

1. INTRODUCTION

Malaria [from the Italian *mala aria* – bad air; English - malaria, ague, marsh fever; French – Paludisme; German – Malaria, Sumpffieber, Wechselfieber; Spanish and Italian – Paludismo; old name – marsh fever, febris intermittens] is the name of a group of closely related severely infectious diseases, which are caused by the appearance and multiplication in the body of blood parasites: primary strain malarial plasmodia. There are four known types of plasmodium that cause malaria in humans: Plasmodium Vivax, which causes three-day malaria; Plasmodium Falciparum, which causes tropical malaria; Plasmodium Malariae, which causes four-day malaria; and Plasmodium Ovale, which causes a strain of three-day malaria. Malaria manifests itself as a general illness, the most characteristic symptoms of which are recurrent bouts of fever, swelling of the kidneys and liver, and anaemia. The periods of fever alternate with interfebrile periods, following which the disease often recurs. Carriage of the disease does not even give rise to immunity against the type of parasites that caused the illness. Local cases of malaria can only be observed in territories in which the Anopheles mosquito is found, since that is the only vector of the human strains of malaria.

The natural spread of malaria across the world first attracted the attention of Soviet and foreign researchers many years ago. The excellent work by V.V. Favr entitled “Experience of medical studies of malaria in Russia” [100] consists of a collection of many facts and literary accounts of the appearance and spread of malaria in Russia. These were expanded on in the following studies: I.A. Kassirsky [37], G.K. Vasilyev and A.E. Segal [12]. The history of malaria in Armenia was studied by A.S. Ktsoyan, and Georgia was studied by P.S. Dzhaparidze [22] and I.I. Topuriya [91-97]. Extensive materials on the spread of malaria in foreign countries have been collected by Hersh [168], A. Laveran [44], Ross [211], Boyd [126], Russell [214-216], Simmons [221], A.Y. Lysenko [49], A.I. Yakusheva and N.N. Dukhanina [110], A.I. Yakusheva [109], and M.G. Rashina [82]. L.J. Bruce-Chwatt [130] devoted his work to researching specific issues relating to the paleogenesis of malaria. The patterns of the spread of malaria in the USSR were investigated in detail by L.I. Prokopenko and N.N. Dukhanina [81]. The individual aspects of the geographical spread of malaria have also attracted the attention of geographers, anthropologists and ethnographers [17, 23, 188, 201, 207, 236].

As a result of these and many other studies, extensive materials have been gathered and published worldwide, which have allowed the spread of malaria across the globe to be studied on complex medical and geographical levels. The only attempt at using a different approach was made not long ago by the American medical geographer Jack May [194] from the perspective of the ecology of the agent, the vector and the human. The author used a large quantity of factual material and quoted several interesting theories of his own. However, the article is only really a formal collection of data on the contemporary spread of anopheles and malaria across the world. The reasons behind the geography of malaria were hardly touched on, and the structure of the nosoarea was not mentioned. The map of the global spread of anopheles is of significant value, although unfortunately it has been compiled from an unusual perspective for Europeans. In general terms, May’s first experience clearly shows that a serious medical and geographical analysis of the natural spread of infectious diseases with particularly complex causes, such as malaria, cannot be carried out without an in-depth understanding of the particular specificities of the infection’s epidemiology.

Malaria, as the subject of a nosogeographical study, is of exceptional interest. This is due to the many aspects specific to this particular infection. Malaria is a transmissible anthroponosis, the mass spread of which is defined by natural and social factors. It is one of the oldest diseases that affect humans, and at the same time it is one of the few infections that mankind has decided to eradicate once and for all. Thanks to the successes achieved in eradicating malaria, the disease’s nosoarea is rapidly reducing, and is now a typical example of a residual nosoarea. Medical geographers are also attracted to the study of malaria by the wide range of materials that have been collected by malariologists all over the world in a vast number of studies of the conditions for the development of the infection and (in the majority of countries) the compulsory registration of patients.

DYNAMICS OF THE SPREAD OF MALARIA DURING ITS ORIGINAL DEVELOPMENT

All researchers agree that human malaria has origins that date as far back as the beginning of mankind. Accompanying man in his movements, malaria spread across a large proportion of the world. The dynamics of the nosoarea during the original development of the disease cannot, for understandable reasons, be traced in detail. However, the existing supplementary data has served as a basis for the development of a variety of interesting and similar hypotheses on the original development of the spread of malaria after this ancient human disease first arose at the dawn of mankind's existence.

2.1 The initial nosoarea

According to contemporary ideas [24, 130] malarial parasites, which were the agents of malaria in animals and later in humans, developed from ancient, independent-living protozoa. The evolution of the parasite included the penetration of the independent-living protozoa into the intestinal tract of a vertebrate, and their adaptation to the epithelial cells of the intestines (Coccidia) and then to the endothelium of the blood vessels and blood cells (Haemosporidia). The penetration into the blood created a precondition for adaptation to a new host: the blood-sucking invertebrate. The older strain of Haemosporidia gave rise to the malarial parasites of amphibians, reptiles and birds, and the evolutionally younger strain gave rise to the malarial parasites of mammals. The oldest forms of primate malarial parasites are the malariae groups with a four-day periodicity (contemporary human and chimpanzee *P. malariae*, and South American monkey *P. brasilianum*), which were isolated and became primate parasites during the eocene period [156]. Approximately 30 million years later, during the oligocene period, Old World monkeys acquired ovale group parasites, which had a three-day periodicity (contemporary human *P. ovale*, and Malay macaque *P. fieldi*) and vivax group parasites with a three-day periodicity (human *P. vivax*, chimpanzee and gorilla *P. schwetzi*, and Asian macaque *P. cynomolgi* and *P. bastianellii*). The *Laverania* subgenus came into being later than the others, different forms of which became parasites of high apes and man (contemporary human *P. falciparum*, chimpanzee *P. reichenowi* and *P. pitheci* of the orang-utans of Sumatra and Borneo) (see diagram1).

The vector of malarial parasites, the *Anopheles* mosquito, existed during the eocene period (60 – 40 million years ago) and possibly earlier [8, 35], i.e. long before the appearance of the first ancestors of man. It is possible that *Anophelini* mosquitoes adapted to feeding from mammals an extremely long time ago, unlike the *Culicini* mosquitoes, which preyed predominantly on birds [192]. Since mosquitoes isolated themselves from other insects many millions of years before the existence of man, it is wholly natural that all malaria vectors were originally *xophiles** or *zoophiles***.

Which primate passed malarial parasites on to humans is still unknown.

There are three existing hypotheses. According to one of the hypotheses (Beklemishev [9] Goar [14]), man, chimpanzees and gorillas inherited their malarial parasites from a common ancestor. During further evolution, the *reichenowi* parasite affecting apes, and the *falciparum* parasite affecting man, became completely different, while the *vivax* and *malariae* parasites remained identical in both hosts.

If that hypothesis is taken to be correct, tropical malaria should be viewed as a true anthroponosis, and three-day and four-day malaria as an anthroponosis in areas where there are no gorillas or chimpanzees and as a zoonosis in the forest areas of Africa, where it may be possible for certain groups of people to come into contact with these species of monkey in natural conditions.

According to the second hypothesis (Beklemishev [9]) man acquired three forms of malaria from chimpanzees in the same period as he first appeared in Africa (at least in the mid-quaternary period).***

In this case, all forms of human malaria can be considered to be ancient zoonoses, which lost their zoonosis characteristics in connection with the establishment of a transmission mechanism that allowed the disease to spread among humans. Regarding three-day and four-day malaria, the above-mentioned hypothesis remains valid.

Livingstone [187] and P.G. Sergiyev and N.A. Tiburskaya [90] arrived independently at the hypothesis that the human *vivax* parasites developed from the *cynomolgi*-like parasites affecting macaques.

This hypothesis relies on the recently established fact that humans were infected with *bastianellii* [149] and *cynomolgi* [122, 137, 181] parasites from low narrow-nosed monkeys. The acceptance of this hypothesis would mean that different types of human malarial parasites have come from different sources: the malaria and *falciparum* parasites from an ancestor shared with pithecooid apes, and the *vivax* parasites

from low narrow-nosed monkeys. It must, however, be added that the *schwetzi* chimpanzee parasite was also passed on to them through low narrow-nosed monkeys (or from man). In the light of these hypotheses, the significance of low monkey malaria as a potential obstacle to the eradication of human malaria is considerably increased. It is well known that low monkeys, which were widespread in the Old World, were hosts for many strains of malarial parasites of the *vivax* group (see diagram 2). It is still unclear from where man contracted *ovale* parasites. According to P.G. Sergiyev (private report, 1966), the *ovale* parasite could be a hybrid of the *vivax* and *malariae* parasites.

The question of the origins of human malarial parasites is not only of theoretical interest. It has recently been necessary to return to the question in connection with the world-wide eradication of malaria [14, 130, 138, 199]. The question of the place of origin of the initial nosoarea is also closely linked to this issue.

It must be stated that the beginning of the initial stage of development of human malaria has not been studied sufficiently. Even in the interesting book written by V. M. Zhdanov, entitled "The Evolution of Human Infectious Diseases" [29] very little attention is paid to malaria. Meanwhile, many of the specifics of the way in which malaria spread still remain unclear. To begin with, there is no consensus on where human malaria originated. Of the few authors who touched on the issue, it is worth remembering Christophers, who as far back as 1934 was of the opinion that human malaria originated in Africa [134].

V. N. Beklemishev, considering that man first appeared in South-East Asia considered two possibilities: firstly, man could have inherited malaria from his predecessors at his place of origin; second, the disease could have been acquired later, and then spread to primitive man who reached Africa from South-East Asia. The author did not give a preference for either of these hypotheses, but his conclusions were clearly in favour of the African origin of human malaria. He came to the following conclusions:

1. The human plasmodia (*P. falciparum*, *P. vivax* and *P. malariae*) are very similar to the chimpanzee plasmodia *P. reichenowi*, *P. schwetzi* and *P. rodhaini*. More recently this conclusion has become even more valid, since it has now been proven that *P. vivax* is a parasite common to chimpanzees, gorillas and man, and that *P. malariae* is common to chimpanzees and man [14].

2. The indigenous people of Africa have the highest resistance to malaria of all peoples across the world.

3. African *A. gambiae* has a marked preference for the blood of primates, and is epidemiologically the most dangerous vector of human and monkey malaria.

In fully agreeing with these parasitological and epidemiological conclusions, we believe that it is possible to add a fourth, zoogeographical conclusion: Africa is the only place in the world where the four types of human malaria agent, *P. vivax*, *P. malariae*, *P. falciparum* and *P. ovale*, exist constantly. Zoogeographers consider the oldest part of the distribution area to be that where the widest variety of forms exist [13, 34]. This hypothesis also concurs with the latest views of primatologists, according to whom primates - the quasi apes of the eocene and early oligocene periods (60 – 30 million years ago) and their descendents in the miocene period (20 million years ago) which were the predecessors of anthropoid apes - were found exclusively in Africa, since that was the only place with conditions suitable for their existence. From there they spread to Asia, which was connected to Africa at that time. Paleontological findings over the past 30 years have shown that the principal area of primate evolution was eastern Africa. It is therefore assumed that it was there that the Hominoidae group divided into ancient anthropoid apes (major anthropoids of the Pongidae family) and the Hominidae family, from which primitive man later developed [30,166].

It should be mentioned that a significant proportion of anthropologists continue to follow the hypothesis that man originated in South-East Asia [71]. Evidently Y.Y. Roginsky and M.G. Levin [85] are correct when they write that "as yet it is not possible to give a preference between the African and Asian hypotheses". However, irrespective of how anthropologists solve this problem, the first appearance of human malaria occurred, by all accounts, in eastern Africa [130].

2.2 The formation of the nosoarea

If we take it that man first appeared in Africa, then we can fully agree with the hypothesis on the direction in which malaria spread from its initial nosoarea developed by Bruce-Chwatt [130] (see diagram 3). According to the author, malaria spread from its place of origin in Eastern Africa across the whole of Tropical Africa, to Mesopotamia, India and China, and along the Nile, where it reached the Mediterranean

countries. Information in world literature demonstrates that by all accounts malaria was known to all the peoples settled in the classical countries: Babylon, Assyria, Egypt, Greece, Ancient Rome, China and India. On the other hand, and this is no less important, there is evidence that malaria spread widely in these countries comparatively recently. Thus, according to Ross [211], there is no basis for assuming that Malaria was present in Greece in the country's early history. Malaria was probably brought to Greece in c.5 B.C. by soldiers and slaves from other countries. It is unlikely that the population of Egypt suffered from malaria in the period before the New Empire. The first mention of febrile illnesses with hypersplenism was made in 1570 B.C. Malaria first appeared on the Nile delta in c. 400 B.C. Even in the first century B.C. malaria had apparently not yet appeared in Alexandria, despite the fact that the city was surrounded by marshland. The ancient Etruscans also apparently did not know of malaria, which only became a problem in the Roman republic in c. 200 B.C.

How and when malaria appeared in America is still unclear. According to one group of researchers, malaria existed in America before the arrival of Columbus. Malaria agents could not have been brought by early man coming from Asia across the Bering Strait to resettle in North America ten thousand years ago during the Ice Age [139]. It is possible that the disease was brought by early seafarers from the countries of South-East Asia, Polynesia and Melanesia, who crossed the Pacific Ocean and settled in Central and South America. According to another group of researchers, malaria appeared in America relatively recently. They believe that it was brought by the Spanish Conquistadors who arrived in the country with Columbus.

A prominent role in the spread of malaria in America was played by the African slaves [118], who were brought to the country in large numbers by slave-traders in the 16th to 18th centuries. Gabaldon [153] and Bruce-Chwatt [130] propose a compromise hypothesis, suggesting that *P. malariae* and *P. vivax* existed in America before the arrival of Columbus, and that *P. falciparum* was brought by the Spanish and the Africans. Thus malaria was able to spread across the world from its place of origin in Africa.

2.2.1. Stages of the formation of the nosoarea

The formation of the nosoarea of malaria could not have taken place over a short period of time. Thus we should first answer the following question: when did malaria start to spread from its original distribution area? At least two of the opinions on the enlargement of the initial distribution area are appropriate. It can be assumed that man, having inherited malaria from his anthropoid ancestors, or having acquired it from his close relatives the anthropoid apes (and *P. vivax* from low apes?) spread the disease further to all of the places he reached during his major settlement of the world. In this case, the age of the disease for all peoples and races should be similar. A second assumption is, however, possible, which is that for a long time malaria was "exclusive" to primitive man in Africa, living within the territory of the initial distribution area, and possibly to a few tribes living in the oldest filial distribution areas. The disease could also only have spread to the other territories inhabited by man during the period when the necessary conditions for its existence developed. In this case, the history of malaria would be very different for different peoples.

It is well known from the history of epidemiology that all different tribes and peoples suffered from different diseases at any one time. Relevant examples can be found in V. M. Zhdanov's monograph "The Evolution of Human Infectious Diseases" [29]. Smallpox, which became a human infection at the dawn of civilization, was for a long time a disease known only to those living in South-East Asia and the eastern Mediterranean. It was significantly later, in the 14th and 15th centuries A.D. that the disease spread to the people of Europe and soon afterwards to America.

It is believed that cholera originated in India, in the Ganges basin and Brahmaputra. It became a human disease at the time of the formation of the ancient river cultures. Cholera remained within the borders of its original distribution area for one thousand years, and it was only at the beginning of the 19th century, during the English colonial wars, that its agent was carried to other countries and the disease spread across the world. (The first pandemic was from 1816 – 1823).

These are however, examples of infections which became human diseases as a result of the adaptation of the parasites of either domestic animals (smallpox) or saprophytes (cholera) to the human body. This adaptation took place at relatively late stages in human development. Of the diseases that man inherited from his predecessors, the agents of which evolved alongside man, V. M. Zhdanov lists herpes, enterobiosis, diseases of the streptococcus, pediculosis and malaria. Unfortunately, the author only looked unjustifiably briefly at the evolution of malaria. The chapters of most interest are those on other ancient,

purely human infections, in particular enterobiosis and herpes.

The conclusion that arises from these chapters falls within our sphere of interest in the following way: having inherited enterobiosis and herpes from his ancestors, man, anywhere in the world, has almost never been separated from these diseases; enterobiosis and herpes have always been, and remain, ubiquitous diseases. It would seem that malaria also falls into this category of illnesses, and yet it is easy to make a serious error by using this analogy.

A very interesting article written by A. P. Markevich, entitled “The origin and development of animal and human parasitofauna” [62] contains the following explanation: “Domestic animal and human parasitofauna have undergone particularly great changes as regards both their and their concomitants’ settling in all inhabited areas of the world. Fellow members of the human “group” have often ended up in completely new ecological situations. Strikingly different living conditions have also developed for parasites that exist independently at all stages, in contrast to those to which they had adapted and in which they had existed for many centuries. The result of this was that some strains of parasite were unable to survive in the new conditions, while others that were more flexible were able to adapt to exist in the maximum variety of geographical areas and are now typical cosmopolites. Above all, cosmopolitanism is characteristic of constant ectoparasites (lice, headlice, itch-mites) and of endoparasites that develop without the involvement of intervening hosts (threadworms, ascarids, whipworms, etc.)”.

The author’s opinion that endoparasites that develop with the involvement of intervening hosts have less capacity for adapting to new conditions is important with regard to the human malaria agent.

The long absence of malaria in America demonstrates that possibility that primitive man disposed of malaria while settling. Irrespective of who brought malaria agents to the continent and when, it is believed certain that it was not present among the ancient Asiatics who travelled to America from Asia across the Bering Strait ten thousand years ago.

In this case, it can be presumed that the ancestors of the Indians had either become free of malaria parasites during resettlement as a result of the climatic barrier (the resettlement took place during the Ice Age, when the conditions for the transmission of infection must have been extremely unfavourable), or that they had lost the parasites even earlier, before the beginning of their movement across the Bering Strait. At the same time, a number of agents of other diseases, for which a climatic barrier did not exist, for example the agents of pinta, were carried to America by Asiatic settlers and began the development of their endemic centre on that continent [164].

It must be noted that the key reason for the restriction in the rate of the dispersal of malaria parasites was their complex transmission mechanism. It is well known that the infection transmission mechanism of malaria is considerably more complex than that of herpes, enterobiosis and pinta. It can only be put into effect through a vector – the *Anopheles* mosquito, and with favourable temperature conditions in the external environment (temperatures of over 16°C). Even if primitive man dispersed mainly across river valleys and around lakes and came into contact with the local species of *Anopheles*, it would have undoubtedly taken a certain amount of time for *Anopheles* to adapt to its new prey, and for the types and cultures of plasmodia brought by man to adapt to the new vector. It must be remembered that originally all species of *Anopheles* were exophiles and zoophiles (see previous footnote). In order to effectively participate in the transmission of human malaria, they had to become synantropes: firstly anthropophiles, and then endophiles. The development of these types of behaviour could not have taken place quickly if we take into account the fact that even nowadays the majority of known types of *Anopheles* have remained “wild”, and many types that are proven vectors have retained pronounced zoophile and exophile characteristics. Regarding the adaptation of the parasites to the new types of *Anopheles*, there are even considerable differences between the contemporary types of *Anopheles* in their receptivity to malaria plasmodia. It is well known, for example, how difficult it is for *A. sinensis* to become infected with the tropical malaria parasite (*P. falciparum*), and for many other types of *Anopheles* to acquire the four-day malaria parasite, *P. malariae*. It is hardly by chance that out of over 400 known types of *Anopheles*, only 25 – 30 types have become major vectors, and that the most epidemiologically effective vector of human malaria is the African *A. gambiae*, which is found on the territory of the initial distribution area. The fact that this type of *Anopheles* is more dangerous than species that became vectors later is demonstrated by the consequences that it has had when carried to other zoogeographical areas. In 1930 it was carried to Brazil, where the local vector *A. aquasalis* had led to hypo- and mesoendemics of malaria, and caused a catastrophic epidemic with a vast death toll. The analogical consequences were that *A. gambiae* was carried to Egypt in 1942, where the local vector *A. pharoensis* had only caused a minor endemic [220].

The conclusion arises that the danger of *A. gambiae* as a vector can be explained not only by the ecological particularities peculiar to it: the time factor is particularly significant, namely since human malaria parasites have had a greater possibility of better adapting to *A. gambiae* than they have to other types of *Anopheles*.

Forcible arguments in favour of the significantly longer history of malaria in Africa, and in its first filial breeding grounds, in comparison with the other regions of the nosoarea are provided by data on the spread of several irregular haemoglobins.

The patterns of the geographical spread of these irregularities have been of interest to representatives of many different sciences, in particular anthropologists and ethnographers. This is understandable, since these irregularities relate to the haematological aspects that have existed for thousands of years and are capable of shedding light on peoples' migration routes [123].

This issue is also of great interest to malariologists as a result of the role that malaria played in defining the general spread of irregular haemoglobins.

Among a large number of irregular haemoglobins, medical geographers pay particular attention to Haemoglobin S. The history of the discovery of this type of haemoglobin and the particularities of the effect of malaria on the carriers of Haemoglobin S have been described in great detail by A. I. Nemirovskaya [70].

Haemoglobinose-S is a genetic molecular disease caused by the presence of the presence of valine, an untypical amino acid, in human haemoglobin molecules.

Children who have inherited this characteristic from both parents (HbSS) often develop fatal haemolytic anaemia. Pathological effects do not usually develop in heterozygous inheritors of the condition (Hb AS), although in certain circumstances their red corpuscles change shape and become elongated and falciformed. Persons with this particular irregularity are considered to be vectors of Haemoglobin S (sicklelema). Under conditions of hypoxia (such as aeroplane flights and narcosis) vectors of Haemoglobin S can suffer from a rupture of the spleen, and more frequently they suffer from haematuria.

An analysis of the available data on the spread of HbS has brought to light some important trends. It seems that this particular irregularity was confined principally to the tropics and sub-tropics of the Old World. It spread widely, despite the fact that homozygous Haemoglobin S carriers generally die before fully maturing and therefore cannot leave descendants. Cases of the appearance of Haemoglobin S have reached 20 – 40 per cent in many parts of Africa, which begs the question why there has been such an increase in cases of the irregularity among that population. It has been suggested that having appeared as the result of a mutation, irregular haemoglobins, although they cause serious pathologies in some individuals, can at the same time increase the chances of survival of the remainder of the population in the tropics who are exposed to a variety of dangers, including parasites. In this regard, particular attention has been paid to tropical malaria as the main cause of infant mortality in Africa, South-East Asia and the Mediterranean countries.

Until now, the link between the spread of haemoglobin S and tropical malaria has been the area studied in the greatest detail. There have been a variety of different arguments, including experimental evidence, in favour of the existence of that link [111,112,115,124].

These experiments have shown that Haemoglobin S provides its carriers with a relative resistance to tropical malaria. This resistance shows against the weaker parasitemia in persons who are not immune, but persons with a certain level of acquired immunity are fully resistant to infection. The results of these experiments concur with a large amount of information collected in mass population studies on susceptibility to *P. falciparum*, and clinical data on the seriousness of the effects of tropical malaria on children with normal and pathological haemoglobin.

As has been demonstrated by studies carried out by Allison [113,114], Vandepitte and Delaisse [230] J and C Lambotte-Legrand [183], Vandepitte [229] and others, in Africa, tropical malaria appears more rarely and is clinically less serious among child carriers of HbS than among children with normal haemoglobin. It is particularly important that the proportion of children with over 1000 parasites per 1 ml. of blood, i.e. a life-threatening quantity [150], is also considerably lower in the group with pathological haemoglobin. As a result of this, malaria mortalities among child carriers of HbS are more than 20 times lower than average (see table 1).

Table 1

Malaria mortality among child carriers of HbS

Place of observation	Percentage of malaria sufferers carrying HbAS (<i>a</i>)	No. of cases of mortality from malaria among all children observed (<i>b</i>)	No. of cases of mortality among malaria sufferers carrying HbAS	
			Estimated number (<i>axb</i>)	Actual number
Leopoldville, Congo [183].	26	23	6	0
Luluaburg, Congo [230].	29	23	7	1
Ibadan, Nigeria [143].	24	27	6	0
Accra, Ghana [143]	8	13	1	0
Kampala, Uganda [208]	19	16	3	0
Total		102	23	1

Nowadays, the hypothesis on the reason for the connection between tropical malaria and haemoglobin S is accepted by the majority of pathologists, geneticists, medical geographers, anthropologists and malariologists [1, 106, 130, 188, 194]. One of the most important conclusions in favour of this hypothesis is the strong geographical correlation between the distribution areas of haemoglobin S and tropical malaria (see Diagram 4).

The first thing that should be noted in comparing the maps of the distribution of haemoglobin S and *P. falciparum*, is the confinement of haemoglobin S predominantly to tropical Africa, i.e. to the territories where the main holo- and hyperendemic origins of malaria are found, and where, as it is well known, *P. falciparum* developed. Very few cases of haemoglobin S have been found in Africa outside the areas of the holo- and hyperendemic origins of malaria.

There is an infrequency of haemoglobin S among persons living on plateaus or in deserts, where malaria occurs rarely, and also in countries and regions north of the Sahara and south of the Zambeze River, where *P. vivax*, rather than *P. falciparum*, is dominant.

It is rare to find cases of haemoglobin S outside Africa. A fairly significant number of cases have arisen only in India, on the Arabian Peninsula, and in the northern Mediterranean (southern Turkey, Greece, Sardinia).

The distribution area of haemoglobin S hardly exceeds the borders of the above-mentioned countries and territories. In the Old World, HbS did not appear south of India, and specifically was not found in Malaysia and Singapore [231], New Guinea [178, 180], Sarawak [232] or Australia [170]; and there were only isolated cases of HbS in Indonesia [147, 148]. Haemoglobin S was almost unheard of among the Aborigines and the American Indians [116, 117]. In the Old World, haemoglobin S appeared exclusively among the descendants of black immigrants from Africa. Thus, in such conditions, when the blacks and their descendants lived in areas that were intensively affected by malaria [Guyana (Georgetown), Suriname], the frequency of carriage of haemoglobin S remained almost the same as among people living in their homelands [177, 233]. However, living for 200 – 300 years in places where there were almost no cases of malaria (Curaçao, the Netherlands Antilles, West Indies) or where there were small endemics (Jamaica), led to a significant reduction in cases of the haemoglobin S irregularity [114, 177, 238]. This information allows us to draw some very interesting conclusions. It can be considered that the frequency of carriage of haemoglobin S by the population of a given country is directly dependent on the time period and intensity with which malaria has developed in that country. We can see that carriage was at its greatest in the countries of tropical

Africa, slightly less in Greece and India, considerably less in Indonesia, and practically non-existent among the aboriginals of Australia and America. This means that occurrences of haemoglobin S are themselves indicators of the history of malaria in a given place, and among a given population. Of course, this conclusion is fair only in relation to those peoples among whom haemoglobin S appeared as a result of a mutation or was introduced into the group from outside (when a race settled in the country). In areas with persistent malaria, not reached by the haemoglobin S gene (e.g. New Guinea), children, who are the sector of the population most susceptible to tropical malaria, are completely unprotected. As a result of the extremely high rate of infant mortality from tropical malaria on the island of New Guinea, particular breeding grounds have developed for holoendemic malaria in which the dominant strain of parasite is not *P. falciparum*, as in the classical breeding grounds for holoendemic malaria in Africa, but rather *P. vivax* [203].

Table 2 shows, in a schematized form, the possible malariological interpretation of data on the frequency of carriage of haemoglobin S among populations living in areas with malaria.

Table 2

Malariological interpretation of data on the frequency of carriage of haemoglobin S

Haemoglobin S	Main types of correlation between malaria endemics and the frequency of carriage of HbS	Typical territorial examples	Interpretation
Has spread	1 – Holo- and hyperendemic malaria. Predominantly <i>P. falciparum</i> . High mortality rate among children with normal haemoglobin compensated by low mortality rate among children carrying haemoglobin S. Carriage of haemoglobin S: 10 – 40 %. 2 – Meso- and hypoendemic malaria. In normal years <i>P. vivax</i> is predominant; in endemic years <i>P. falciparum</i> is predominant. The advantage for vectors of haemoglobin S regarding tropical malaria do not always compensate for the deficiencies in the spread of this irregularity (homozygous vectors are unable to survive). Carriage of haemoglobin S: less than 10 %.	Tropical Africa; India. Some tropical African countries, many breeding grounds in India; Greece.	In other similar conditions, the greater the carriage of haemoglobin S, the older the breeding ground for malaria, and the greater the role played by <i>P. falciparum</i> in its development.
Does not exist	1 – Holo and hyperendemic malaria. Predominantly <i>P. vivax</i> . Outcome of becoming infected with tropical malaria for children who are not immune depends only on the usual factors affecting the body's resistance (mortality is very high). 2 – Meso- and hypoendemic malaria. <i>P. vivax</i> is always predominant or only when there is no endemic. Malaria is not a cause of death.	New Guinea; part of the territory of South America. European countries; part of the territory of South America	The lack of haemoglobin S bears witness either to the past isolation of a particular race (people), or to the limited duration of the existence of malaria, or to both of the above.

Thus a number of important conclusions and considerations allow us to suppose that for quite a long stage in mankind's history, malaria remained confined exclusively, or predominantly to its initial distribution area, tropical Africa. During settlement across the world, a significant proportion of primitive people spontaneously freed themselves of their ancient diseases. Large territories populated by man, particularly those outside tropical regions, were either completely free from malaria, or the disease was extremely limited in its diffusion. The conditions for the wide spread of malaria outside its initial distribution area evidently only began to develop in the Aeneolithic era (c. 4000 B.C.) through the development of agriculture, the transition from a nomadic to a settled way of life, and the increase in population density. During this period, in the areas where malaria had already "taken hold", it began to spread more widely, and it also began to take root in the places where the population had thus far been free

of the disease. It is highly likely that malaria started to take root in places previously free of the disease even later, during the Bronze Age (c. 2500 B.C.), through the development of seafaring and long voyages to war, which allowed the large-scale carriage and transmission of the infection. The expansion of the nosoarea continued uninterrupted for a very long time, right until the end of the 19th / beginning of the 20th Century.

2.2.2. The formation of the distribution areas of the individual types of malaria agent.

The distribution area of human malaria was covered by the disease's four strains, each of which is caused by a specific type of parasite.

The development of the different types of human malaria parasite was completed either before or at the time of the first appearance of man. The distribution areas of all of the types of human plasmodia must have been formed in accordance with the ecological particularities of each type of parasite. The factors of particular importance were the parasite's reaction to a new type of vector, to different temperature conditions, and its potential for genetic adaptation.

2.2.2.1.

DISTRIBUTION AREA OF *P. VIVAX*

P. vivax spread earlier and wider than the other types of malaria parasite, and finally occupied almost the entire group distribution area of malaria, where the four types of parasite developed together. In some countries, three-day malaria was almost the only type of local malaria (England, Germany, France, northern USA), or it quickly prevailed over the other types (France, the Netherlands).

P. vivax was able to spread so widely owing to some of its specific characteristics. It develops inside the vector in lower temperature conditions than other types of parasite (see table 3).

Table 3

Comparative temperature limits for the development of human malaria agents

Type of parasite	Lowest threshold for development (°C)	Duration of spore incubation (days)		Total heat (degree – hours) for completion of spore incubation*
		20°	25° C	
<i>P. vivax</i>	16	19	10	105
<i>P. falciparum</i>	18	23	12	111
<i>P. malariae</i>	18	30	16	144
<i>P. ovale</i>	?	?	15 - 16	?

It is natural that owing to this characteristic, *P. vivax* was able to spread under a variety of different conditions, from the initial distribution area considerably further into temperate climatic zones than was possible for the other types of parasite.

Just as significant, was the diversity of the geographical varieties (of groups of strains) of *P. vivax*. The variety of strains discovered during experimental studies on *P. malariae*, *P. falciparum* and *P. ovale* were epidemiologically few in comparison with those of *P. vivax*. (See table 4).

Table 4

Classifications and intensity of the main varieties of human malaria parasite strains

Type of Parasite	Varieties of high epidemiological significance			Varieties with a second level of epidemiological significance	
	Incubation	Type of recurrences	Infectiousness for mosquitoes	Seriousness of bouts of illness	Ease of treatment
<i>P. vivax</i>	++*	++	+	++	++
<i>P. falciparum</i>	–	–	++	+	++
<i>P. malariae</i>	–	–	+	–	–
<i>P. ovale</i>	–	–	+	–	–

Since there is such a diversity of varieties of *P. vivax* this has led to the development of a range of classifications for them. The main method of classification is by type of course of infection of different groups of *P. vivax* strains, which have been grouped into two subspecies: *P. vivax*, and *P. vivax hibernans*. Strains causing illness in humans after a short incubation period were classified in the first group, and those causing illness after a long incubation period were put in the second category [75].

Taking into consideration the peculiarities of the strains of the Chesson group [144], P. G. Sergeev and N. N. Duchanina proposed differentiating between three groups of *P. vivax* strains: a) strains causing illness after a short incubation period, which recurred periodically after short intervals; example: Chesson strain; b) strains causing illness after a short incubation period, which recurred after longer intervals, 7 -11 months after the original illness; example: the “southern strains” described by Soviet authors, and the Mak Koi, Saint Elizabeth and Madagascar strains described by foreign authors; c) strains causing illness after a long incubation period (8 – 14 months); example: the “northern strains” described by Soviet authors.

As N. N. Duchanina clearly demonstrated [27], the spread of different groups of *P. vivax* strains in the USSR has been quite natural. Some were exclusively predominant in the south of the Soviet Union, and others in the central and northern regions. The border between the areas where the southern and northern strain groups were dominant was at approximately 48° - 52° north. In other countries, *P. vivax* strains causing illness after a long incubation period were predominant in Finland [167], the Netherlands [225, 226], Sweden [146], England [190] and Germany [169]. It should be noted that local occurrences of three-day malaria caused by Chesson group strains have definitely not been registered either in the USSR or in any other European countries. Current experimental and epidemiological data on the spread of the geographical varieties of *P. vivax* are summarized in the map in diagram 5.

The diagram shows that the different groups of strains were confined to certain parts of the distribution area of *P. vivax* that had specific temperature conditions. “Northern strains” are predominant in temperate climate conditions, where the transmission season is limited to 1 – 2 summer months. Here, in the majority of cases, the agent has only one possible route of passage through the vector, and must stay in the human body until the following year, when once again the conditions will be favourable for the further spread of the infection [74]. According to Sergiyev [86, 87], *P. vivax* strains with long incubation periods developed through a long process of evolutionary selection while *P. vivax* was being carried by man from the tropics to places with temperate climates.

In hot climatic conditions with longer transfer seasons (3 -5 months or more) “southern” cultures are predominant, which cause illness after a short incubation period. The recurrences that are characteristic of this illness take place at long intervals, which start at the beginning of the following transmission season.

During the epidemic season the cultures of this group are able to complete several passages through the vector, and above all, have adapted in order to live in the human body during periods that are unfavourable for transmission.

Chesson group strains are confined to a comparatively small distribution area, including the island of New Guinea, numerous small islands in the southern part of the Pacific Ocean, and probably the Malaysian archipelago. Studies in the regularity of the spread of the strains of this group are sorely lacking. The reasons for the narrowness of the distribution area and for why these strains do not exist on other territories with similar climates, specifically Africa and South America, are still unknown. Of all the types of *P. vivax* cultures, only the Pacific Ocean cultures have proven capable of forming breeding grounds for holoendemic malaria where they predominate over *P. falciparum* [203]. We are inclined to look at the peculiarity of the distribution area and some of the characteristics of the Chesson group strains as one of the indications of their special origin. It can be assumed that these Pacific Ocean strains developed from cynomolgi, parasites similar to those of the low Old World monkeys (see above).

P. vivax has proven to be an exceptionally flexible type of human malaria parasite, which has allowed it to spread over the widest distribution area.

An important advantage of *P. vivax*, in respect of the expansion of its distribution area, is also the duration of the infection it causes in humans. As Levine and Harper [185] and Downs et al. [142] demonstrated, military troops infected with three-day and tropical malaria very quickly rid themselves of *P. falciparum* when they arrived in places unaffected by malaria, but the process of “losing” *P. vivax* was extremely slow. Analogical data were collected in the USSR by observing inhabitants of Moscow who had been re-evacuated back from the Central Asian Soviet republics [63].

Despite the significantly wide distribution area of *P. vivax* in comparison with the distribution areas of other malaria parasites, the number of people infected with three-day malaria has always been smaller than the number infected with tropical malaria [126]. This can be explained by the fact that in hyperendemic breeding grounds, where the greatest number of people suffering from malaria is concentrated, the proportion of *P. vivax* is relatively small. Exceptions to this are the breeding grounds in the distribution area of the Pacific Ocean strains of *P. vivax*. In breeding grounds in tropical Africa, there is considerably less infection with three-day malaria than with tropical malaria, and in a large proportion of western Africa, *P. vivax* is hardly known [155].

2.2.2.2. *DISTRIBUTION AREA OF P. FALCIPARUM*

None of the particularities of the non-African strains of *P. falciparum* that have thus far been discovered (see table 4 above) can be considered as an adaptation for existence in temperate climates. The movement of this type of parasite to areas with temperate climates could only have taken place within the climatic limits that were still appropriate for its initial behaviour. Since the infection had a significant number of sources, outbreaks of tropical malaria arose in separate years in latitudes as far as 61° north (Solvychevodsk, see [26]), and at altitudes as high as 2590 metres (Kenya, see [154]). However, such outbreaks were typical examples of temporary “occurrences” of tropical malaria outside the permanent borders of its distribution area. In the past, the stable border of *P. falciparum*'s distribution area in the northern hemisphere was at 45 – 50° north [26], and in the southern hemisphere was at 20° south [153]. Tropical malaria can only sustain itself in the long term in places where the temperature conditions allow at least two consecutive passages of the agent through the vector during the course of one epidemic season [77].

It appears that as a result of the short duration of the tropical malaria infection, *P. falciparum* penetrated territories that had previously been free from malaria later than the other types of parasite. The example of America has already been mentioned. The different forms of malaria took root in a similar order in Australia [172] and Turkey [197]. *P. falciparum*, rather than *P. vivax*, determined the high-altitude malaria border in only one place in the world: the African mountains [154, 158, 176, 239]. At the same time *P. falciparum* has not spread widely in the equatorial climate of South America, and in the Amazon basin, for example, *P. vivax* is predominant [58]. This is possibly because *P. falciparum*, which has recently arrived in America, has not adapted adequately to the local vectors.

Despite its significantly smaller distribution area, *P. falciparum* infects more people than *P. vivax* and *P. malariae*. According to Morton's evaluation [196] tropical malaria accounts for 50 per cent of the world's malaria cases, three-day malaria accounts for 43 per cent and four-day malaria 7 per cent. *P. falciparum* is responsible for 98 per cent of deaths out of all fatal cases of malaria.

2.2.2.3 *PARTICULARITIES OF THE DISTRIBUTION AREA OF P. OVALE*

Until recently the distribution area of *P. ovale* had not even been described approximately. There were also no qualified reports on where in the world this mysterious type of human malaria parasite has been found. Lacan's reports [182] began to fill that gap.

It should be noted that Lacan, like many other authors before him [126, 216] lists all of the possible findings of the parasite, irrespective of how reliable they are. Meanwhile, it has already been proven that the cases of *P. ovale* described in the USSR are not reliable [76]. The majority of other instances of *P. ovale* being detected outside Africa are also unreliable [189] and nowadays the only indisputable breeding grounds for local *ovale* malaria are those in Tropical Africa, New Guinea and the Philippines. The distribution area of *P. ovale* is unique in size, form and structure: in size, it is considerably smaller than the distribution areas of any of the other three types of human malaria parasite; in form it is interrupted by the trans-Indian section. The areas with the highest and lowest density of *P. ovale* distribution are both found in Africa: the highest density being confined to the north coast of the Gulf of Guinea and the lowest being the remaining part of the distribution area. In the area with the highest density, 10 -15 per cent of the population is infected with *P. ovale*, and in the remaining areas 1 -2 per cent of the population is infected (see diagram 6). The Pacific Ocean section of the distribution area can be considered to be the section from which the infection has disappeared, since *P. ovale* only appears there sporadically.

Looking at the distribution area of *P. ovale* as a whole shows that both of its sections are confined to territories with average equatorial and subequatorial climates.

It can be assumed that this confinement is dependent on the temperature limits on the development of *P. ovale*. However, in that case, the reasons for the generally limited nature of the *P. ovale* distribution area, in comparison with that of *P. malariae*, and for the fact that *P. ovale* does not occur in Central and South America, which have the same climatic conditions as tropical Africa, remain unknown. Meanwhile, there are grounds for believing that *P. ovale* was carried to those places more than once, particularly during slave trading. The climatic particularities also do not explain the extremely rare occurrence of *P. ovale* in the Pacific Ocean section of the distribution area. At the same time, the structure of the African section of the *P. ovale* distribution area correlates well with the climatic indicators (see diagram 6). The principal parts of the optimum *P. ovale* distribution area are confined to the equatorial forest and wooded savannah regions. The effects of *P. ovale* in West Africa naturally decrease as one moves north, in relation to the decrease in the density of its distribution.

P. ovale is spread over an area occupied by three different types of anopheles that carry malaria: *A. gambiae* in Africa, *A. punctulatus* in New Guinea and *A. minimus flavirostris* in the Philippines (see diagrams 6 and 8). In experimental conditions the different strains of *P. ovale* also infected vectors from other regions (*A. m. atroparvus*, *A. albimanus*, *A. quadrimaculatus*). Thus the particularities of the distribution area of *P. ovale* cannot be connected to differences in the vectors' fauna. On the other hand, the principal African part of the *P. ovale* distribution area is limited only to the optimum distribution area of *A. gambiae*, and specifically to the part where *A. gambiae* forms breeding grounds for hyper- and holoendemic malaria. It is possible that the development of persistent and intensive breeding grounds for malaria caused by such a stenotropic parasite as *P. ovale* could only occur with the strength of an effective vector, i.e. *A. gambiae*.

The particularities of the spread of ovale malaria have led some researchers to the idea that the illness could be zoonotic. Languillon [184], for example, suggests that *P. ovale* could be a regular parasite for monkeys, specifically chimpanzees. The possibility of *P. ovale* being transmitted to chimpanzees by *A. gambiae* has been proven through experiments [128].

Although the distribution area of *P. ovale* is wider than the distribution area of chimpanzees and in places also covers the distribution area of low narrow-nosed monkeys, this does not preclude the possibility of this particular malaria parasite having been circulated between humans and monkeys. The fact that analogues of human *P. ovale* were not discovered in anthropoid apes (as they were in the cases of *P. vivax* and *P. malariae*) does not mean that they did not exist.

The racial composition of the population is the same for both sections of the *P. ovale* distribution area. In Africa it is found exclusively in areas with black populations and in New Guinea in areas with Melanesian populations. According to Soviet anthropologists these two races, which both come from the equatorial race, have closely related origins [18, 72, 84]. Regarding the Philippines and Madagascar, the Mongoloid populations of these islands have a considerable number of equatorial characteristics, and in the Philippines, above all, groups of pygmies still exist, who are directly related to the equatorial race.

Relative or full resistance to some diseases can be a racial characteristic. It is well known that black Africans have an innate resistance to *P. vivax*. This resistance has remained among black Americans. Bray [127] believes that *P. vivax* cannot exist among pure black populations, although there are some black individuals who do not have this resistance. In areas with maximum spread of *P. ovale* (Nigeria, Ghana, Cameroon, Liberia, Gambia) *P. vivax* hardly exists. The three-day malaria agent is only found permanently in East Africa, where the peoples are predominantly of European origin (Arabs, Indians, Europeans) and transitional Ethiopian races, and in Madagascar, where the population is Mongoloid. In this connection, the occurrence of *P. ovale* in these places, as far as can be judged, is less noticeable than in West Africa. The peoples of Melanesian races from the Pacific islands do not display a resistance to *P. vivax*, and *P. ovale* only occurs very rarely in that area. Although when comparing the Donaldson strain and the Liberian strain of *P. ovale* it was discovered that both black and white Americans are equally susceptible to both strains [175], this does not exclude the fact that in natural conditions extremely subtle differences can arise in the body's susceptibility to the parasite and in the development of immunity, which as yet are not understood. In the light of contemporary data on the different occurrences of irregular haemoglobins (see above) and the possibility of other biochemical particularities in the blood of different nationalities, it can be suggested that the mutual relationship between the host and the parasite develops in black peoples differently to how it develops in peoples of European descent for example.

Thus none of the investigated factors (climate, vector fauna, distribution area of monkeys, racial particularities of the population) explain in themselves the uniqueness of the *P. ovale* distribution area.

It appears that the explanation should be sought in the complex effects of these and possibly some other factors.

There is no doubt that the wide distribution of *P. ovale* is hindered first and foremost by its biological particularities as a parasite. The short infection period among patients with the ovale infection as a result of the low and inconstant production of gametocytes, the low intensity of vector infection, and the duration of spore incubation (15 – 16 days at a temperature of 25° C in comparison with 10 days for *P. vivax* in the same conditions) all reduce the possibility of the parasite being transferred from the patient to a healthy person, particularly in areas with ineffective vectors and seasonal transmission.

Some of these characteristics are also found in *P. malariae*, but they are seen much more clearly in *P. ovale*. It appears that such characteristics could explain the spotted distribution peculiar to both of these parasites within the malaria distribution area. The long duration of infection in four-day and ovale malaria is clearly an evolutionary adaptation, which compensates for the particularities of their biology that are not favourable for the survival of parasites.

In view of the above, when isolated vectors of *P. ovale* arrived in places where ovale malaria did not exist, the probability of transmission from a patient to a healthy person was reduced to nil, and this could, to a certain extent, explain why *P. ovale* did not spread from Africa, where malaria had a stronghold, and why it does not exist in America, despite all the types of malaria having been brought to the continent on a large scale by the African slaves, and where a number of parasitic diseases, including tropical and four-day malaria have taken root.

Considering that the particularities of the *P. ovale* distribution area are one of the unsolved mysteries of malariology, we propose that the problem can be unravelled by carrying out a more in-depth medical and geographical analysis of available and routinely collected data on the spread of this type of human malaria parasite across the world.

2.3. External borders of the nosoarea

The distribution area of malaria has never reached global proportions, and will never be able to do so. The worldwide spread of malaria is impeded by: the limited spread of Anopheles; the fact that some of the areas where the mosquitoes can be found are uninhabited by man; the fact that many types of Anopheles are ineffective malaria vectors, owing to their biological and ecological particularities; and, finally, the impossibility for a given type of effective vector to contribute to malaria transmission due to insufficient warmth for completing the parasite's development cycle within the mosquito in certain parts of the distribution area that are occupied by this type. As will become clear, the implications of each of the abovementioned reasons for the limited size of the nosoarea are extremely different.

2.3.1. Distribution area of Anopheles

Anopheles mosquitoes act as vectors of human malaria. Human malaria does not develop in any other type of mosquito or in other anthropoid parasites*. It thus follows that the nosoarea cannot be wider than the distribution area of Anopheles.

2.3.1.1. DISTRIBUTION AREA OF ANOPHELES MOSQUITOES AND CONDITIONING FACTORS

The distribution area of Anopheles is extremely wide, but nonetheless does not cover extreme northern and southern latitudes, high altitudes and some deserts. Factors such as climate (temperature, precipitation, humidity, winds), relief, type of soil and vegetation influence the spread of Anopheles. The nature of the influence of each of these factors on the vector's distribution area is unique and multifaceted.

Of the climatic elements, temperature is the most significant. The vital functions of the Anopheles larvae that are most resistant to the cold cannot be carried out below temperatures of +10°C. In the northern zone of the USSR, *A. maculipennis* can only survive if the temperature conditions remain constantly warm enough to allow the development of at least two generations [103]. It is temperature that defines the borders of the Anopheles distribution area. The northern border of the Anopheles distribution

area is formed by *A. maculipennis*, its subspecies *messeae* in Asia, *atroparvus* in Europe and *freeborni* and *occidentalis* in North America. The southern edge of the Taiga was the natural northern border of the *A. maculipennis* distribution area. In dense forests with cool summer conditions, there are no water supplies suitable for larva growth, and this type of *Anopheles* has not been found in natural Taiga. Man's deforestation of the Taiga in the past allowed *A. maculipennis* to break through that barrier and it travelled as far as the climatic border of its distribution area. According to data published by V. N. Beklemishev and A. N. Zhelochovstev [10], this border concurs with the isolines along which the average daily temperature is higher than +10°C for 85 days of the year.

By taking into account the information collected over the past 20 years, the climatic border of *A. maculipennis* proposed by these authors could be made more accurate. It has been proven that *Anopheles* (and malaria) has spread along the river Lena, further north than 62° north, i.e. it has gone beyond the isoline indicated in the abovementioned work. Data published by E. S. Kalmykov [33] on the borders of the regions of stable and unstable *A. maculipennis* reproduction in Archangelsk oblast' and Komi ASSR, and similar data, published by G. M. Shub [107], on the Karelsk ASSR also show that these borders lie north of the indicated isoline. There are reports that *A. maculipennis* has been discovered in Finland at 68° 20' north [162], and in Canada it has been found inside the Arctic Circle [152]. Combining the maps of the areas of stable and unstable *A. maculipennis* reproduction in Archangelsk Oblast' and Komi ASSR, and the most northern findings of this strain in Yakutsk ASSR, the Kolsk peninsula, Finland and Canada, with temperature maps [2, 136, 227] demonstrates more accurately that the northern border of *A. maculipennis* distribution coincides with the isoline for 70 days each year when the temperature is higher than +10°C.

In the southern hemisphere the *Anopheles* distribution area occupies all inhabited dry land, except for the extremities of America, south of 40° south, and the islands of New Zealand. The factors defining the southern border of the *Anopheles* distribution area are still unknown. It is suggested that in addition to the low temperature, lack of humidity is also a limiting factor [163].

At any latitude the majority of *Anopheles* strains are confined to low and moderate altitudes, up to approximately 1000 metres above sea level. With an increase in altitude the fauna of malaria mosquitoes decreases. They can only reproduce at very high altitudes in the tropics and subtropics, and even in those areas cannot do so at altitudes above 3500 metres. As they moved north and south away from the equator, the altitude boundaries of *Anopheles* distribution reduced. This was due to the relatively large drop in temperature in the mountains in temperate climate zones. The altitude boundaries in the distribution of the different types of *Anopheles* (including those that are proven vectors), as well as the maximum altitude of registered malaria breeding grounds, are summarized in reference table 2 (see appendix).

Precipitation and humidity also have a known effect on the distribution of *Anopheles*. Thus *A. superpictus* is widespread in eastern Georgia, which has a dry climate, but is almost unheard of in western Georgia, owing to the unfavourable influence of the relatively high air-humidity on the imago [35]. In East Africa during the dry season, *A. gambiae* can be found at altitudes of 1000 metres above sea level, and during the wet season can be found at up to 1800 metres, and even as high as 2100 metres [209]. During the rainy season in South Africa, *A. gambiae* can be found anywhere from the valleys to the mountains [141]. With the help of the wind, some strains of the vector (for example *A. pharoensis*) can spread tens or even hundreds of kilometres from the place where they reproduce and even cause outbreaks of malaria [157, 217].

Land relief in itself is not a factor defining the distribution area of *Anopheles*. Biotopes of *Anopheles* can be found on flat land as well as in mountainous areas, on the bottom of the world's deepest cavities (around the Dead Sea) and at the highest altitudes of the different mountain chains (the Pamirs, the Himalayas, the Andes, etc.). However, the indirect influence of relief is extremely significant and manifests itself through both malaria parasite hosts: mosquitoes and man.

The nature of relief defines the water drainage system, the availability, area and type of water supplies, and whether they are suitable for inhabitation by *Anopheles* larva [5]. It perhaps would not be out of place to mention that in itself, the area of *Anopheles*-inhabited water sources, in particular marshes, still does not predetermine whether malaria will develop in a particular place. An example of this is in northern Vietnam, on the marshy delta of the Red river, which is inhabited by the majority of the population, almost none of whom are infected with malaria, despite the vast numbers of the zoophiles *A. vagus* and *A. sinensis*. An overwhelming proportion of malaria breeding grounds in the country are

confined to the mountains, and well-drained areas where *A. minimus*, a relatively rare but effective vector is found [52]. This apparent paradox still surprises European physicians, who by tradition only associate malaria with marshy areas. As Hackett appropriately says [163], the lack of malaria in some marshy deltas in the tropics is not surprising if one remembers that malaria is linked not to a specific type of water supply, but rather to a specific type of Anopheles.

Frequently within the boundaries of one strain of Anopheles, the strain's numbers vary in different relief areas, a fact which is reflected in the structure of the nosoarea. In respect of *A. minimus* in northern Vietnam, this was noticed by Tumanov [228]; in respect of *A. maculipennis* in Georgia by G. I. Kanchaveli [35]; and in respect of *A. superpictus* in the western Pamirs by A. Y. Lysenko et al. [57]. In the western Pamirs, the numbers of *A. superpictus* and the population's contraction of malaria, as a rule, decrease as the altitude increases. The increase in *A. superpictus* has only been sufficient to support high level endemic malaria in one area, up-stream of the river Pyanzh, in Rushon district (on the site of an old, untended lake, at an altitude of 2000 metres above sea-level). Owing to the particularities of the relief of that site, lowland river malarial breeding grounds with high endemic levels developed from the hypoendemic malarial ravine landscape. In northern Vietnam, the optimum region in the distribution area of a particular vector, *A. minimus*, is confined to the Middle Mountains. In both outward directions, in the high mountain regions and hilly sub-mountainous areas, the numbers of *A. minimus* (and infection among the population) decrease. Another interesting particularity has been proven: depending on the form of the mountains, the highest border of the *A. minimus* distribution area (and nosoarea) reaches as far as 700 – 800 metres above sea level in some regions, and from 1200 – 1400 metres in others [51].

Relief is also known to predetermine human settlement. Vast mountain ranges and deserts still remain uninhabited by man, as a result of which they are malaria-free.

Thus land relief significantly determines the greatest “gaps” in the Anopheles (see diagram 8) and malaria (see diagram 15) distribution areas, and to a lesser degree the infection among the population at different altitudes within the borders of the distribution area of the same type of Anopheles.

Soil types affect the chemical composition of surface water sources, to which the different strains of Anopheles are particularly sensitive. *A. darlingi*, the main malaria vector in South America, prefers fresh water with a neutral or slightly acidic Ph. In contrast, *A. aquasalis* thrives in water with a high salt content. Appropriate places for this strain to multiply are found almost only in coastal areas. In certain regions in the states of Pernambuco and Seara (Brazil) have soil with a salt content that also provides the chemical composition of water in their local water sources necessary for the survival of *A. aquasalis*, as a result of which the distribution area of this vector stretches deep into the country [58].

Two examples can be given to support the idea that the influence of vegetation can be highly significant. As B. N Beklemishev and A. N. Zhelokhovtsev [10] noted, *A. maculipennis* cannot develop in water sources that are found in natural Taiga. Here, the dense forest vegetation creates a natural barrier. At the same time, the presence of malaria in parts of the southern states of Brazil and several regions of the island of Trinidad depends exclusively on a large quantity of epiphytes of the bromelia family, unique forest cisterns of water, which are appropriate breeding places for *A. cruzi* and *A. bellator* (in the state of Santa Caterina in Brazil) and *A. bellator* (Trinidad) [58, 204, 213]. The mass spread of bromelia is only possible in certain forest vegetation, on which they support themselves. If there is a small number of bromelia, the number of sub-species *Kerteszia* mosquitoes is not sufficient to be of epidemiological significance (for example in Venezuela).

Thus the northern, southern and high-altitude borders of the Anopheles distribution area are determined principally by climate (temperature and precipitation), and relief and vegetation are of indisputable significance. The internal construction of the distribution area of different strains of Anopheles is defined by many factors, the particular significance of which depends on the specific ecological particularities of each individual strain.

It should be noted that the formation of the Anopheles distribution area is not yet complete. Thus, Anopheles has arrived on many island territories relatively recently, following the establishment of contemporary modes of transport. An example of this is that *A. albimanus* was transported to Barbados in 1927 and *A. punctulatus* to the island of Rennell in approximately 1833 [219]. At the same time, some islands still remain free from Anopheles, despite the fact that it has been carried to them from neighbouring territories with endemic malaria. Such islands include Fiji, New Caledonia, New Zealand, the Marshall Islands, the Caroline Islands, the Bahamas, the Galapagos Islands, Hawaii, Tahiti, Samoa and several others (see diagram 7). The reasons for these islands' “immunity” against Anopheles (an

expression used by Scott) remain unknown, although Baxton [132] addressed this puzzling issue some time ago*.

There are few examples of territories where *Anopheles* can be found but which have not been settled by man. Thus Perry [202] reported that *A. farauti* existed without man on Russell Island and P. A. Petrisheva [79] discovered *A. superpictus* in an uninhabited part of the Karakum.

2.3.1.2 DISTRIBUTION AREA OF STRAINS OF ANOPHELES KNOWN TO BE VECTORS

According to data issued by Russell et al. [216], 65 species and subspecies of *Anopheles* are proven vectors of human malaria. According to our more accurate data, there are in fact 80 (see appendix 1). This figure includes species and subspecies, individuals of which were found to be infected in malaria breeding grounds. The figure reflects the general biological pattern, according to which usually only a portion of the types within a given species (family) of anthropoda is apt to become a vector of a disease agent. Out of the total number, more than 400 species of *Anopheles*, only 20% are vectors. The epidemiological significance of anthropoda in general, and specifically *Anopheles*, is defined by many biological and ecological factors, the most important of which are considered to be susceptibility to infection, number, the degree of the relation with man and his living environment, and the activity and life-span of the vector [4, 7, 25]. As a rule, dangerous malaria vectors tend to be species that are large in number, feed primarily off man, are active for a reasonably long season, and species of which a large percentage of females live long enough to acquire sporozoids in their salivary glands (an epidemiologically dangerous age). Depending on specific local conditions, each strain of *Anopheles* responds to these needs to different degrees [21]. One and the same strain may be a major vector in one location (*A. sinensis* in China), and yet under different conditions may be of very little epidemiological significance (*A. sinensis* on the delta of the Red River in the Democratic Republic of Vietnam). A number of strains are dangerous vectors across a vast portion of the nosoarea (*A. gambiae*, *A. darlingi*, *A. m. messeae*), and others are of purely local significance (*A. sergenti* in the oases of the Sahara, and *A. hispaniola* in the Atlas mountains).

Data on the spread of the strains of *Anopheles* that carry malaria in different countries (see appendix 1) show that, even in tropical conditions, there are few countries in which a large number of vector strains have been registered. Usually, in each given country one or two important vector strains have spread, which also define the specific type of malaria illness. Since the distribution area of these important vectors covers a number of neighbouring countries, the overall malariological situation in the world is defined by 25 – 30 strains of vector.

The most effective malaria vectors in the world are *A. gambiae* and *A. funestus* in tropical Africa and *A. punctulatus* in New Guinea; they are highly sensitive to infection by human plasmodia, and a large proportion of them live to an epidemiologically dangerous age, and they differ greatly in their anthropophile and endophile characteristics. Their distribution area covers parts of the nosoarea with the highest level of infection among the population: holoendemic areas. Hyperendemic malaria breeding grounds in South and Central America are caused by *A. darlingi* and *A. albimanus*, in South-East Asia by *A. fluviatilis*, *A. culicifacies*, *A. sudaicus*, *A. maculatus* and *A. minimus*, and in the Mediterranean countries and the Near and Middle East by *A. maculipennis labranchiae*, *A. m. sacharovi*, *A. sergenti*, *A. stephensi* and *A. superpictus*. Epidemic malaria breeding grounds in temperate regions have been formed by mosquitoes of the *maculipennis* group: *quadrimaculatus*, *freeborni* (North America), *messeae* in Asia and *atroparvus* in Europe (see diagram 8).

2.3.2. TEMPERATURE LIMITS ON PARASITE DEVELOPMENT

The best known and most studied limiting effect is had by low temperatures, which define the northern and high-altitude borders of the spread of malaria in general, and specifically the individual forms that the disease takes.

Even before the discovery of the agent and vector of malaria, the great Russian physician and medical geographer N. I. Toropov noted the following in his monograph “The experience of medical geography in the Caucasus with regard to intermittent fevers” [98]: “Fever does not exist in places where the average summer temperature is lower than 16.2°C” (page 250). A little while later, but also before the discovery of the malaria agent, the German medical geographer Hirsch [168] came to

a similar conclusion. He took summer isotherms of 15 - 16° to be the border of the distribution area of autochthonous malaria (page 178). The explanation for why the borders of the distribution area of local malaria are governed by temperature came later, when Grassi [160] and Jancsó [174] ascertained through experiments that *P. vivax* does not develop in mosquitoes in temperatures below 15.5 - 16°. Here it is appropriate to stress the great opportunities provided by the medical-geographical method that allowed N. I. Toropov and Hirsch to discover the important pattern before such time as the reason for it could be understood.

Since the temperature threshold for malaria parasite development (16°) is higher than the corresponding threshold for the development of *Anopheles* larvae (10°), temperature limits the spread of malaria more severely than it does the spread of *Anopheles*. For this reason only, the distribution area of malaria must be smaller than the distribution area of *Anopheles*. In fact, *A. occidentalis* (of the *maculipennis* group) has been registered in Canada inside the Arctic Circle, up to 69° north [198], but the breeding grounds for local malaria have never reached further north than 50°. In Sweden, *A. maculipennis* has been discovered up to 68 – 69° north, but the breeding grounds for local malaria reach a maximum of 66° [145].

Annual fluctuations in summer temperature condition the continuous mobility of the northern and high-altitude borders of the distribution areas of *Anopheles* and malaria [104]. In places located on the northern and high-altitude climatic borders of the nosoarea, the microclimate inside buildings is of considerable significance. In the northern regions of the USSR, the summer temperature inside people's houses and in livestock sheds is a few degrees higher than the outside temperature [45]. Similar information has been found in high mountain villages in Kenya; only constant fires in huts create the necessary temperature conditions for complete spore development in mosquitoes and the transmission of malaria [154]. This is why, according to the author, preparing food in a kitchen built outside the home would be sufficient to eradicate the conditions necessary for epidemic outbreaks of tropical malaria. Comparisons between the registered most northerly breeding grounds for local malaria and climate charts shows that the northern border of the distribution area of malaria coincides reasonably accurately with the isoline for recurring temperatures above 15°C for 30 days per year.

In that regard, we believe that the isoline for temperatures of over 15°C for 30 days per year is a more accurate demonstration of the northern border of the nosoarea, than the July isotherm of 16°, which foreign malariologists [125, 159, 163] often consider to be the northern border of the malaria distribution area.

Very little research has been carried out into the effects of constant, very high temperatures, such as those found in the oases of tropical deserts. According to Hackett [162], the absence of three-day malaria and, in contrast, the significant spread of four-day malaria in some oases of the Sahara is likely to be linked to the oppressive effects of temperature on the spore formation of *P. vivax*.

2.3.3. ECONOMIC ACTIVITY OF THE POPULATION AND MIGRATION

Of many socio-economic factors, economic activity and migration have had the greatest influence on the formation of the malaria distribution area.

For a long time man facilitated the expansion of the malaria distribution area through his economic activity. The establishment of permanent settlements resulting from the transition to a settled way of life, the development of irrigation farming, trade and seafaring all facilitated the formation of new malaria breeding grounds in territories that were formerly free from the disease, and increased infection among the populations in breeding-ground countries. The expansion of the nosoarea was particularly intensive in the eighteenth to nineteenth centuries, when the dissociation between countries that had been characteristic of earlier social formations disappeared. Large capitalist powers had a subjugating influence over economically underdeveloped countries, and colonization took place. During the colonial wars, links were established with formerly isolated territories. As a result of the wars and crises, the migration process strengthened, which allowed the agents of the disease to spread among all peoples and races. Epidemics occurred simultaneously in colonizing countries and colonies [102].

Illness and death caused by malaria rose sharply during this period. Deforestation, irrigation, and large-scale building of railways and roads, military fortifications and other buildings that generally did not undergo any sort of sanitary inspections, led to the establishment of a vast number of man-made places where *Anopheles* could breed. "Man-made malaria" developed alongside natural malaria.

Deforestation of the Taiga allowed breeding grounds for malaria to develop on the northern border of the *A. maculipennis* distribution area (see above). The malaria distribution area in Malaya expanded greatly as a result of mass deforestation of rainforests. In the virgin forests in the heart of the country the water sources were shaded and *Anopheles* could not breed in them. The destruction of the vegetation that shaded water sources allowed *A. maculatus*, a very effective vector in Malaya, to penetrate former forest areas, and as a consequence, dense malaria breeding grounds arose [218]. Similar human activity led to the expansion of the *A. quadrimaculatus* distribution area in the USA, and thus the expansion of the malaria distribution area [125]. The spread of malaria in many countries was facilitated by the introduction of rice growing in paddy fields, the creation of ponds for fish farming, and damming rivers and irrigation canals.

Global experience demonstrates that in the past, the initial phases of settling new lands always coincided with a worsening in the malariological situation. Malariologists have distinguished three stages in the settling of new lands [5, 151, 186, 237]. The first, when the land had only just begun to be settled, was characterized by an influx on non-immune workers, the arrival of new strains of agent, and an increase in vector quantity. In circumstances where there were few agricultural livestock, insufficient food and poor medical services, epidemics broke out and mortality rates were high. At the second stage land cultivation was typical, which was large-scale, and involved bringing in seasonal workers. From there, along with well-equipped villages, there were still many primitive settlements for seasonal workers, among whom malaria outbreaks occurred, which also affected the local population and were exacerbated by poor medical services. The third stage was characterized by efficient land use, a fall in migration, an increase in numbers of agricultural livestock and an improvement in medical services. Malaria took its victims gradually.

It is thought that over half the world's cases of mortality from malaria have been a direct result of irrational activity, from a hygiene perspective, on the part of man [151].

2.3.4. THE FURTHEST BOUNDARIES OF THE NOSOAREA

During its period of maximum spread, at the end of the nineteenth and beginning of the twentieth centuries, the distribution area of malaria was vast (see diagram 15). It is clear that this was a zonal nosoarea. It covered a vast area of the globe from the Tropic of Capricorn and stretched almost to the Arctic Circle. The malaria distribution area should be considered to have been complete during this period, since it occupied almost all of the territory inhabited by man that had climatic conditions to suit the ecological requirements of the vector and the parasite. The few "gaps" in the nosoarea generally appeared in large mountain ranges (Tianshan, the Himalayas), deserts (the Gobi, Karakum, the Sahara, the Arabian desert, the Great Sandy Desert in Australia, the Kalahari, etc.) and some islands (Sakhalin, Hokkaido, New Caledonia, New Zealand, etc.). Malaria was widespread in all climatic zones except the Arctic. As a rough approximation, one could consider that the borders of the global nosoarea coincided with the borders of the combined distribution area of the 12 most important strains of vector-*Anopheles* (see diagrams 15 and 8).

What allowed malaria to spread so extensively in comparison with other infectious diseases?

According to V. N. Beklemishev [9], the greatest advantage in spreading a disease is held by the agents of transmissible diseases for which man can serve as an epidemiologically significant source of infection and the vector has become sufficiently synatropic. In the case of malaria, man is almost the only source of infection. Vector-*Anopheles* spread across the world long before the first appearance of man [212], and over time, many strains of this species acquired not only synatropic, but also anthropophile characteristics. Consequently, the spread of the infection was carried out by man himself, creating breeding grounds for malaria wherever he settled within the *Anopheles* mosquito distribution area. The duration of the infection allowed the agent to be preserved while man moved, and weak post-infection immunity did not prevent malaria from taking root even in places with small populations [29].

3. STRUCTURE OF THE MALARIA DISTRIBUTION AREA DURING ITS PEAK PERIOD

Until recently, insufficient attention was paid to studying the structure of nosoareas. In particular, there was no clearly defined understanding of the term "nosoarea structure".

3.1 Definition of nosoarea structure

In biogeography, there are understood to be internal “constructions” within the structure (or topography) of a distribution area, i.e. population density, or the nature of the spread of one or another of the forms across the whole distribution area” [34]. A similar definition was given by Y. A. Isakov [32], according to whom the study of the structure of a distribution area is its “subdivision into categories “similarly permitted by the environment”, from natural conditions on which the seasonal distribution of the species depends, constancy of its habitation of a territory in different years, and its number”. This is what we mean when we talk about the optimum and minimum parts of a distribution area [69] or the centre of species’ density [13]. It is considered that the densest number of a given species is confined to the optimum part of the distribution area, and that this part of the distribution has the most favourable conditions for the existence of that species. The further one moves towards the peripheries of the distribution area, the smaller becomes the area of biotopes appropriate for the survival of the species, and the lower the species becomes in number. The concepts of “danger zones” [108] in agricultural entomology, and of species dispersion zones in zoogeography [78] have been developed on this basis. As with feral herd diseases, epizootologists differentiate between stable epizootic areas and developing epizootic areas [42, 101].

The issue of the structure of disease distribution areas has only just begun to be developed by medical geographers. A. A. Shoshin [105] pointed out the need to study the structure of nosoareas, although he did not define the details of the task. It is likely that the first possible approaches to studying nosoarea structures (of malaria, for example) were discussed at the second Scientific Conference on Medical Geography, held in Leningrad [60].

Developing these points of view, we believe that the following issues should be worked on when studying the structure of the initial distribution area of malaria:

a) Subdividing the nosoarea into sections of stable and unstable endemics (“permanency of a species’ settlement of a particular territory in different years” according to Isakov); b) subdividing endemic malaria territories with similar levels of infection among the population into groups of holo-, hyper-, meso-, and hypoendemic malaria (“species density”); c) subdividing the grouped malaria distribution area into species distribution areas, and separating areas occupied by individual subspecies and groups of strains of the malaria parasite; d) separating sections with similar malaria seasons (“seasonal species distribution”).

Developing all of these issues would lead to the establishment of specific indicators for the epidemiological differences within the nosoarea, with the final aim of differentiating the treatments and prevention methods appropriate to the particularities of each different group. There is almost no experience in studying the structure of residual distribution areas of infectious diseases.

In the case of malaria, we believe that the residual nosoarea should be characterized in two main ways. Firstly, it should be subdivided into parts according to difference in risk of infection for people who are not immune (in particular new arrivals), and second, according to the probability of malaria reappearing in cured territories in the event of the arrival of a source of infection.

The final results of a study on nosoarea structure should be the detailed mapping of its different aspects.

3.2. Principles of the subdivision of malariogenic territories

The following four principles for are the most widely used to subdivide malariogenic territories [56]: climatic, zoographic, landscape and subdivision by level of endemic.

3.2.1. Malariological zoning using climatic indicators

The dependence of the spread of malaria on climate was noted earlier than its dependence on any other factors (see above, section 2.3) and as early as 1900, Celli [133] set out the malariological (or to be more precise, parasitological) characteristics of what were considered at the time the world’s three main climatic zones. He believed that temperate climate zones were characterized by the considerable spread of *P. vivax* and the absence of *P. malariae*, subtropical and tropical climate zones were characterized by the predominance of *P. falciparum* and a greater or lesser proportion of *P. vivax*. Later, Gill [159] not

only set out the malariological characteristics of the world's principal climatic zones in more detail, but also specified the partial coincidences between "climatic zones of malaria" (diagram 9) and different climate zones. As critical values, defining the possibility of malaria transmission, he took the mid-month isotherm of the hottest month of the year (July or August) to be over 15.6°C, and the respective midmonth humidity to be greater than 63%. For a long time, Gill's "climatic zones of malaria" were the only example of a breakdown of the disease's global distribution. His map was later misquoted by many authors as being a "malarial" map. Thus Professor Pampana produced a copy of Gill's map in his monograph "A textbook of malaria eradication" [199] under the title "Endemic types of malaria".

The technique used by Gill (appropriating malariological characteristics to a major area or zone according to climatic features) was adapted by some authors for the zoning of malarial territories on individual continents (South America [153]) and countries (Ceylon [179] and Brazil [131]).

Climatic indicators were used slightly differently to develop malarial typographical maps of Tanzania and Kenya [119, 120]. The authors divided the malariogenic territory of these countries into types of zone with malaria transmission seasons of different durations (see diagram 10). This approach was more thorough than the first since it took into account not only climatic indicators, but also the particularities of the vector.

3.2.2. Malariological zoning using the principle of zoogeography

There is only one known example (see diagram 11) of zoning the global distribution area of malaria using this principle [191]. A map of 12 malarial regions, into which Macdonald divided the global nosoarea was "compiled taking into account the world's zoogeographical zones, to which different species of animal, including Anopheles, are confined". Thus, this was an attempt to break down the nosoarea according to vector species. Indeed, the author also mentions that in compiling the map "there was no intention of studying these areas precisely, it was more an attempt to define territories, within which the epidemiology of malaria was constant, owing to temperature, precipitation, the physical particularities of the land and other factors, as well as the spread of strains of Anopheles". In fact, this subdivision of malariogenic territories is based on the author's theory on the existence of two extreme epidemiological types of malaria – stable and unstable malaria. Breeding grounds for stable malaria are created by particularly effective vectors, which are characterized as extremely aggressive towards man and as having a strong probability of survival in high temperature conditions, which are favourable for the parasite's development in the mosquito. On average 0.025 bites of a human in one night is sufficient for these vectors to become and remain highly infectious. The author attributes the following strains to the group of vectors that create breeding grounds for stable malaria: *A. gambiae*, *A. funestus*, *A. minimus minimus*, *A. fluviatilis*, *A. maculipennis sacharovi* and *A. maculipennis labranchiae*. Vectors that rarely attack man and have a weak probability of survival, (*A. culicifacies*, *A. philippinensis*, *A. maculatus*, *A. minimus flavirostris*, *A. stephensi*, *A. maculipennis messeae* and *A. aquasalis*) form breeding grounds for unstable malaria. The transmission of infection in such breeding grounds is sustained only by large numbers of mosquitoes biting humans on average between one and ten times per night.

There is no reason to disagree with the author regarding his proposed classifications of epidemiological types of malaria and the conditions for the intensity of their transmission. At the same time, we believe that the structures defined by the author are only reasonable for centres of high density in the distribution areas of the vectors, where the particularities inherent in the individual strains of Anopheles are fully apparent. However, it is well known that the peripheries of the distribution area constitute a significant proportion of the territory occupied by any species of vector. Here, by nature, even the most effective vector is unable to create intensive malaria breeding grounds. Such breeding grounds for hypo- and mesoendemic malaria are found in Africa in the distribution area of *A. gambiae* and in northern Vietnam in the distribution area of *A. minimus* etc. In at least one of these areas, Macdonald cannot be epidemiologically accurate, and thus his principles of zoning cannot be considered to be wholly satisfactory (see also below, section 3.3.2).

3.2.3. Malariological zoning and typological mapping using the principle of landscape

The question of the confinement of malaria to specific types of landscape was first raised by Tumanov. In his monograph “L’anophélisme en Extrême-Orient” (Anophelism in the Far East) [228] he clearly separated many malariological types of landscape in northern Vietnam, which differed according to the presence of effective malaria vectors and the level of their infection with malaria parasites. Since he did not have any parallel material on the population’s infection with malaria, Tumanov could not carry out an in-depth epidemiological analysis, and therefore did not come to any theoretical conclusions.

The first scientific proof that the spread of malaria and the particularities of the disease’s epidemiology depend on type of landscape was provided by V. N. Beklemishev [5]. His starting point was that it was necessary to “give a malariological analysis of all factors existing for the spread of malaria across all landscape areas, and through analysis create a natural classification system for the types of malaria breeding grounds found within individual landscape zones”. He believed that “the degree of malariogenesis of each landscape zone and each landscape is characterized by its number and intensity of malaria breeding grounds, and depends on a combination of conditions, both natural and social, which influence malaria’s development: climate, mosquito fauna, the geological construction of the area, drainage system, vegetation, population density and migration, agricultural methods, etc.”.

The landscape principle has been used by malariologists as a basis for the landscape-epidemiological zoning and typological mapping of separate parts of the nosoarea. A substantial geographical unit (zone, region, province) was classified in the zoning process, and was assigned a special characteristic. This method was used by V. N. Beklemishev [5] in the section of his work that deals with the division of the Soviet Union into malarial zones. He demonstrated that in as far as the main factor defining the regional distribution of malaria is climate, the malaria zones in the USSR (the malaria-free north, the epidemic malaria zone and the endemic malaria zone) more or less coincide with the general landscape-geographical zoning.

Later, this approach was successfully adopted by G. I. Netsky and M. M. Itskovich [73] in the malariological zoning of the west Siberian lowlands. In accordance with the zones defined by V. N. Beklemishev, they identified from north to south: a malaria-free zone, an unstable epidemiologically effective temperature zone, and a stable epidemiologically effective temperature zone.

In mountainous countries, one of the first zoning projects was carried out by A. A. Ustinov [99]. The author gave detailed malariological characteristics to four geomorphological “zones” in Abkhazia, and in doing so noted that “in the majority of cases the breeding grounds in one geomorphological zone are so similar, that they should be classed together as one type...”. Of course, that conclusion is due to the author’s exaggeration of the landscape-zoning principle. Evidence that malarial breeding grounds in one geomorphological zone are epidemiologically different can even be found in the author’s own work. Thus in characterizing a cavernous geomorphological zone he writes (page 23): “different measures are required for curing breeding grounds, owing to the fact that they are not the same (!)”.

The work of G. I. Kanchaveli [36] contains a malariological zoning of Georgia, which is based on the geomorphological division of the republic and numerous entomological materials compiled by the author. The author defined “7 malarial landscape regions with 13 zones” in the republic (excluding Abkhazia). Each “malariogenic region” and “malariogenic zone” was epidemiologically different. The more similar zones were separated by G. N. Gordadze [15], who studied the changes in climatic conditions from west to east (the influence of the Black Sea) and from north to south (the influence of geographical coordinates).

Thus irrespective of the basis on which malariological zoning is carried out (by climate, vector or landscape) the regions that have been separated are not sufficiently epidemiologically similar, and therefore cannot serve as a basis on which to plan anti-malaria activities. It is significant that V. N. Beklemishev [5] considered the subdivision of the USSR into malariological zones to be a vital step towards establishing a scientific basis for planning eradication measures. More recently he considered planning on the basis of landscape and typology. He clearly pointed out that “... in order to plan nationwide activities it is absolutely necessary that there is some kind of general theory on malarial breeding grounds, and that they are typified. We should know which main types exist, and how these types are distributed geographically across the USSR. Above all, to the same end, it is necessary to develop typological plans for eliminating the main types of breeding ground. Thus, typifying malarial

breeding grounds is one of the fundamental scientific and practical tasks in the fight against malaria”.

The first serious specific work on typifying malaria breeding grounds according to landscape was carried out by A. S. Klug in 1941 [39]. The author described four landscape types for malaria breeding grounds in Bashkiria: flood-land, steppe, ravine-springs and mountains, and he proposed typified systems of activity for curing them. He did not, however, compile a typological malarial map of Bashkiria.

In 1958 a group of Azerbaijani malariologists [3] typified the malaria breeding grounds in Azerbaijan. Their work is of methodological interest. It demonstrates, above all, the authors' dissatisfaction with a purely regional approach to zoning. Having given the malariological characteristics of two landscape regions and several landscape zones, the authors went a step further and identified characteristic types of malaria breeding grounds within each of landscape region (15 types in total). They discussed in detail the particularities of activities which should be carried out in conformity with the particularities of each type of breeding ground. The work, however, was never completed as the authors did not publish typological malarial maps of Azerbaijan, i.e. a document that would serve as a conclusion to the whole zoning of the territory [64].

Taking into account the theories put forward by V. N. Beklemishev, and the experience of typifying malarial breeding grounds reflected in the works of A. S. Klug [39], and L. V. Ivanova and A. I. Nemirovskaya [31], A. Y. Lysenko and co-authors [59] typified the malaria breeding grounds in Tajikistan. The final aim of typifying the breeding grounds was to compile a landscape-typological malarial map of Tajikistan.

The main stages in compiling a typological malarial map of this mountainous country were [50]:

1. Using an average scale landscape or topological map (scale 1:100 000 or 1: 250 000) to choose routes to be investigated with coverage of the whole variety of orohydrographical conditions in the territory studied;
2. Carrying out a complex investigation of the places and populations along the chosen route;
3. Typifying the malaria breeding grounds using study materials;
4. Sorting the data collected by comparing the types of malaria breeding grounds identified and all the remaining inhabited parts of the given area and grouping together similar types of breeding grounds in malariogenic landscapes;
5. Carrying out a conclusive investigation in the parts of the identified malariogenic landscapes, which for any reason have not been sufficiently proven to belong to a given type (defining the boundaries of malariogenic landscapes more accurately);
6. Characterizing each class of malariogenic landscape using all of the materials collected: investigation results, demographic and economic statistics, etc.

The borders of the initial malarial territories in Tajikistan and the borders between the country's five types of malariogenic landscape, which were identified in 1955 and specified in more detail in 1956, are shown on the map in diagram 12, which was first published in 1965 [53]. In a similar way, a typological map of northern Vietnam was compiled later (see diagram 13).

It is interesting to compare the maps of malariogenic landscapes and their characteristics in two mountainous countries: Tajikistan and northern Vietnam (see diagrams 12, 13 and table 5). Table 5 shows that there are similarities and differences between the two countries. The similarities lie in the fact that the majority of the malariogenic landscapes are of the same type, and are of similar epidemiological significance (types of landscape confined to hilly, low and medium mountainous territories). Of the differences, the most important to remember are the very different levels of significance of ravine-river malariogenic landscapes (highly significant in Tajikistan, and of very little significance in Vietnam) and the different levels of danger of the predominant strain of parasite (*P. vivax* and *P. falciparum* respectively).

Landscape typological mapping served in both countries as a basis for developing programmes for combating malaria, which were defined according to the particularities of the different types of malariogenic landscape. The programme for combating malaria in Tajikistan has been completed, and the programme in northern Vietnam is being successfully implemented [41, 52, 53].

Everything that has been said about zoning using landscape typological maps illustrates the high level of precision of that method in respect of separating individual epidemiological malariogenic differences. Owing to the particularities we have mentioned, this principle of subdivision provides a

strong scientific basis for developing tailor-made plans for both cure and prevention activities. It has already been noted [54] that this principle of typifying breeding grounds and malariogenic landscapes allows prognoses to be made for the potential risk of breeding grounds developing in different parts of the nosoarea, and as a result of this it is possible to make a prognosis regarding possible changes in conditions.

Table 5
Comparative malariological characteristics of two mountainous countries: Tajikistan and northern Vietnam

Tajikistan					Northern Vietnam				
Vectors	Length of	Level of		Proportion of population living on the territory of a given malariogenic landscape	Vectors	Length of	Level of epidemic		Proportion of population living on the territory of a given malariogenic landscape (%)
A. m. sacharovi A. superpictus A. pulcherrimus	6 - 7	High	P. vivax	5(9.0)	(A. Minimus	Mainly free of malaria			67.5
>>	>>	>>	>>	19.0		None			
A. superpictus	5	Low	>>	10.0	A. Minimus	4 - 6	Low	P.	9.0
(A. superpictus)	(5)	(Low)	>>	(10.0)	A. Minimus	5 - 7	Average	P.	9.0
A. m. sacharovi	4 - 7	High	>>	15.0	A. Minimus A.	6 - 8	High	P.	13.0
A. superpictus	3 - 5	low	>>	2.5		None			
None					A. minimus	3 - 4	Low	P.	1.0

3.2.4. Developing typological malarial maps according to epidemic levels

It was noticed many years ago that the level of infection among the population in long-standing malaria breeding grounds in the tropics was typical of that type of breeding ground. The more typical this level is, the more stable the conditions are that define the existence of the breeding ground. S. D. Moshkovsky [67], having studied the quantitative side of this issue, came to this conclusion as follows: “for each combination of epidemiological conditions there exists a level of infection among the population. This rate of infection becomes apparent at the endemic level typical of the given combination of epidemiological parameters”.

Endemic level tends to be judged based on the level of the splenic index for children aged 2 - 9. Classifications of malaria epidemics are based on the following figures (World Health Organization):

Hypoendemic malaria - splenic index for children aged 2 - 9 from 0 - 10%.

Mesoendemic - splenic index for children aged 2 - 9 from 11 - 50%.

Hyperendemic - splenic index for children aged 2 - 9 over 50%, and as high for adults.

Holoendemic - Parasitic index for infants constantly above 75%. Splenic index for adults: high (in the case of the New Guinea type) or low (in the case of the African type).

The experience of many countries shows that in the vast majority of cases the classification of breeding grounds by endemic level measured using the splenic index for the standard age group (children aged 2 - 9) is wholly satisfactory for comparing breeding grounds and compiling malariological maps. The method of typological mapping of malariogenic territories using infection level among the population has been widely applied in different continents.

The “malarial map of India” (diagram 14) is an example of a “malarial” map constructed using population infection indicators. This map uses the distribution area to indicate the locations of malarial territories. The distribution area is subdivided into types of malariogenic territory, which differ according to their endemic level. The evidence used to explain the absence of malaria in non-malariogenic territories (places higher than 1500 metres above sea level, and malaria-free plains) has become legendary. It is clear that this map, which was completed by qualified specialists at the Indian Malaria Institute, fully satisfies the needs of epidemiologists and medical geographers.

3.3. Compiling a map of “the structure of the worldwide malaria distribution area based on primary endemic levels”

The wide range of materials published during the time when the spread of malaria was at its most extensive could be summarized in a map.

When we began to compile the map of the structure of the worldwide malaria distribution area based on initial endemic levels, we were aware of the complexity of the task, caused by the need for large-scale collection and analysis of materials. Certain detailed summaries on the spread of malaria in some countries, which could have been included in the map, were not found in the available literature. Neither were there any summaries of malarial maps, published in different countries. Compiling the map was also made difficult by incomplete factual data on the spread of malaria in many countries and the fact that the materials were in a wide range of formats.

3.3.1. Basic requirements of the map of “the structure of the worldwide malaria distribution area based on primary endemic levels”

The requirements of the map were summarized as follows: A. The map must reflect as accurately as possible the structure of the primary malaria distribution area, i.e. the distribution area at its prime.

For the vast majority of countries, this period coincided with the end of the 19th and the beginning of the 20th centuries. The “malarial potential” of many northern European countries and North America reached its maximum earlier, between the end of the 18th and the mid-19th centuries. In general terms, we included in the nosoarea all territories in which at one time or another local malaria breeding grounds had been registered. In this respect we maintained the same point of view regarding the distribution area of malaria as had been expressed by specialists in feral herd diseases, regarding the borders of the distribution area of the agent of endemic zoonoses. An example of this is that B. K. Fenyuk [101] proposed that the

distribution area of the vector of the plague be referred to as “the whole territory in which enzootic plague has appeared in any form over recent years, including areas that have been subject to epizootic occurrences that are located outside the boundaries of stable epizootic regions”. Recently this point of view has been strongly supported by V. V. Kucheruk [42].

B. The breakdown of the nosoarea on the map must be carried out according to one indicator: endemic level.

We have tried to identify four differences within the borders of endemic malarial territories (hypo-, meso-, hyper-, and holoendemic regions) and individually in regions with severe epidemic malaria (as understood by B. N. Beklemishev [5]).

C. The main version of the map should be produced on a scale of no less than 1:30 000 000 with national borders marked according to the Political Map of the World (Moscow, 1966). The issue of the precision with which State borders were marked was very significant in connection with the map's future use in the drafting of a map of “the structure of the contemporary malaria distribution area according to risk of infection”, which is planned for publication in a periodical and will be used to plan and implement precautionary measures to prevent the spread of malaria in the USSR*.

3.3.2. Analysis of the map of the “structure of the worldwide malaria distribution area based on primary endemic levels”

This map (diagram 15) clearly demonstrates the differences in endemic levels within the nosoarea that had been reached between the end of the nineteenth and the beginning of the twentieth centuries. Malaria had only reached holoendemic levels in two parts of the nosoarea: tropical Africa and the island of New Guinea. In Africa, the breeding ground of holoendemic malaria was formed by *Anopheles gambiae* and *Plasmodium falciparum*, and on the island of New Guinea by *A. punctulatus* and *P. vivax* (Chesson strains), and also by *P. falciparum* (see page 15). The main breeding grounds for hyperendemic malaria were also confined to tropical Africa, but a significant number of them developed in the Mediterranean, Western and Central Asia, the Indochinese Peninsula and Hindustan. In the New World comparatively small sections of the distribution area of hyperendemic malaria arose only in Central and South America. *P. falciparum* developed alongside the breeding grounds for hyperendemic malaria, and was transmitted by effective vectors including *A. gambiae*, *A. minimus*, *A. maculatus*, *A. culicifacies*, *A. maculipennis labbranchiae*, *A. maculipennis sacharovi*, *A. superpictus*, *A. darlingi* and *A. albimanus* (see diagrams 15 and 18).

The largest parts of the nosoarea with mesoendemic malaria were confined to South America, the northern and southern extremities of tropical Africa, Western, South and South-East Asia, the southern regions of the USSR and the People's Republic of China. The different mesoendemic parts of the nosoarea varied in respect of species of vector and natural climatic conditions. The moderate degree of malaria infection among the population in these parts had a variety of causes. In some parts, the intensive spread of malaria was prevented by unfavourable climatic conditions, which limited the epidemiological effectiveness of such dangerous vectors as *A. gambiae* (the northern and southern extremities of its distribution area in Africa). In other situations, the climatic conditions were conducive to intensive transmission, but the local anopheles fauna did not include effective vectors (extensive regions in Indonesia, Malaya and other countries). In several parts, infection did not reach very high levels owing to the small population (the Amazon basin). More often than not, the population's moderate level of malaria infection was a result of all three of these factors.

Everything that has been said about mesoendemic malaria areas is also relevant to hypoendemic malaria areas, with the only exception that in these areas the main limiting factors were the ineffectiveness of the vector, and unfavourable climatic conditions (the Soviet Far East, the Deccan Plateau in India, etc.).

The epidemic malaria region includes two large tracts of land. The largest of the two was confined to the northern peripheries of the nosoarea (northern Europe, the northern part of the European and Asian parts of the USSR and North America), where *A. m. atroparvus* and *A. m. messeae* were malaria vectors. The second, which was not sufficiently defined, was confined to northern Australia. Several small parts of the epidemic malarial zone (not indicated on the map) were listed in Africa, at the high-altitude border of the nosoarea, in India and in North America.

It is interesting to compare the map of the structure of the nosoarea based on endemic levels with Macdonald's map of the epidemiological regions of malaria (see diagram 11). It is sufficient, for example, to compare Macdonald's South American and Indo-Persian regions with the relative parts of the nosoarea

on our map, in order to prove what is written above (section 3.2.2.) on the epidemiological differences of the areas that were identified by Macdonald using the regional principle.

When characterizing the map of the structure of the worldwide malaria distribution area based on primary endemic levels, attention should be paid to its main cartographical particularities. In content it should relate to thematic, and in this case nosogeographic (malariological), maps. In its method of identifying differences it is typological by design, general in view, and small-scale. To a certain extent the map refutes the malariogenesis inherent in the given territory and several characteristics that are derived from it (primary risk of infection, access to treatments, potential danger of malaria developing when brought in to malaria-free areas, etc.). An important aspect of this map is its possible use for developing summarized maps and in particular extremely important practical maps of the structure of the worldwide distribution area according to risk of infection (see below section 5.2).

4. DYNAMICS OF THE DISTRIBUTION AREA FOLLOWING THE BEGINNING OF MASS ANTI-MALARIA ACTIVITIES

From what has been said above, we can see that the borders and structure of the malaria distribution area are defined by a combination of complex natural and social factors. The natural consequence of any changes in these factors is inherent in changes in the nosoarea. During its initial formation, the distribution area of malaria was progressive (see N. S. Kamyshev, [34]). Its borders widened, the population's infection with malaria increased and the different types of malaria parasite attained maximum distribution. However, during its formation, there were also circumstances in which the nosoarea diminished in certain areas.

There is reason to believe that the Red River delta, which was at one time a malarial area, gradually became free of malaria as a result of continual settlement and development into a mass area of uninterrupted rice fields, which meant that the conditions necessary for the main Indochinese vector, *A. minimus*, to breed, no longer existed [17]. The differences between the reclaimed plains, which were almost free from malaria, and the highly infected mountain areas were so significant that they had a decisive influence on settlement. In Vietnam and Cambodia, some peoples, particularly the Khin, only settled in the flat, malaria-free territories (see diagram 16). We suggest describing the border between the mountainous malarial areas, which were inhabited by small mountain tribes, and the malaria-free plains, which were almost exclusively inhabited by the Khin, as the "Dobby ethno-malariological line" (named after the geographer that compiled the map used in diagram 16).

According to P. Guru [17], the Khmer people, at the height of their civilization, developed the territory of ancient Cambodia so well that malaria did not pose them any problems. It was only when the Siamese destroyed the irrigation channels that malaria once again reached hyperendemic levels in that area. These, and several other similar examples, demonstrate that the broadening and regression processes of the nosoarea took place simultaneously.

There were different reasons for the regression of the malaria distribution area. These reasons can be split into two main groups: inadvertent activities connected with man's economic activity, and activities carried out specifically to combat malaria. Thus it is possible to differentiate between the period of spontaneous reduction of the nosoarea, and the period of organized anti-malaria activity.

4.1. Spontaneous regression period

The conditions required for a significant reduction in some parts of the malaria distribution area began to form in the 18th Century. The development of land cultivation and general land reclamation in economically developed and densely populated countries of Western Europe and the USA led in several cases to the reduction of breeding areas for mosquitoes, and the general increase in animal breeding and the transition to stabling of farm animals led to the increased deflection of mosquitoes to domestic animals. This factor was of particular epidemiological significance in the distribution area of *A. maculipennis*, some subspecies of which are pronounced zoophiles. Neither the reduction in breeding areas for mosquitoes as a result of land reclamation and nor zooprophylaxis were targeted anti-malaria measures, but these types of human economic activity had a decisive influence on the spread of malaria in several countries. Malaria infection among the populations of these countries gradually reduced. The number of malarial breeding grounds decreased, and areas of malaria-free anophelism developed [6, 126, 161, 191]. The spontaneous eradication of malaria took place in Great Britain, Belgium, Norway, France, Germany, Switzerland,

Finland, Poland, Czechoslovakia, Austria, the Baltic States, Belarus and the northern USA. The eradication was sustainable, and even when a large number of sources of infection were carried from the military front during the First World War, the consequences were limited: many small breeding grounds appeared, but the number of local people who contracted malaria in those areas was limited and the breeding grounds themselves did not survive for very long.

Spontaneous eradication spread through European countries and the northern USA and also took place in Japan, Australia and Argentina. All of the countries in which malaria was spontaneously eradicated were located on the peripheries of the nosoarea. On the whole, these were countries with temperate climates, where the conditions for malaria transmission had never been particularly favourable. It should be mentioned that in Tsarist Russia, with its underdeveloped economy, the process of the spontaneous disappearance of malaria was weak. The necessary conditions only began to develop after the Great October Revolution, during which time widespread targeted anti-malaria measures were taken across the USSR, and even in the northern regions the eradication of malaria was principally a result of those activities.

4.2. Dynamics of the nosoarea during the organised fight against and eradication of malaria

Although the reduction of the nosoarea during the spontaneous regression took place mainly as a result of untargeted activities (the development of land cultivation and livestock breeding), the role of quinine treatment, which was widely used at the end of the nineteenth and beginning of the twentieth centuries, should not be underestimated. Naturally the development of methods for combating malaria and the more widespread use of targeted anti-malaria activities increased the effects on the nosoarea. In this regard, the period in which active measures were taken to combat malaria, starting at the beginning of this century, can be divided into two separate periods.

The first period, or the period of the organised move to combat malaria, continued approximately until the end of the Second World War, when DDT began to be used. It was during this period that the main changes to the nosoarea occurred. The measures that were taken resulted in weakening the intensity of malaria transmission in breeding grounds, as a consequence of which illness and death from the disease reduced. The number of parts of the nosoarea with high epidemic level indicators decreased and its mosaicism increased as a result of irregular eradication. During this period, the nosoarea only reduced in regions with epidemic and hypoepidemic malaria, where the conditions were unfavourable for the survival of the disease.

In breeding grounds with high endemic levels, during the time before DDT was discovered, it was possible to temporarily reduce illness, but it increased again when measures were weakened (see the classic example in the Khamidie Kabardino-Balkar Autonomous Soviet Socialist Republic [83]).

The Soviet Union can serve as an example of the maximum changes in the nosoarea that were achieved during the period in which organized measures were employed to combat malaria (see diagram 17). Far fewer changes were seen in the vast majority of other countries.

During the eradication period, which began when DDT began to be widely used (1946 – 1949) the nosoarea began to reduce in size. Major results were achieved during this period in the Soviet Union. Thanks to considerable earlier success during the measures to combat malaria and the broad introduction, along with DDT, of other new effective treatments (bigumal and chioicide), the reduction of the nosoarea in the USSR took place at an unprecedented speed (see table 6).

During this period malaria was successfully eradicated in several other territories in the tropics (Venezuela, Mexico, India and the Democratic Republic of Vietnam).

Table 6.

Number of areas cured of malaria before 1956 [89]

Soviet Union Republic	Total number of regions	Number of regions cured of malaria	
		Number	%
RCFCR	2766	1966	71.1
Ukraine	868	736	84.8
Belarus	192	157	81.8
Uzbekistan	179	82	45.8
Kazakhstan	218	83	38.1
Kirgyzia	67	36	53.7
Tajikistan	55	9	16.4
Turkmenistan	50	35	70.0
Georgia	83	9	10.8
Azerbaijan	71	5	7.0
Armenia	34	21	61.8
Moldova	63	35	55.5

As a whole, the changes that took place in the worldwide distribution of malaria during the organized measures to combat the disease and during the eradication period can be characterized by the following two indicators:

Firstly, the structure of the nosoarea changed considerably. At the beginning of the twentieth century almost all of the malaria breeding grounds were “untouched”, whereas now, such breeding grounds only remain in certain parts of Africa, on the island of New Guinea and in some countries in South-East Asia (southern Vietnam, Laos, Cambodia and Indonesia). In the vast majority of the remaining part of the nosoarea, the epidemic process was suppressed, as a result of which illness and death from malaria reduced significantly. There are no comparative statistics on illness and death caused by malaria in different countries of the world, and the dynamics of illness caused by the disease can only be characterized using evaluative indicators. An evaluation of the number of malaria-sufferers in the world and in India (a country with a relatively high number of sufferers) is shown in table 7.

Secondly, the worldwide malaria distribution area reduced in size. The nosoarea currently amounts to approximately 55% of the territory it covered at its peak.

Table 7

Dynamics of illness caused by malaria over the past 30 years (evaluative data)

Date	Number of malaria sufferers (in millions)	
	In the world	In India
1930s	700	100
1952	350	75
1955	250	37
1959	140	1
1964	115	0.2
1965	107	0.1

5. STRUCTURE OF THE CONTEMPORARY MALARIA DISTRIBUTION AREA

It has already been pointed out that the planning and implementation of measures for the prevention of malaria among Soviet citizens working in hot countries, as well as activities to prevent malaria from being brought into the USSR from the tropics, must be based on an in-depth knowledge of the structure of the contemporary malaria distribution area and the ability to update that knowledge in accordance with future changes [60].

It is considered [55] that these needs can only be satisfied by a map (or series of maps), characterizing the structure of the contemporary malaria distribution area as fully as necessary, according to risk of infection. Such an in-depth map would facilitate an evaluation of the contemporary malariological situation in any area of the world from the most important point of view: specific epidemiological danger.

5.1. Methods of evaluating risk of malaria infection

The concept of risk of infection has existed in malariological literature for a considerable period of time. R. Ross [211] introduced the term “Inoculation rate”, which he interprets as a range of chances of a non-immune person (a newborn baby or a person newly arrived in an area) of becoming infected with malaria in a given place in a given period of time (week, month or year). S. D. Moshkovsky [67] interprets his own term “loemopotential” in a similar way (“the probability of infection for a new person in a given breeding ground in a given period of time”). In accordance with the aim of our research, the concept of the risk of malaria infection is understood to be the chances of non-immune persons becoming infected with malaria in a given breeding ground in a given period of time. Thus both R. Ross and S. D. Moshkovsky in particular, paid considerable attention to the methods of quantitatively defining the ranges they had proposed (according to the inoculation rate and loemopotential). For our aims it is not necessary to define the range of infection risk accurately. It is possible to fully complete a three-stage infection risk assessment based on the four main differences identified in the structure of the primary nosoarea. We have made the following assessment:

Primary endemic level	Risk of infection
Holoendemic/ Hyperendemic	High (++++)
Mesoendemic	Medium (+++)
Hypoendemic	Low (++)

As we have already mentioned, however, a large part of the contemporary nosoarea is characterized by a regression, which has taken place principally as a result of active anti-malaria measures. The question therefore arises: how can risk of malaria infection be assessed in the different parts of the contemporary (remaining) nosoarea?

It is clear that under the influence of mass prevention measures, the primary endemic level, and therefore the respective infection risk level, decreases. Infection risk reduction should be greater, the more developed the eradication programme is in a given part of the nosoarea. On the other hand, the risk of infection towards the end of a given phase of an eradication programme should generally speaking be smaller, the lower the level of infection of the population was in the given region before the campaign began.

Naturally, at the end of an eradication campaign, there should be almost no risk of infection, irrespective of how high the primary endemic level was in the region. As global experience has demonstrated, the intensity of malaria transmission quite naturally reduces from one phase of an eradication programme to the next. As a result of this, risk of infection depending on the initial endemic level and on the stage of implementation of the malaria eradication programme in a given part of the nosoarea can be quite accurately defined on the following scale (see table 8).

Table 8

Scale for evaluating infection risk in parts of the remaining malaria distribution area

Initial endemic level	Stage of implementation of eradication programme				
	preparatory	attack		consolidation	follow-up
		Second year	Third and fourth years		
Holo- and					
Hyper-	++++	+++	++	+	-
Meso-	+++	++	+	-	-
Hypo-	++	+	-	-	-

++++ High

++ Low

- Almost non-existent

+++ Medium

+ Very low

5.2. Compiling the map of the structure of the contemporary malaria distribution area according to risk of infection

The proposed principle for evaluating infection risk in the various areas of the remaining nosoarea is complex in nature, and relies on two vital preconditions: the initial endemic level and the stage of implementation of the measures taken to suppress the epidemiological process. It is clear that the map of the structure of the nosoarea according to risk of infection must be a synthesis, combining the indicators of two maps: the first being of the structure of the malaria distribution area according to initial endemic levels, and the second of its structure as conditioned by malaria eradication programmes. Naturally the accuracy of such a map depends greatly on the accuracy of the two analytical maps used to compile it. These two maps are not equivalent. The above-mentioned map of the structure of the nosoarea according to initial endemic levels is a basic map. In theory, its content should not be changed, with the exception that individual parts of the nosoarea could be reclassified according to additional information, which was unknown at the time the map was drawn up. It should reflect the dynamics during the implementation of malaria eradication programmes, or the successful results of campaigns to combat malaria in the countries where they were implemented. This map therefore has to be updated regularly.

5.2.1. Evaluation of the status of malaria eradication programmes across the world

The need to evaluate the status of malaria eradication programmes in different countries arose immediately when the campaign to combat malaria began. It was clear that the evaluation must be simple, in order that anyone involved in the implementation of eradication programmes could understand the indicators that were used. At the same time, the main evaluation could not include traditional indicators of illness rates, since not all countries had registers of malaria patients and the extent to which existing registers had been completed differed greatly from country to country, which meant that patient figures could not be compared.

The ultimate aim of the worldwide eradication of malaria was to eliminate the disease among the population living on the territory of the initial nosoarea. The number of measures required to meet that aim depended on two indicators: the number of people living in the territory of the nosoarea, and the size of the nosoarea. These two indicators were used by WHO as an assessment of the initial malariological situation in a country both before and during eradication programmes.

The programme was divided into four stages (preparatory, attack, consolidation and follow-up¹) and its dynamics were characterized mainly by the population in an original malaria territory that was in transition between the earlier and later stages of an eradication programme.

It can be considered that on the whole, this method of general analysis was effective. It was simple, clear, understandable to people without qualifications in malariology and could be used for comparative study. Of course, one must not forget that it did not reflect the initial intensity of the spread of malaria among a given population living in a specific part of the nosoarea and as a result the analysis was

noticeably restricted.

Alongside the qualitative assessment indicators, WHO has, for a long time, been using cartographical methods to define the spatial characteristics of the dynamics in the reduction of the malaria distribution area. Examples of these maps from 1962 - 1964 have been published in the WHO Chronicles [46, 47, 48] and one has been published in the abstract journal "Medical Geography" (1962, 36.5.98).

It should be noted that although they are based on existing national maps, these maps are not always sufficiently accurate. We have therefore conducted our analysis of the implementation of malaria eradication programmes using not only general data from WHO, but also factual data on each country (if they were available). The information below on the status of malaria eradication programmes across the world is based on WHO data, which we have made more specific for several countries.

5.2.2. European countries

The eradication of malaria is almost complete in European countries. In 1965, 615 cases of malaria were registered in Europe, including across the whole territory of the USSR (681 million people), of which only 104 were new local cases. It is very important that achievements in respect of malaria across Europe have been maintained for several years, despite the constantly increasing influx of sources of infection from other, non-European countries.

5.2.3. Asian countries

The majority of Asian countries were under colonial rule for a long time. Malaria spread almost uncontrollably in these countries until the end of the Second World War. With wars of independence being fought in many countries, and the appearance of DDT, a powerful and relatively cheap method of destroying mosquitoes, it became possible to combat and eradicate malaria. Asian countries began trying to eradicate malaria at the beginning of the 1950s. The largest malaria eradication programmes began in India in 1953 and in the Democratic Republic of Vietnam in 1958.

Lack of economic development, poor health services and political instability are holding back the implementation of malaria eradication programmes in many Asian countries. In several countries, programmes have even been stopped (Southern Vietnam, Laos and Cambodia). The current status of malaria eradication programmes in Asian countries is shown in table 9. The table shows that in several countries where the spread of malaria was limited (Israel, Lebanon) and also on several islands (Cyprus, Taiwan), the disease has almost been completely eradicated. Malaria has also been eradicated from significant parts of the territory of many other countries. Generally speaking, approximately 60 per cent of the population of the original malarial territories live in areas in Asia (excluding The People's Republic of China and the People's Democratic Republic of Korea) from which malaria has been eradicated, and which are in either the follow-up or consolidation stages of a programme. It is expected that this figure will reach 80 per cent over the next two to three years.

In spite of that, the conditions for the total eradication of malaria in Asia are not particularly favourable. A large number of countries and territories (see table 9) are still not involved in malaria eradication programmes, and many of the programmes being implemented are unable to surmount local difficulties. In Afghanistan and several other countries, the issue of curing malaria among nomadic tribes has not been resolved, and in Thailand and Burma problems have been encountered in malaria eradication among the national minorities living in mountainous and wooded areas. The uninterrupted spread of malaria across the continent is facilitated by the ancient Muslim custom of visiting sacred places, particularly Mecca. Above all, new difficulties are arising in the implementation of eradication measures. In several countries, local malaria vectors have developed a resistance to insecticides. In some countries (Iraq, Iran) this has allowed malaria outbreaks to occur in protected territories [173]. Strains of *P. falciparum* that are resistant to malaria treatments, including chloroquine, which is widely used, have also been detected (Southern Vietnam, Thailand, Cambodia, Malaya) [140, 205, 206].

Table 9

Presence and stage of implementation of malaria eradication programmes in Asia (according to WHO statistics dated 31 December 1965)

Programme status	Countries and territories	Population (in thousands)		Population distribution in original malarial territories, currently at different stages in eradication programmes (%)			Proposed date for ending eradication programmes
		Total			Attack stage	Consolidation and follow up stage*	
Almost complete malaria eradication Programme currently being implemented	Israel, Cyprus, Lebanon, Ryukyu Island (Japan), Singapore, Syria, Taiwan	27 188	21 905	-	-	100	
	Aden (Brit.)***	1 122	1 122	-	-	21.6	unknown
	Afghanistan	15 873	6 609	-	83.2	16.8	1970
	Burma	25 070	20 448	-	52.0	48.0	1973
	D.R. Vietnam**	19 355	7 500	-	56.6	43.4	unknown
	India (+ Bhutan)	488 023	472 504	-	20.0	80.0	1969
	Indonesia***	106 432	106 432	1.3	14.3	52.7	unknown
	Jordan	1 991	1 091	-	27.5	72.5	1966
	Iraq	7 173	4 609	-	100.0	-	1968
	Iran	13 690	16 746	28.1	24.1	47.8	1969
	Nepal	10 093	5 305	11.1	88.9	-	1971
	Pakistan***	103 965	92 890	20.8	52.7	24.1	1976
	Sabah (Brit.)	549	465	-	59.4	40.6	unknown
	Sarawak (Brit.)	851	719	-	27.0	73.0	1968
	Hongkong (Brit.)***	3 956	3 956	-	-	80.4	unknown
	Thailand	31 050	31 050	14.8	72.4	12.8	1973
	Turkey	32 485	32 485	-	28.4	71.6	1968
	Philippines***	32 787	8 868	-	54.9	42.6	1969
	Ceylon	11 380	7 412	-	2.0	98.0	unknown
		Total	915 845	820 211	3.7	27.9	61.1
No eradication programme	Aomyn (Port.), Brunei (Brit.), Southern Vietnam, Oman, Yemen, Cambodia, Qatar (Brit.), PDR Korea, China, South Korea, Laos, Madagascar, Maldives, Oman and Masqat (Brit.), Bahrain, Saudi Arabia, Timor (Port.)	851 228 (75 359)****	40 690 ****				
	Total	1 794 261**** (1 018 392)****	882 806 ****				

5.2.4. African countries

“In the African tropics, malaria constitutes a constant and insidious threat, killing a large number of children, sapping the energy and strength of the population and to a large degree contributing to a vicious circle of disease, poverty and ignorance. However, as a result of a lack of acute epidemic outbreaks and relative immunity to infection among the adult population, this constant loss of life and manpower is not immediately obvious. This could explain, but not change, the fact that in some African countries only limited measures have been taken to cure and prevent the disease, with preference being given to programmes to combat endemic diseases that affect all age groups equally, such as trypanosomiasis, tuberculosis, smallpox, cerebro spinal meningitis, leprosy, etc”. [11]. This was how a leading WHO malariologist, L. J. Bruce-Chwatt, explained the lack of development of malaria eradication programmes in Africa. We believe that the reasons were much more complex.

Until the end of the Second World War, when the majority of African countries were under colonial rule, the fight against malaria was limited, and was conducted almost exclusively for the protection of Europeans. The greatest successes during that period were achieved in countries that had a significantly large population of European origin (Algeria, Tunisia, Morocco, the United Arab Emirates, the Republic of South Africa). Reasons for implementing large-scale anti-malaria measures in the interests of the local population arose later, after the African wars of independence.

In some small countries and on several islands malaria eradication programmes began to be implemented (Swaziland, the Green Cape Islands, Mauritius, Zanzibar), and in others pilot projects were set up on the recommendation of WHO, which aimed to ascertain the possibility of eradicating African malaria breeding grounds using up-to-date resources and methods. The long-term experience of implementing these projects showed without any doubt that eradicating malaria was much more complex in tropical African conditions than in any other continent. In many holoendemic malaria breeding grounds it has not been possible, using any known methods, to interrupt the transmission of the infection [11, 165, 193]. It is possible that this is a manifestation of the aspects particular to Africa that caused it to be the first malaria distribution area. On the other hand, we cannot ignore the fact that WHO clearly did not wish to delve deeply into the particular problems of eradicating malaria in Africa, or to play an active role in financing eradication and anti-malaria activities. Thus the harsh legacy of the colonial past (economic weakness, a lack of trained malariologists, insufficient medical staff) and the evasiveness of WHO in providing assistance were the true fundamental reasons behind Africa's failure to eradicate malaria.

The current situation of malaria in Africa is shown in the figures in table 10. The table shows that only two per cent of Africa's population lives in regions in which malaria has been eradicated.

A considerable danger is also caused by the disorganized nature of activities that are currently being carried out in Africa, which are leading to a widespread resistance to insecticides in *Anopheles*, and to medicines in malaria parasites.

A resistance to dieldrin in *A. gambiae* has been registered in many West African countries, and has reached such a level that it “represents a serious threat to the continent, since resistance in *A. gambiae* could easily spread anywhere with the development of transport technologies, in particular aviation” [40]. Evidence of *A. gambiae* developing a resistance to diadrine has also been found in East African countries and Madagascar. Thus further delays in implementing malaria eradication programmes in Africa could worsen the already pessimistic prospects for eliminating the disease among the African peoples.

Table 10

Presence and stage of implementation of malaria eradication programmes in Africa (according to WHO statistics dated 31 December 1965)

Programme status	Countries and territories	Population (in thousands)		Population distribution in original malarial territories, currently at different stages in eradication programmes (%)		
		Total	Including in original malarial territories		Attack stage	Consolidation and follow up stage*
Almost complete malaria eradication	Libya, Swaziland (Brit.) , Somalia (France)	2 205	290	—	—	100.0
Programme currently being implemented	Zanzibar	338	338	—	100.0	—
	Mauritius (Brit.)**	769	769	—	—	97.5
	Cape Verde (Port.)**	232	232	—	45.3	10.8
	Southern Rhodesia (Brit)**	4 347	4 238	—	—	3.5
	Republic of South Africa	18 108	4 901	—	1.0	99.0
	Total	23 794	10 478	—	4.7	55.2
No eradication programme	Other African countries	287 390	256 754	0	0	0
	Total	313 209	267 522			2.0

5.2.5. American countries

In many American countries the fight against malaria became large-scale in the 1920s. As a result of this, in several countries, illness and death from the disease not only reduced, but also ceased completely in certain parts of the nosoarea (Argentina, Chile, USA). In 1951, a malaria eradication programme began in Venezuela. In 1954, the 14th Pan American Sanitary Conference adopted a recommendation on reforming all national programmes to combat and eradicate malaria. The current status of malaria eradication programmes in America is shown in table 11. The American part of the nosoarea has decreased in size owing to the eradication of malaria in the USA, Chile, the majority of Mexico, Venezuela, Guyana and some islands of the West Indies. In total, over 60 per cent of the population of original malarial areas of the continent currently live in regions from which malaria has been eradicated. An extremely large part of the remaining distribution area is confined to Brazil, and there are small parts in Guatemala, Colombia, Nicaragua, Paraguay and Haiti. The malaria eradication process in these countries is particularly difficult. Poor economic development and political instability are impeding the implementation of malaria eradication programmes, which require coordination at the national level and stable funding. In Amazon basin countries (Brazil, Venezuela, Peru, Colombia, Bolivia), malaria eradication has also proven difficult, owing to the particularities of the population and way of life [58]. In all of the Central American countries (with the exception of Costa Rica), a resistance to DDT and dieldrin has been discovered in the main malaria vector, *A. albimanus*. This vector has also been found to be resistant to dieldrin in Colombia and Ecuador [171, 173]. In Colombia, Brazil and Guyana, strains of *P. falciparum* have been discovered, which are resistant to malaria medicines [121, 195, 210]. In Haiti, Colombia and some regions of the central plateau in Brazil, the interruption of malaria transmission has been made more difficult by vectors preying on man outdoors.

Thus the prospects for malaria eradication in America, despite the progress that has been made, cannot be considered as bright as the American regional office of WHO claims.

Table 11

Stage of implementation of malaria eradication programmes in America (according to WHO statistics dated 31 December 1965)

Programme status	Countries and territories	Population (in thousands)		Population distribution in original malarial territories, currently at different stages in eradication programmes (%)			Proposed date for ending eradication programmes	
		Total			Attack stage	Consolidation and follow up stage*		
Almost complete malaria eradication Programme currently being implemented	British Honduras, Virgin Islands (Brit., USA), Barbados (Brit.), Guadeloupe (Fr.), Puerto Rico (USA), Saint Lucia (Brit.), USA, Trinidad and Tobago, Chile, Jamaica	212 283	53 731	-	-	100.0		
	Argentina	22 577	2 877	7.2	28.1	64.7	1969	
	Bolivia	4 373	1 387	-	15.4	84.6	1968	
	Brazil	82 512	31 259	32.4	33.5	34.1	1971	
	Venezuela	8 862	6 617	-	3.8	96.2	1967	
	Haiti	4 709	3 624	-	100.0	-	1968	
	Guatemala	4 513	2 024	-	54.4	45.6	1967	
	Guyana	655	655	-	1.5	98.5	1967	
	Dutch Guyana (Suiname)	345	205	-	32.7	67.3	1968 1969	
	Guyana (France)	38	38	-	7.9	92.1		
	Honduras	2 122	1 855	-	18.0	82.0	1967	
	Dominican Republic	3 641	2 985	-	88.2	11.8	1969	
	Colombia**	17 872	9 293	-	21.7	76.1	1968	
	Costa Rica	1 486	453	-	40.4	59.6	1967	
	Cuba	7 535	2 296	-	100.0	-	1969	
	Mexico	41 566	21 272	-	36.6	63.4	1968	
	Nicaragua	1 783	1 713	-	57.4	42.6	1969	
	Panama	1 269	1 219	-	100.0	-	1968	
	Panama Canal (USA)	50	50	-	2.0	98.0	1968	
	Paraguay	2 144	1 781	100.0	-	-	1970	
	Peru	11 735	3 879	-	38.6	61.4	1968	
	El Salvador	2 961	2 487	28.4	71.6	-	1968	
	Ecuador	5 106	2 814	-	52.2	47.8	1968	
		Total	227 854	100 779	12.7	38.4	48.6	
		Grand total	440 137	154 510				

5.2.6. CHARACTERISTICS AND ANALYSIS OF THE MAP OF THE STRUCTURE OF THE CONTEMPORARY MALARIA DISTRIBUTION AREA ACCORDING TO RISK OF INFECTION

The map (diagram 18) shows the borders of the original nosoarea (these are the same as the borders on the map of the structure of the malaria distribution area according to original epidemic level) and identifies four types of region, which differ according to risk of infection. The structure of the whole nosoarea is presented on a political map. The structure of the part of the nosoarea in each country is shown in as great a detail as was permitted by the materials available and the scale of the map. The map as a whole reflects the situation at the end of 1965. Analysis of the map brings to light several important

particularities of the contemporary distribution area, which are of both purely malariological and general medical and sociological interest.

All degrees of risk of infection are represented in the remaining nosoarea. The risk of infection has remained high across a large area of tropical Africa, in Indo-China, Southern China, and on the islands of Kalimantan and New Guinea. In these countries one has a higher probability than anywhere else of being infected with *P. falciparum*. The parts of the remaining nosoarea with a medium risk of infection are confined to tropical Africa, Pakistan, Southern China, and in particular South America. A large number of small malaria breeding grounds have remained in the Amazon basin, the elimination of which will evidently not be achieved in the immediate future. It is important to note that malaria has been eradicated in two large parts of the nosoarea, located in the tropics: part of the territory of Venezuela and India. India's success is of particular significance from the point of view of malaria being brought into the USSR, since it is a country with which the USSR has strong economic and cultural links. The Democratic Republic of Vietnam has also been particularly successful in eradicating malaria, and risk of infection is now minimal across a large proportion of its territory.

The map clearly shows the regressive nature of the contemporary malaria distribution area. In a large proportion of the original nosoarea, risk of infection has decreased to almost zero. All of this territory can now be regarded as a potential nosoarea. The potential nosoarea covers the territories from which malaria has been eradicated, including the Soviet Union, European countries, the USA, Venezuela, Chile, Argentina, Bolivia, India, Australia and several other countries. Approximately 45 per cent of the territory of the original nosoarea, when it was at its largest, has now been cured of malaria.

In conclusion, we believe that it is imperative to note that the method of evaluating territory according to its potential danger of epizootic development (e.g. the development of plague) proposed by N. P. Mironov [65], is theoretically similar to our method. We consider this to be evidence that the problem of carrying out evaluations of "nosogenic" territories according to the intensity of the actual or potential epidemiological (or epizootic) process is beginning to be solved.

6. CONCLUSION

Recently, the geographical aspects of malaria have attracted the attention of a wide range of specialists, frequently not working in medicine.

Along with epidemiologists and medical geographers, this group includes socio-geographers, anthropologists, ethnographers, haematologists, historians, economists and demographers. This interest in malaria has not come about by chance. Many specialists are interested in carrying out first-hand studies of the infection, particularly in parts of the world where it constitutes a serious social problem. Some of them actively assist medical staff with malaria eradication projects, working on related issues, such as population migration, reactions of different ethnic groups to anti-malaria measures being taken, the possible role of monkeys as a natural infection store, etc. A new subject area for study is the economic and demographic consequences of successful malaria eradication.

Another group of specialists are interested in malaria as a potential indicator in anthropological, ethnographic and historical investigations.

Irrespective of why non-medical specialists are interested in malaria, medical geography in general, and in particular malariology, are having a positive impact on this cooperation. It is to a significant extent because of this interest shown by specialists from related fields that it has become possible to carry out the present study on the structure and dynamics of the worldwide malaria distribution area.

The materials that we now have at our disposal allow us to suppose that the point of origin of human malaria was Tropical Africa. It was there, at the dawn of mankind, that the original malaria distribution area arose, from where it later spread almost across the whole world. The appearance of the original nosoarea in Africa was made possible by factors such as the wide variety of monkeys, from which man inherited and acquired malaria parasites, the presence of an effective vector, *Anopheles gambiae*, and the very favourable climatic conditions, which facilitated the intensive transmission of the infection, even when population density was low.

The first filial nosoareas evidently arose in Mesopotamia, India, China and the Mediterranean. The broad spread of malaria took place in the Eneolithic period, when population density increased and migration processes were strengthened. The Ancestors of the American Indians did not bring malaria with them, and it was brought to the New World by seafarers, who travelled to America from Polynesia

and Micronesia. It is possible that *Plasmodium falciparum* was brought to America from Africa some time later, during the slave trade. In Western Europe, malaria only spread widely during the first Century A.D. On many islands (Mauritius, Reunion) malaria appeared with the influx of Europeans, and on some (Fiji, New Caledonia, New Zealand, etc.) malaria was not, and still has not, been found. The nosoarea reached its maximum size during the transition to capitalism, at the end of the 19th and beginning of the 20th Centuries.

It is most likely that all four types of human malaria agent spread from Africa. *Plasmodium vivax* covered the largest distribution area, and during its evolution developed several subspecies (groups of strains). This species spread to the outskirts of the whole nosoarea, with the exception of a few regions in Western Africa.

The very particular, small and disconnected distribution area of *P. ovale* still remains unexplained.

The collective distribution area of all forms of malaria reached north almost as far as the border of the *Anopheles* mosquito distribution area (62 - 66° North), and south to 32° South; the highest malarial breeding grounds were registered at 3500 metres above sea-level. By the end of the maximum nosoarea period, almost 700 million people had malaria (out of 1700 million people) and almost 7 million died of the disease each year.

There were significant differences within the initial malaria distribution area, owing to the differences in natural and social conditions in its different areas. There have been two attempts to define the differences in the structure of the nosoarea using maps. These maps are Gill's map of climatic malaria zones, and Macdonald's map of epidemiological malaria regions. In both cases, the zoning of the nosoarea was carried out on a regional basis, as a result of which the differences defined differ considerably from the significant epidemiological variations. In this work, a typological malarial map of the initial nosoarea has been developed at the E. I. Martsinovskiy Institute of Medical Parasitology and Tropical Medicine. The map shows five types of territory, which differ in their initial endemic levels. Malaria breeding grounds with the highest possible level of infection (holoendemic malaria) developed in two parts of the distribution area. In Tropical Africa these were formed by *Plasmodium falciparum* and *Anopheles gambiae*, and in New Guinea by *P. vivax* (Chesson strains) and *P. falciparum*, and *Anopheles punctulatus*.

The malaria distribution area is unique in its high level of mobility. Even during its optimum period, it began to reduce as a result of the spontaneous disappearance of malaria in the peripheral regions (North America and Western Europe), where the conditions for the spread of the infection were least favourable. The main reason for the regression of the nosoarea was unintentional human activity (agricultural land development, and intensive livestock breeding), as a result of which epidemic malaria regions transformed into regions with malaria-free anophelism.

Although the targeted fight against malaria only began at the beginning of the 21st Century, it has drastically changed the nosoarea of the disease. Particularly significant changes have taken place over the past ten years, during the implementation of malaria eradication campaigns all over the world. European countries eradicated malaria first. In Europe, by the end of 1965, only a limited number of malaria breeding grounds with local cases of the disease remained (in Albania and Greece). In Asia and America, approximately half of the population of original malarial territories now live in malaria-free regions. Only the African part of the nosoarea has remained almost unchanged in size and structure. The current nosoarea covers only 55% of its past maximum territory and the only unaffected breeding grounds that have remained are in Africa, New Guinea and a few countries in South-East Asia. The number of malaria patients is steadily decreasing: from 140 million peoples in 1959, to 115 million in 1964 and 107 million in 1965.

From typological malarial maps and WHO maps, which show the status of malaria eradication campaigns across the world, a summarized map has been compiled, which classifies territories by risk of infection. This can serve as a basis for the scientific planning of malaria prevention activities among Soviet citizens working abroad, and for preventing malaria from being brought into the USSR.

Many important issues related to the patterns of the global spread of malaria have not been fully investigated. These include:

1. Factors determining the particularities of the distribution areas of *Plasmodium ovale* and the Chesson strains of *P. vivax*;
2. Reasons for the absence of *P. vivax* from the West African part of the nosoarea;
3. Reasons why in tropical areas malaria parasites have become resistant to medicines, and *Anopheles* mosquitoes have become resistant to insecticides.

The study of the structure and dynamics of the worldwide nosoareas of infectious diseases is opening up a range of opportunities for understanding the patterns of their geographical distribution and is strengthening the basis for the scientific planning of large-scale eradication and prevention measures.

SUMMARY

The worldwide malaria distribution area has been studied in detail. The origin of malaria as a human disease and the formation of its initial and filial distribution areas are discussed. New data on the links between malaria and abnormal haemoglobins have been studied, in order to understand the genesis of the malaria distribution area. The dynamics of the initial nosoarea with and without the use of organized anti-malaria measures have been studied. An analysis has been carried out into the main factors defining the contemporary nosoarea. The precise spread of species of *Anopheles* that are proven vectors has been compared with a list of all species across the world. The particularities of the species distribution areas of the malaria parasite have been considered. A map has been compiled, showing the spread of the main groups of *P. vivax* strains, the distribution area of *P. ovale* has been marked out for the first time, and an analysis has been carried out into the factors which could explain its unique nature. The task of studying the structure of a nosoarea is defined using the example of malaria. This includes the division of the nosoarea into regions of stable and unstable epidemics; the subdivision of the territory of endemic malaria into parts with similar levels of infection among the population; the subdivision of the general malaria distribution area into species distribution areas and the isolation of regions occupied by subspecies and groups of parasite strains; and the isolation of regions with similar seasonal malaria occurrences. The residual nosoarea should be subdivided into parts that have a similar risk of infection for non-immune persons (in particular new arrivals) and the probability of malaria reoccurring in territories from which it had previously disappeared in the event of sources of the infection being imported. The first maps have been introduced that show the worldwide malaria distribution area according to initial endemic level and risk of infection (valid for the end of 1965). The discussion of the formation and structure of the worldwide malaria distribution area facilitates a deeper understanding of the very specific epidemiology of the disease and allows for the planning of activities for malaria prevention in formerly infected territories.

(Footnotes)

* Exophiles are mosquitoes, which digest blood in their natural surroundings (outside)

** Zoophiles are mosquitoes, which prefer to feed off animals, even if there is the possibility of feeding off humans.

*** If we take it that man first appeared in South-East Asia.

* According to the calculations of S. D. Moshkovsky [66, 68].

* ++ high intensity

+ low intensity

- none

* There are isolated cases of Aedes, Culex and Mansonia mosquitoes being infected with human and monkey malaria parasites in laboratory conditions [see 234, 235]. The possible epidemiological significance of this is not yet clear.

* The border between the group of Pacific Ocean islands that are free from Anopheles, and the neighbouring malaria-infected territories is referred to by ethnographers as "the Baxton Line" [201].

** In Tajikistan these exist along with other low mountainous malariogenic landscapes

* During epidemic outbreaks

* The respective map of Asian countries has been published [55], and the map of African countries has been submitted for publication in the atlas of Africa [61].

¹ The aim of the attack stage is to interrupt the transmission of malaria, usually with the help of the intensive use of DDT. During the consolidation stage the remaining malaria breeding grounds should be eradicated, and the follow-up stage consists of preventing malaria from being reintroduced into territories in which it has been eradicated.

* In these zones malaria transmission has stopped and the risk of infection is either very low or does not exist.

** According to preliminary data provided by the Ministry of Health of the Democratic Republic of Vietnam in 1965.

*** Anti-malaria measures are not being taken across the whole territory.

**** Excluding data for the People's Republic of China and the People's Democratic Republic of Korea.

* In these zones malaria transmission has stopped and the risk of infection is either very low or does not exist.

** Anti-malaria measures are not being taken across the whole territory.

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