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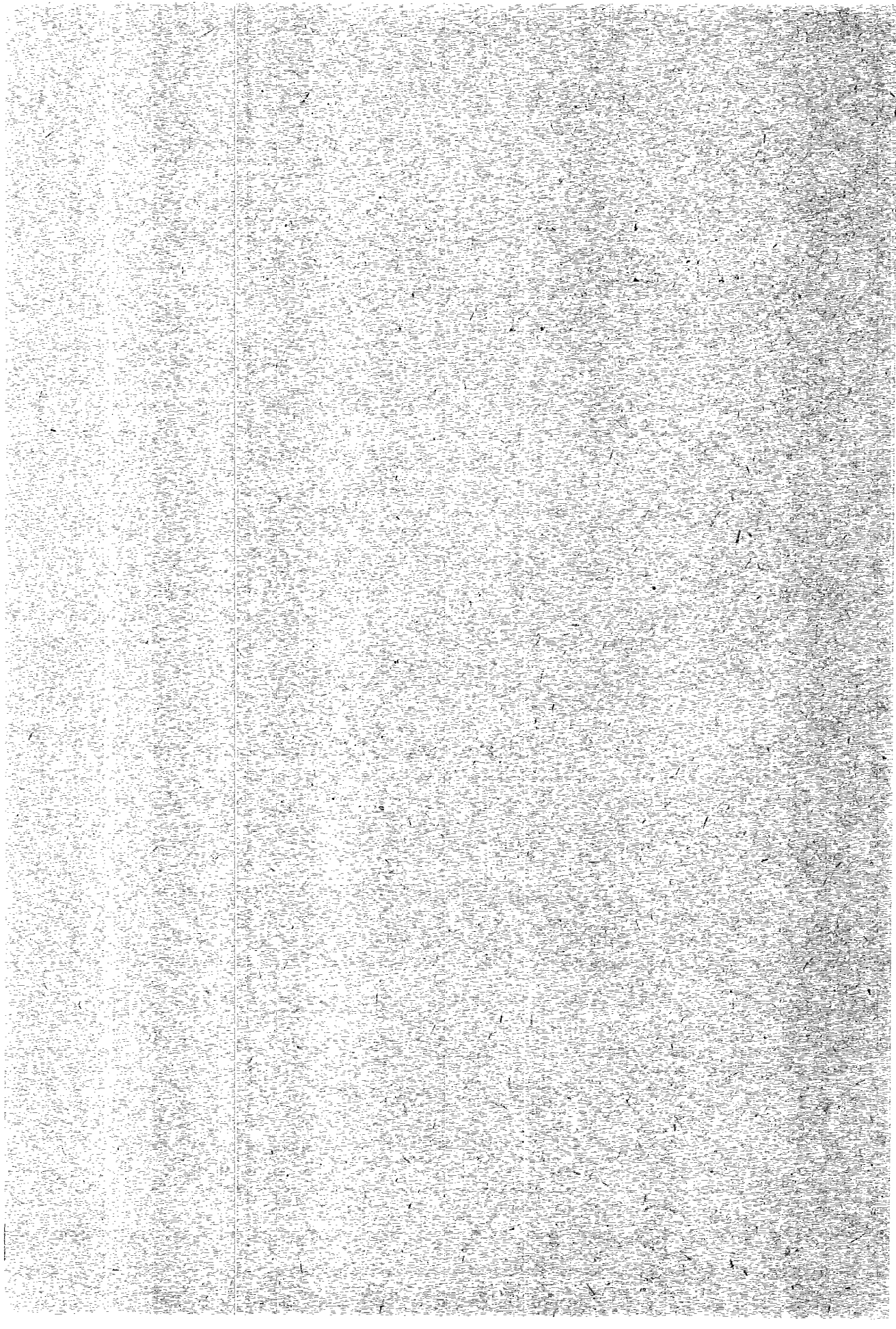
RECENT FINDINGS BEARING ON
THE EPIDEMIOLOGY OF MALARIA
IN EUROPE

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The return of the soldiers to their homes after the World War brought about one very extraordinary situation. Chronic cases of malaria were distributed to every part of Europe, and towns, villages and farms were stocked with reservoirs of gametocytes. This resulted in epidemics of malaria covering a period of years in certain regions, but the most striking fact is that over wide areas with large rural populations nothing happened at all in spite of the presence of anopheline mosquitoes. Hardly any new malarious districts were created, since the increase in incidence occurred usually where the disease had never completely disappeared before the War. Over large parts of Germany, France, England and North Italy there were no secondary cases among the wives and children of the repatriated soldiers.

There were many theories as to why local anophelines were not infected by the imported gametocytes, and it was even suggested that man, or the mosquito, or both had in some manner become resistant to the infection. The phenomenon occurred, however, only where *A. maculipennis* is the malaria carrier, and as this is a domestic anopheline which is found in stables in much larger numbers than in dwellings, the conviction has grown that in recent times domestic animals have in large measure substituted man as its preferred host.

In fact, Hackett and Missiroli (1931), by the use of the precipitation test, were able to show that in non-malarious areas in Italy almost none of the anophelines contained human blood.

The question then arose as to what factors had operated to dissolve the association between *A. maculipennis* and man in some areas and not in others. There was a division of opinion among the malariologists. Some thought that the anophelines must be biologically different in the malarious and non-malarious places. Thus, Roubaud distinguished two strains, one zoophilic by instinct and the other indiscriminate in its food preferences. Others, however, held that the anophelines were more or less homogeneous but that the difference lay in the living conditions of man and his domestic animals. James (1929) thought that malaria had virtually disappeared in England during the course of the last century

because of higher standards of living of the people, especially in the matter of housing. The dwellings are no longer as attractive to anophelines as before and so they tend to resort almost exclusively to stables. Marchoux (1929) suggested that *A. maculipennis* is above all a parasite of animals and when these are rare or unstabled, the anophelines have no other retreat than the house. This school believes that where there is a strong contrast in microclimate, i. e. in cleanliness, light, temperature, humidity and other physical conditions, between houses and stables, the anophelines will confine their attention to the animals and ignore human beings.

There is good evidence on both sides. Roubaud proposed the theory of zoophilism as early as 1920, and later found that the zoophilic *maculipennis* had on the average more maxillary teeth than the undifferentiated one. In Holland, van Thiel (1926), and de Buck, Schoute and Swellengrebel (1927) were able to prove that *maculipennis* was divided into two races by size, color and a number of biological characters, and that one of these races was the sole cause of malaria in Holland. There was a great search then for structural differences by which it might be possible to divide *A. maculipennis* into its races or subspecies.

Falleroni (1926) had previously reported that *maculipennis* females did not all lay the same kind of egg. He described at least four kinds which he had observed in Italy, two of which he considered to be of genotypic importance and to which he gave names: *A. maculipennis* var. *labbranchiae* to the gray eggs dappled with wedgelike spots, and *A. maculipennis* var. *messeae* to the dark eggs of an irregular checkered pattern with two transverse bars. Martini, Missiroli and Hackett (1931) gave importance to this discovery by an analysis of the *maculipennis* populations of Germany and Italy. Eventually five separate subspecies were set up, each characterised by a different egg type. Other differences have since been discovered in certain larval hairs and in the male hypopygium, but the egg remains the basis of our present classification of the subspecies. No other character serves to differentiate so many groups without overlapping.

That these egg types really represent true subspecies is shown in various ways. A given female lays only one type of egg. Areas are known in which each subspecies, according to its egg type, is found in pure strain. A study of such strains, both in laboratory and field, shows that they differ even more in biological characters than in physical. In choice of breeding places, in sexual habits and in winter behaviour, each race shows a certain adaptation to the conditions of its environment, which is characteristic of it wherever it is found. De Buck, van de Torren and Swellengrebel (1933) have shown, by attempts at cross-mating in the laboratory, that viable hybrid generations cannot be obtained. There is, therefore, a barrier to hybridization in nature. This in itself points very strongly to the genotypic importance of the differences between the subspecies.

Since we have each of the races in pure strain in some part of Europe, it is possible to observe their individual relationship to the spread of malaria. One of the earliest observations was made by Grassi in 1921, in a marshy but well cultivated area near Naples. Passing the night in the house of one of the peasants, he was surprised to find that neither he nor anyone else in the house had been bitten by the anophelines, breeding in huge numbers in the canals and filling the stables. He concluded that the local *maculipennis* must be a separate race which did not bite

human beings, but, by instinct, depended upon animals alone for food. We have since determined that the race in this area, Orti di Schito, is a pure strain of *A. maculipennis maculipennis*, which we consider the type and refer to, for convenience, as *typicus*. It is characterised by an egg with two black bands across a bright gray field, and is the easiest to identify of all subspecies. Wherever we have found this race it seems not to be concerned in malaria transmission.

The same may probably be said of *melanoon*, a new variety of which not so much is known. The female lays a uniformly black or dark egg flecked with white, and breeds in fresh water marshes and rice-field areas. It has many affinities with *messeae*. The race *labranchiae* is limited to the littorals of southern Italy, southern Spain and North Africa and is always associated with intense malaria. It is very similar in physiology and behaviour to *A. elutus (sacharovi)*. It is convenient for the purposes of our studies to include *elutus* with the subspecies of *maculipennis* to which it is so closely allied. In fact, if one of the American races of *maculipennis* should prove not to have the group of straw colored hairs in the fringe at the tip of the wing¹, the principal basis of the distinction between *A. elutus* and *A. maculipennis* would fail. These two species are very resistant to heat and dryness and seem rather tolerant of the differences between houses and stables and visit both freely under almost all circumstances.

The subspecies *messeae*, which breeds in the great inland river valleys and fresh water marshes, is bound very strongly to stables and is rarely induced to enter dwellings. However, on occasion, where it is produced in great numbers and there is a relative scarcity of domestic animals, it will attack man and, in a few localities, is reported to be a vector of mild malaria. It probably causes some sporadic cases in North Italy and, according to a recent report of Martini and Zotta (1933), an endemic of a certain intensity in parts of Roumania.

And finally in *atroparvus* we have a subspecies ordinarily feeding on cattle and only exceptionally found in dwellings. The egg lacks the two distinctive symmetrical bars of *messeae* and *typicus*, and has a pattern composed of cuneiform dark spots springing from the sides of the egg and tapering obliquely toward the center; these tongues sometimes fuse across the median line to form irregular thin bands.

In general it is clear that the degree of association with man, naturally the most important factor in the spread of malaria, seems to depend in large measure on racial instincts and adaptations. Hence those who have contended that the *maculipennis* of malarious regions differs biologically from that of non-malarious regions are fully justified. There is no doubt that under identical circumstances, the various races of *A. maculipennis* behave differently. It is equally clear that this is not a complete explanation of the local distribution of *maculipennis* between dwellings and stables. This appears most convincingly in the behaviour of *atroparvus* under varying conditions of environment. This important and widespread race is the cause of whatever malaria there is in Europe north of the Alps, and of that northern Spain and Roumania as well. In other and much wider zones, however, where it is prevalent, it does not cause any malaria at all. In one place it is apparently restricted to stables very closely when in search of blood; in another it is a facultative feeder upon

¹ As seems likely from a personal observation of the author on two newly-hatched specimens in California.

man. Its range includes the whole northern coast of Europe from France through Belgium, Holland and North Germany to Danzig and beyond; we do not know much about its distribution in the Soviet Union. In this extensive area why is it a malaria carrier only in North Holland and the adjacent region of East Friesland in Germany? The difference must lie not in the biology of the mosquito (for that is the same), but in some combination of circumstances connected with its surroundings. And the same influences must be at work, though in less degree, upon the other subspecies.

The relative numbers of *A. maculipennis* which bite man or animals in any zone will therefore depend:

- a) on which subspecies are present in the zone;
- b) on the local conditions of human and animal life.

The presence of one subspecies rather than another is important because, like species, they differ from one another in preferences and sensibilities. One race may have a less restricted range of host than another, or what may turn out to be the same thing, a broader microclimatic adaptation. Thus we find *labranchiae* and *elutus* biting freely under conditions distinctly unfavorable to *messeae* and *typicus*. We may sum this up by saying that stabular attraction acts more powerfully on one race than on another, though we are ignorant of the exact mechanism. It may be working through an instinctive host preference, or through a complex of physical conditions surrounding the source of blood-supply.

The microclimatic factor is important because, with a given subspecies, less frequent contact with man may depend on the degree of contrast between the physical conditions of the human dwelling and those of the animal quarters. This seems most true of very sensitive races, least true of the more tolerant ones. To such forms as *labranchiae* and *elutus* it cannot be said that slight differences have been proved to be of much importance. These races are resistant to widely varying microclimates and find no physiological barriers anywhere within their range which prevent them from seeking human as well as animal blood. Under such circumstances animals cannot be said to deviate *anopheles* so much as to dilute the blood-supply, adding to the host population a quantity of unsusceptible individuals which serve to nullify a considerable percentage of infective bites. To *typicus* and to a less degree, *messeae*, the contrast between bedroom and stable is usually too great to permit of any range of choice. These two subspecies are practically bound by their instinct or microclimatic leanings to the domestic animals. *Atroparvus*, as we have seen, occupies an intermediate position.

Whatever the influence which limit the overflow of *maculipennis* from stables to dwellings, we must draw a distinction between complete deviation and effective deviation. Individuals of all the subspecies are often found in houses and containing human blood, and to this extent the deviation by animals may be considered incomplete.

Effective deviation is established when these visits to man are not sufficiently frequent to fulfil the conditions for malaria transmission. Effective deviation can evidently be upset for a certain length of time, or prevented altogether by other factors than meteorological ones, or the microclimatic preferences of a given subspecies. Among such extraneous influences are an influx of gametocyte carriers, which tends to multiply the possibilities of malaria transmission; a scarcity or diminution in the number of domestic animals, which may act to provoke an overflow of *anophelines* into dwellings; or the rate of production of the *anophelines* them-

selves, which may attain a disproportionate density. A slight change in any of these factors may cause an invasion of human dwellings by *A. troparvus* for example, and thus make of it a malaria carrier in one district while it remains innocuous in another. Thus malaria is associated with war and disaster, and with pioneering conditions in which a primitive standard of living on the part of man is combined with an unrestricted production of anophelines and a paucity of domestic animals.

Summary

Peculiarities in the markings and structure of the egg enable us to divide the species *A. maculipennis* into five varieties which are considered to be true subspecies because of the biological differences between them, as shown particularly in choice of breeding place, and infertility of cross-mating. The instinctive preferences of each subspecies determine in a broad way its contact with man and hence its relation to the spread of malaria, but this is modified by the physical conditions of dwellings and stables (temperature, humidity, etc.), to which some races are more sensitive than others. Thus *typicus* and *melanoon* are virtually confined to stables in their search for blood, and *messeae* has only a slightly greater latitude of choice. *A. troparvus* is less narrowly restricted by its food or microclimatic preferences and under certain conditions enters bedrooms freely. *Labranchiae* and *elutus*, however, have a tolerance for a wide range of physical conditions and will take either human or animal blood as occasion offers. These two races are associated with the most intense malaria. But any subspecies may become a carrier if effective deviation by domestic animals is upset or prevented by disproportionate anopheline density, paucity of animals or an influx of gametocyte carriers, such as may often occur in the wake of disaster, or under primitive or pioneering social conditions.

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НОВЕЙШИЕ ДАННЫЕ ОБ ЭПИДЕМИОЛОГИИ МАЛЯРИИ В ЕВРОПЕ*Л. В. Гакетт* (Рим)

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Из экспериментальной малярийной станции

Особенности рисунка и структуры яиц позволяют разделить вид *A. maculipennis* на пять разновидностей, являющихся истинными подвидами, различающихся по их биологическим особенностям и в частности по местам выплода и не скрещивающихся между собой. Инстинкты комаров, в значительной степени обуславливающие степень контакта с человеком, а следовательно, и роль в распространении малярии, неодинаковы у разных подвидов *A. maculipennis*. Разные подвиды обладают разной степенью чувствительности к колебаниям температуры, влажности и других физических факторов, определяющих выбор помещения (хлева, жилые помещения и т. д.). Подвиды *typicus* и *melanoon* повидому почти исключительно идут в хлева; *messeae* отличается несколько большей широтой во вкусах. *Atroparvus* еще менее прихотлив в отношении микроклиматических условий и в известных условиях охотно летит в человеческое жилье. *Labranchiae* и *elutus (sacharovi)* выдерживают значительные колебания физических условий и без разбора пьют кровь человека и животных. Последние два подвида встречаются в наиболее малярийных местностях.

При высокой плотности комаров, малом количестве домашнего скота или большом притоке гаметоносителей любая разновидность *A. maculipennis* может поддерживать малярийную эпидемию.