MECHANISM OF MALARIA TRANSMISSION IN THE PROVINCE OF NORTH HOLLAND

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(With 3 Figures in the Text)

THIS paper deals with the following problems[1]:

(1) Rate of infection in *Anopheles maculipennis atroparvus* and *messeae*.

(2) Seasonal incidence of anopheline malaria.

(3) Carrying forward of malaria from one season to another.

(4) Transmission of malaria from one village to another.

(5) Extinction of foci of anopheline malaria.

(6) Correlation between anopheline malaria in one year and human malaria in the next.

(1) NATURAL MALARIA INFECTION IN TWO SUBSPECIES OF ANOPHELES MACULIPENNIS

Dissection of females, identified by the shape of their salivary glands during the period of sexual inactivity and by the structure of the floats in mature ova during the period of sexual activity, has yielded the results shown in Table I.

Table I. *Rate of natural malaria infection in* A. maculipennis atroparvus *and* A. maculipennis messeae

	In animal habitations			In human habitations		
Subspecies dissected	No. dissected	No. found infected	% infected	No. dissected	No. found infected	% infected
A. m. atroparvus	2465	7	0·28	37,407	2212	5·91
A. m. messeae	8	0	—	2,028	1	0·05

In human habitations the rate of natural infection of *atroparvus* is 118 times as high as that of *messeae*. As a consequence, in the following sections, the term "anopheline infection" is understood to apply to *atroparvus* only.

(2) SEASONAL INCIDENCE OF ANOPHELINE MALARIA

Fig. 1[2] records in weekly periods the mean outdoor temperature at the nearest meteorological station, Amsterdam (19 km. to the South-east of the

[1] See our paper (June 1936) in *Quarterly Bulletin Health Organisation, League of Nations*, **5**, 295–352.

[2] The figures of anopheline infection, blood-feeding and fertility in 1935, have been previously published in half-monthly periods, but the corresponding figures for 1936 have not, neither have

village of Uitgeest), the fertility of *atroparvus* (% females carrying ova of Christophers' stages 4 and 5), the blood-feeding of that subspecies (% engorged females), the incidence of human malaria (including relapses) and the incidence of salivary infections in *atroparvus* in Uitgeest. The last-named data are also recorded for some neighbouring villages.[1]

(a) *The periodicity of anopheline malaria is not associated with winter*
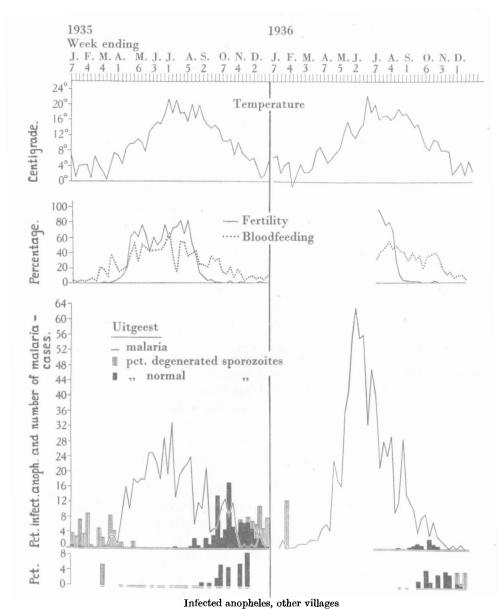
There are two salient features indicated in this diagram: (a) The first is the abrupt decrease of anopheline fertility in the second week of August, which closely coincides with the more gradual increase of anopheline malaria. The fall of the one and the rise of the other occur when the mean temperature is still at 16° C. or higher. In the third week of April, on the other hand, when the mean temperature is still under 10° C., fertility approaches the maximum it will continue till August. Simultaneously, the last traces of the preceding year's anopheline infection are carried away by females which leave the houses to oviposit.

(b) The second feature is that the blood-feeding of *Anopheles* does not decline together with fertility. Notwithstanding various ups and downs it is on the whole maintained on a level but little below that of full summer,[2] from the middle of August, when fertility begins to decline until the beginning of November when blood-feeding also begins to decline. The three months, August–October, represent the period of *gonotrophic dissociation*,[3] so important for the development of anopheline malaria in human habitations, since it does away with egg-bearing and its consequences which militate against malaria transmission, without interfering with blood-feeding.

It is the decline of fertility in August, coupled with continued blood-feeding, which sets anopheline malaria going and so indirectly determines next year's human malaria. The only part winter plays in this process is to check it, (a) perhaps,[4] by reducing the blood-feeding and (b) at a later date by causing

those relating to temperature and human malaria. The data recorded in Fig. 1 are based on a large table which we omit. We can vouch for the reliability of the anopheline figures as they are based on weekly dissections which averaged 378 in Uitgeest and 198 in other villages. The other figures require no comment.

[1] The reason why the infection of *Anopheles* in Uitgeest is so much lower in 1936 than in 1935, whereas it has decreased but slightly in the other villages, is that the houses were sprayed with insecticides, with the purpose of destroying infected *Anopheles*.

[2] This does not apply to the records of 1935. They are too low in autumn because, in that year, we did not note down the percentage of engorged females on the day following their capture but on the day of dissection. This considerably reduced the number of engorged females, if the mosquitoes captured were too numerous to dissect them all on one day, as often happened in autumn.

[3] Swellengrebel (1929), *Ann. Inst. Pasteur*, **29**, 1370.

[4] In 1936 the decline of blood-feeding coincided with a fall in outdoor temperature below 10° C. in the beginning of November. But in 1935 its rise commenced by the end of February, when the outdoor temperature was well under 5° C.

Upper curve. Mean weekly outdoor temperature at Amsterdam.

Middle curve. Uninterrupted line: Mean weekly rate of fertility of *Anopheles mac. atroparvus* (percentage of females carrying ova of Christophers' stages 4 and 5). Observations interrupted from 1 January until 8 July 1936. Dotted line: Mean weekly rate of blood-feeding in *Anopheles mac. atroparvus* (percentage of engorged females). Observations interrupted as described above.

Lower curve. Weekly number of malaria cases in Uitgeest.

Columns. Upper row: Weekly rate of salivary infections in *Anopheles mac. atroparvus* in Uitgeest. Black columns: normal sporozoites. Shaded columns: degenerated sporozoites. The observations have been interrupted wherever the double base-line is absent. Lower row: The same as upper row but referring to neighbouring villages not subjected to house-spraying.

Fig. 1.

the degeneration of the sporozoites, which coincides with a fall of the mean outdoor temperature to below 5° C. in the second week of December.

The epidemiology of malaria in any country, tropical or temperate, whose principal insect vector shows well-marked and regularly recurring rises and falls in the rate of fertility, will resemble the epidemiology of malaria in this country, so long as the decline of fertility does not entail the loss of the insect vector's appetite, as happens, for instance, in *Anopheles mac. messeae*.

In making this assertion we do not lose sight of the epidemiological feature which is peculiar to Holland—the long incubation of malaria in the human host. It is well brought out in Fig. 1 by the waves of anopheline and human malaria alternating at a period of 8–9 months instead of coinciding. But it is the decline of anopheline fertility which decides when the wave of anopheline malaria shall rise and, consequently, when man shall acquire his malaria infection. The length of the incubation fixes the time when he shall fall ill.

(b) *How far into the autumn fresh anopheline infections continue to occur and how long they take to mature*

In the village of Uitgeest a number of houses were repeatedly sprayed with insecticides in the autumn of 1936. The immediate effect of this was to clear the houses of all mosquitoes. *Anopheles* found in houses subsequently must have come from elsewhere and, if they were infected, they must either have brought the infection from elsewhere or they must have acquired it in the sprayed house after the spraying. In the houses, referred to later, infected *Anopheles* could not have been imported because no foci of anopheline infection existed in the neighbourhood. Hence, infected *Anopheles* found in these houses after the spraying must have ingested the parasites on the spot, the earliest possible date of infection being the day after the spraying.

In three houses, D., O. and L., all mosquitoes were destroyed by spraying on 25 August, so the earliest possible date of infection was 26 August. On 11 September, 16 days later, we found in house D.: 81 *Anopheles*, 2 carrying oöcysts, 1 with mature oöcysts; in house O.: 29 *Anopheles*, 8 carrying oöcysts, 2 with mature oöcysts; in house L.: 218 *Anopheles*, 1 carrying mature oöcysts, 1 carrying sporozoites.

In house T., all mosquitoes were destroyed by spraying on 6 October, so the earliest possible date of infection was 7 October. On 27 October, 21 days later, we captured one *Anopheles*, which was found to carry sporozoites.

It is obvious that the time recorded here as required for the development of the sporozoites is to be regarded as a maximum. Moreover, house-spraying as a method of fixing the earliest possible date of infection defeats its own ends, particularly if the season is advanced, because *Anopheles* sufficiently active to fill the depleted houses become increasingly rare. So we conclude that fresh infections can be acquired at least as late as 7 October and that such an infection takes 21 days to mature at the longest.

(3) The carrying forward of malaria parasites from one year to another

The following family history shows how this carrying forward is brought about, by *Anopheles* taking malaria parasites to a house in autumn and infecting the human inmates in whose bodies they pass the winter, spring and summer. In the next autumn the same human inmates reinfect *Anopheles* which are some five generations younger than the original vectors.

Family O., 2 parents and 5 children from a non-malarious area, settled in Uitgeest on 16 July 1935. On 18 October none of the 4 schoolchildren O. had enlarged spleens and none carried parasites. Their house O. was 25 m. away from house T., sheltering 22 infected *Anopheles* (among 56) on 30 September; on 12 November there remained only 14 *Anopheles* in house T., none was infected. On 12 December house O. was found to shelter 3 infected *Anopheles*, among 335, carrying none but degenerated sporozoites. These must have been derived from house T., as no other neighbouring house contained infected mosquitoes. Moreover, they must have invaded house O. some time before 12 November, because on that date the stock of infected *Anopheles* in house T. was exhausted. At that time their sporozoites were presumably still normal, since they are normal in most *Anopheles* in the beginning of November (Fig. 1).

Father O. was the first to suffer by the presence of these mosquitoes: he had malaria on 19 December, after an incubation of 3 months or less. The other members of the family must have been infected at about the same time, but their protracted incubation was of the usual length. They all had malaria in 1936: on 30 May, 12 June, 12 July, 8 August (2 patients) and 8 September. Three became parasite carriers.

No anopheline infection was detected on repeated visits to this house in July and August. But on 11 September 1936, we finally found 8 mosquitoes (among 29) carrying mature oöcysts.

(4) How malaria is carried from one village to another

It is conceivable that a pregnant female *atroparvus* carrying sporozoites in summer (as we have seen them do, although rarely), leaving the village in which it became infected in order to deposit its eggs, carries its infection to some other village. But we never saw this happen. The flight of sexually inactive sporozoite-carrying *Anopheles*, moreover, is much too short (we rarely found them more than 100 m. away from their foci of infection) to allow of their spreading malaria from one village to another. Hence we believe that the following is an instance of the usual way a village in this country becomes infected with malaria.

In a hamlet, near Wormerveer, of 64 inhabitants dispersed through 16 houses, a 17th house came to be occupied by the 10 members of family K. on 8 November 1933. Before, they had been living in Wormerveer, where 3

had malaria in 1930, 1 in 1932 and 4 in 1933; in their new abode 3 had malaria in 1934, 1 in 1935, 1 in 1936 and 3 were permanent carriers since November 1934.

In house K. we found 107 *Anopheles* infected among 441 in the autumn of 1934 and 44 among 497 in the autumn of 1935. In the autumn of 1934 we captured all the *Anopheles* we could find in every house of this hamlet and detected 1 *Anopheles* infected out of 3 in house S., 1 infected out of 40 in house W.R. (both 55 m. distant from K.) and 3 infected out of 307 in house G. (next door to K.). As no malaria had occurred in these houses for at least 5 years it may reasonably be concluded that their infected mosquitoes came from house K. The subsequent history of these houses was as follows:

The inmates of house S. never had malaria. Two inmates of house G. had malaria in August and November 1935; 3 others did not fall ill till May, June and July 1936. Probably all were infected in 1934, as we never found a single infected mosquito on repeated visits to house G. in August, September and October 1935.

In house W. R. malaria was still further postponed, as it did not make its appearance (one patient) until June 1936.

Malaria occurred in 3 houses where no infected *Anopheles* had been detected in the autumn of 1934 and 1935. Three inmates of house J.R., next door to house W.R., had malaria in June 1935; three had malaria in house Sm. 30 m. distant from K., and 1 case occurred in July 1936 in house M., 40 m. distant from K.

Consequently the immigrants had caused malaria in 6 and probably in another 7 of the 48 neighbours living at a distance of 65 m. or less from house K. There was no malaria in 1934, the first year after the family K.'s arrival. The explanation is that they settled in the hamlet on 8 November 1933, too late in the season to start fresh anopheline infections, since *Anopheles* rarely become infected after 31 October (see our paper cited on p. 62).[1]

(5) How foci of anopheline malaria become extinct

It often happens that infected *Anopheles* found in a certain house considerably decrease or completely disappear within 2 or 3 years, without any outside intervention (house-spraying).

The cause of this extinction of a focus of anopheline malaria is obvious if: (a) the human parasite carriers or (b) the total anopheline population inhabiting a house have been greatly reduced in number or have wholly disappeared. This was the case in:

(a) Family Oe., in whose house we found, during the autumn, 19 infected *Anopheles* in 1934, 23 in 1935, but no more than 2 in 1936. No member of the family had malaria later than 1932; hence anopheline infection wholly depended upon two permanent carriers, detected among the children in October 1934, but in whose blood no more parasites were to be found in the autumn of

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[1] Malaria disappeared from this hamlet in 1937, anopheline infection had done so already in 1936. Consequently, the coming and going of malaria entirely depended on family K.

1936. So the decrease of anopheline infection was due to that of the human parasite reservoir.

(*b*) Family R., who had 4 malaria patients and 2 parasite carriers among their 8 members in 1935; in 1936 they had 2 malaria patients and 4 parasite carriers. In 1935, 52 *Anopheles* were found infected among 172 captured on three visits; in 1936 none was infected among 8 *Anopheles* captured on four visits. Here the extinction of the focus was due to lack of *Anopheles*. As an interesting detail, we may add that the lack of *Anopheles* was strictly localized to the particular house occupied by the family during late summer and autumn of 1936 and to which they had moved on 1 August. The new house and the old were in the same street, 75 m. apart. But the attic of the old house possessed secluded, dark shelters next to the bedrooms, difficult of access and therefore never cleaned out, in which all of the 172 *Anopheles* were captured. The attic of the new house, on the contrary, had nothing but well-lighted bedrooms, where *Anopheles* had little chance to stay undisturbed.

The cause of the extinction of a focus of anopheline malaria is less obvious if no well-marked reduction can be observed either in the number of human carriers or in the *Anopheles* inhabiting the house.

This was the case in family Ko., in whose house we found, during the autumn, 28 infected anopheles out of 152 in 1934, but no more than 2 out of 307 in 1935, 3 out of 198 in 1936 and 1 out of 162 in 1937. Among the six human inmates 5 had malaria in 1934, 4 in 1935, 4 in 1936 and 3 in 1937. One child was carrying parasites from November 1934 onward and was still doing so in May, 1937. There was thus no obvious reason why anopheline infection should deteriorate, though in fact it did so.

We also know of families where anopheline malaria completely disappeared, notwithstanding the continued existence of parasite carriers and malaria patients. The following is an instance. Family K. had an autumnal anopheline malaria of 107 infected out of 441 in 1934, 44 out of 497 in 1935 and none out of 79 in 1936. Among the 10 inmates 3 had malaria in 1934, 1 in 1935 and 1 in 1936. Three children were carrying parasites from October 1934 onward and were still doing so in November 1936. So the parasite reservoir remained the same[1] and still anopheline infection disappeared.

We believe that this failure of the parasite carriers to infect *Anopheles* is *one of the causes of the extinction of a malaria epidemic. It is probably to be* explained by a local population of parasites losing their vigour from always having to circulate among the same group of "healthy" human carriers living in the same house, with never a change, except for a short interlude of insect transmission once a year. This supposition is supported by the experience in house T. (see family history O. in § 3, p. 66), a focus of anopheline malaria in 1935, where mosquito infection never revived in 1936, although there were 3 parasite carriers and 4 malaria patients. But in house O., to which the T. strain of malaria parasites had been transplanted in 1935 and where some of

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[1] It did become extinct in 1937.

the patients had recently developed into "healthy" carriers, anopheline infection flourished in 1936, as much as repeated sprayings would allow. It probably was the change to fresh "healthy" carriers entailed by this transplantation, which made the difference between house O. and house T.

It is significant in this respect that the best anopheline infections in 1936 were found in families who had malaria for the first time. Among 18 families who had suffered from the disease in a preceding year the rate of anopheline infection was 32 out of 2006, i.e. 1·6%, whereas it was 51 out of 434, i.e. 11·7% in 12 families who had malaria for the first time.

It is the "healthy" carrier more than the malaria patient who infects *Anopheles*. But if he remains a carrier too long he loses his infectivity. With due regard to the fundamental difference between the two cases, the state of things is not unlike that which results from repeated small doses of salvarsan given to a G.P.I. patient in the course of a fever cure. His fever disappears, his parasites diminish in number, but not so much as to become incompatible with anopheline infection, male gametocytes being present, and still *Anopheles* do not become infected on taking his blood, whereas they succeed in this by feeding on a G.P.I. patient whose blood contained even less parasites, but who had become afebrile without doses of salvarsan.[1]

(6) How anopheline malaria in one year is related to human malaria in the next

The question to be answered here is this: Are the *Anopheles* we find infected in late summer and autumn of one year responsible for the malaria in the next year? This may seem a superfluous question, but the following will show that it is not.

(a) *Malaria in houses with and without infected* Anopheles *in the preceding year*

Among 67 houses, with 516 inhabitants, sheltering infected *Anopheles* in late summer and autumn of 1935, 42 (63%) were malaria-houses in 1936; 124 (24%) of their inhabitants had malaria that year. Among 131 houses, with 567 inhabitants, where no infected *Anopheles* were found during the same period in 1935, 45 (34%) were malaria houses in 1936; 77 (13%) of their inhabitants had malaria that year.

Consequently, the incidence of malaria in the houses with infected *Anopheles* is not quite twice that in houses where no such mosquitoes were found in the preceding year.

This conclusion underrates the effect of the presence of infected *Anopheles*, for the following reasons:

(i) 18 houses, out of the 25 with infected *Anopheles* in 1935, but without malaria in 1936, were examined for the presence of parasite carriers or persons

[1] Swellengrebel, de Buck & Kraan, *Roy. Acad. of Science at Amsterdam.* Session of 20 March 1937.

with enlarged spleens; they were found in 11. Such houses may remain free from malaria for years. So long as they continue to produce anopheline malaria they will swell the list of examples of infected *Anopheles* failing to cause human malaria. The following was another example of this:

Family D., who had much malaria in 1934, but none in 1935. In 1935 and 1936 there were 5 parasite carriers. As 35 infected mosquitoes (among 573) were found in the autumn of 1934, the house was listed, in 1935, as an example of anopheline infection without malaria. As 124 infected mosquitoes (among 1726) reappeared in the autumn of 1935, the house would have been put on the same list in 1936 but for the birth of a child on 13 March 1935, who, consequently, was exposed to the autumnal anopheline infection of that year and responded to this exposure by having malaria on 25 June 1936.

(ii) It sometimes happens that when a house is invaded by infected mosquitoes in the autumn of one year, that malaria fails to appear in the next year, but that it makes its appearance in the next year but one. We know of two houses of this kind, in which no malaria had been known to occur in any of the 5 preceding years. Infected *Anopheles* were detected in October 1934, 6 in one house and 1 in the other, but not in 1935; neither was there malaria in 1935. But in 1936 2 persons suffered from the disease in the first house and 1 in the second.

(iii) We know (see our paper cited on p. 62) that infected mosquitoes escape from autumnal foci of anopheline infection and invade neighbouring houses within a radius of 100 m. But it is very difficult to find them there. Consequently, it is probable that there exist a number of houses, within a circle of 100 m. radius around a focus of anopheline infection, in which malaria occurs through infected mosquitoes which escape detection.

(b) *Distribution of malaria around the foci of the preceding year's anopheline infection*

As was pointed out in the preceding section, most of the infected *Anopheles* which escape from the houses where large numbers became sporozoite carriers (the foci of anopheline malaria) and enter neighbouring houses without being detected, will remain within a distance of 100 m. from these foci. Hence, if we find human malaria accumulating around the preceding year's foci of anopheline malaria, i.e. if we find malaria patients most numerous near these foci and diminishing in number with increasing distance, it becomes highly probable that the anopheline malaria, produced by the foci in one year, is the cause of the human malaria in the next.

In order to test this idea we have described two circles around each of the more important foci of anopheline malaria in 1935. The outer circle, with a radius of 100 m., represents the *range of influence* of the focus; the inner circle, with a radius of 50 m., is the *central range of influence*; what is left of the outer circle is the *peripheral range of influence*. By counting the houses with infected

mosquitoes of 1935 and the malaria houses of 1936, inside and outside these areas,[1] we obtained the results recorded in Table II.

Table II. *Position of:* (A) *the houses with infected mosquitoes in 1935 and* (B) *the malaria houses in 1936, with regard to the foci of anopheline malaria in 1935.*

Area in which the house sheltering infected mosquitoes was situated	Total no. of houses in these areas	Number of houses sheltering infected mosquitoes with					
		20 or more infected *Anopheles*	%	6–15 infected *Anopheles*	%	1–5 infected *Anopheles*	%
Central range of influence	271	12	4·4	11	4·0	30	18·4
Peripheral range of influence	338	1	0·3	2	0·6	14	4·1
Outside the range of influence	162	0	0	0	0	6	3·7

Area in which the malaria house is situated	Total no. of houses in these areas	Number of malaria houses with					
		4–9 patients	%	2–3 patients	%	1 patient	%
Central range of influence	271	19	7·0	32	11·8	56	20·7
Peripheral range of influence	338	2	0·6	24	7·1	46	13·6
Outside the range of influence	162	1	0·6	8	5·0	40	24·7

Figs. 2 and 3 give the same data as Table II A and B in the shape of a plan of the village of Uitgeest. For the sake of simplicity the outer circles have been omitted from the picture.

Fig. 2 shows the houses graded according to the number of infected mosquitoes they sheltered in 1935. Nearly all houses with 6 or more are lying inside the inner circles; but the houses with 1–5 readily transgress these narrow bounds, and some of them even the wider ones (Table II A).

Fig. 3 shows the houses graded according to the number of their malaria patients in 1936. With few exceptions the houses with 2 or more patients are found clustering around or between the foci of anopheline malaria.

This is also brought out by Table II B, showing that the density of human malaria declines with the increasing distance from the foci of anopheline malaria. The houses with 4–9 patients decrease rapidly with the increase of that distance; the houses with 2–3 patients do so more gradually; the one-patient houses, on the contrary, after decreasing in the peripheral range of influence, considerably increase their (relative) number outside this range.

Table II A shows the distribution of the houses with infected mosquitoes, which is so obviously analogous to that of the malaria houses in the succeeding year that there is no need to go into details. There is one important difference however: the houses with the lowest number of infected mosquitoes are scarcer outside than inside the peripheral range of influence, whereas it is just the reverse with the one-patient houses.

This distribution of the malaria houses suggests that the *Anopheles* from the foci of mosquito infection have infected four-fifths of the malaria houses. Part of the remaining fifth, lying outside the 100 m. limit, may still have received

[1] Two houses with 3 patients and 12 with one patient lying outside the central range of influence have been attributed to that area, because infected anopheles were found in them in 1935. These houses are omitted in Fig. 3.
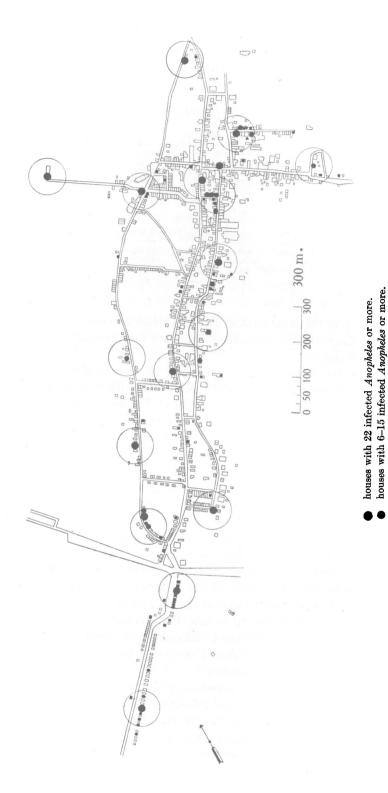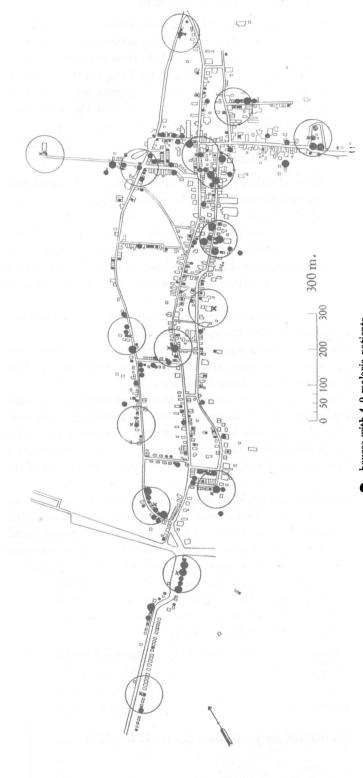
Fig. 2. Plan of the village of Uitgeest. Distribution of anopheline malaria in 1935. The circles with a 50 m. radius mark the central range of influence of the more important foci.

● houses with **22** infected *Anopheles* or more.
● houses with **6–15** infected *Anopheles* or more.
● houses with **1–5** infected *Anopheles* or more.

300 m.

0 50 100   200   300

Fig. 3. Plan of the village of Uitgeest. Distribution of human malaria in 1936. The circles with a 50 m. radius mark the central range of influence of the more important foci of anopheline malaria in 1935.

● houses with 4–9 malaria patients.
● houses with 2–3 malaria patients.
● houses with 1 malaria patient.
× site of the foci of anopheline infection in 1935.

300 m.

0 50 100   200   300

their infection from these foci, because infected mosquitoes are actually seen overstepping this limit (Table IIA). But the striking accumulation of 40 one-patient houses outside this limit renders it probable that the greater part of them did not become infected by *Anopheles* coming from the foci. Perhaps they derived their malaria from the few *A. mac. atroparvus* which we found infected during their period of sexual activity in July and the first half of August[1] (14 in all out of a total of 2219 infected *Anopheles*).

CONCLUSIONS

1. The rate of malaria infection in nature is more than a hundred times higher in *Anopheles mac. atroparvus* than in *A. mac. messeae*.

2. The periodicity of anopheline malaria is the effect of the periodically recurring intermissions in the fertility of *A. mac. atroparvus*, associated with continued blood-feeding. These intermissions occur independently of temperature.

3. *Anopheles* can become malaria-infected at least as late as 7 October. An infection acquired at that time takes no more than 3 weeks to reach the salivary glands.

4. Winter contributes to the shaping of the epidemiology of malaria in Holland by causing the sporozoites to degenerate.

5. *Anopheles* spread the malaria parasites from man to man and from house to house in autumn. Man keeps them alive till the next transmitting season.

6. Man spreads malaria from village to village.

7. Anopheline malaria dies out in a house by the deterioration of the human parasite reservoir or by the lack of *Anopheles*, resulting from the removal of appropriate places for *Anopheles* to hide in. But it can also become extinct, notwithstanding the presence of numerous *Anopheles* and of human parasite carriers, because these carriers lose their infectivity before they get rid of their parasites.

8. The failure of infected *Anopheles*, staying in a house, to cause malaria in the human inmates of that house during the next year is due to a partial immunity or to an unusually long period of incubation of the human host.

9. The incidence of human malaria is highest near the foci of anopheline malaria of the preceding year. The scattered cases of malaria (one-patient houses) do not all conform to this rule. Their distribution suggests that a certain number (less than one-fifth) of the malaria houses are infected by *Anopheles* carrying sporozoites during the period of their sexual activity in the second half of July and the first half of August.

[1] As has also been suggested by van Thiel (1934), *Nederl. Tijdschr. v. Geneesk.* **78**, 997–1007 (English summary on p. 1007).

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