Map of the World on Mercator's Projection showing the Climatic Zones of Malaria.

Zones of Malaria
- Temperate Zone
- Sub-Tropical Zone
- Tropical Zone
- Equatorial Zone

[The isotherms used in the construction of the map are derived from temperature data reduced to sea-level.]
Malaria Commission; League of Nations 1924, Geneva
MALARIA IN THE NETHERLANDS

by

N. H. SWELLENGREBEL

and

A. DE BUCK

AMSTERDAM

SCHELTEMA & HOLKEMA LTD.
Finally we come to an example which is the most puzzling of all, namely to the quartan fever which, in 1936, attacked the chairman of the malaria commission of the Sanitary Council, the late professor Aldershoff. He had never lived in any malarious part of the country, but he had visited the Balkans some sixteen years before. However, we are not going to blame another country for the malaria which occurs here. We always feel hurt when we hear the Germans saying they have no malaria except on the Dutch border. So we will not pay others with the like coin and we shall charge Professor Aldershoff’s quartan to our own account.
Fig. 2. Malaria at Amsterdam. Comparison of the monthly incidence in 1857 and 1922. Continuous line: tertian 1857; dotted line: quartan 1857; broken line: tertian 1922.
Malaria in The Netherlands 1938
NH Swellengrebel and A De Buck
it may suffice to summarize the situation by saying: North-Holland, the land largely reclaimed from the sea, is malarious; South-Holland and the adjoining parts of Utrecht and Guelders, the ancient resistant peat-land, are healthy.
Malaria in The Netherlands 1938
NH Swellengrebel and A De Buck
fixed rule came to be ignored. In October of that year we found a spleen-rate of twenty-five per cent among schoolchildren, of the age of six and older, living in the village of Uitgeest. Most of the enlarged spleens, we should add, were palpable on deep inspiration only *. Since then, Dr. de Rook has successfully extended our work, primarily for the purpose of giving a lead in the search for foci of anopheline infection. He found spleen-rates ranging from nineteen to twenty-seven per cent in some little-explored villages of North-Holland near the new polder. Among the immigrant schoolchildren of the
Asymptomatic *Plasmodium vivax* carriage in The Netherlands

Beside the malaria patients there exist healthy carriers. We do not know that they are really healthy and, for our present purpose, we do not care either. All that matters is that they do not feel sufficiently ill to call in their physician, although they can do so as often as they like, being members of the sick-club. Their number may be quite considerable on occasion. Among a group of 264 persons *,


78 of whom had had malaria during the year, 103 healthy parasite-carriers were detected. Out of these, 67 had no malaria during the whole year, the others had, although they were quite well at the time their blood was examined.

<table>
<thead>
<tr>
<th>had</th>
<th>50 parasites per 100 leucocytes including male gametocytes</th>
<th>7</th>
<th>12-25 parasites per 100 leucocytes, with male gametocytes in 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>6-9</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>1-5</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>1-5</td>
<td>1,000</td>
<td></td>
</tr>
<tr>
<td>59</td>
<td>1-5</td>
<td>6,000</td>
<td></td>
</tr>
</tbody>
</table>

Malaria in The Netherlands 1938

NH Swellengrebel and A De Buck
Fig. 19. Infected anopheles in houses with healthy carriers (right section) and without healthy carriers (left section), but with summer patients in both. White or shaded columns: number of houses; the shaded portions indicate the number of houses with an average of two summer patients. Black columns: number of infected mosquitoes caught in these houses.
High infection rates

after that time. Here is an example of the change in the rate of anopheline infection observed in one single house:

<table>
<thead>
<tr>
<th>Month</th>
<th>Date</th>
<th>Anopheles infected</th>
<th>Total</th>
<th>Infection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>August</td>
<td>16th; 10</td>
<td>10</td>
<td>118</td>
<td>8%</td>
</tr>
<tr>
<td>September</td>
<td>20th; 79</td>
<td></td>
<td>307</td>
<td>26%</td>
</tr>
<tr>
<td>October</td>
<td>17th; 84</td>
<td></td>
<td>219</td>
<td>38%</td>
</tr>
<tr>
<td>November</td>
<td>27th; 75</td>
<td></td>
<td>232</td>
<td>32%</td>
</tr>
<tr>
<td>December</td>
<td>17th; 38</td>
<td></td>
<td>101</td>
<td>38%</td>
</tr>
<tr>
<td>December</td>
<td>30th; 20</td>
<td></td>
<td>77</td>
<td>26%</td>
</tr>
</tbody>
</table>
A family, in the village of Wormerveer, who had suffered much from malaria previous to June 1932, came to occupy a house on October 15th 1934. The house had been vacated by a second highly malarious family on October 1st. A few days before the second family moved out of the house, and during the weeks it was left unoccupied, we had detected quite a number of infected anophelae. We had captured not nearly all of them, as we perceived on revisiting the house (now occupied by the new family) in the beginning of November. One of the new occupants, a girl of fourteen months who had never had malaria before, was evidently infected by them, since she was found to carry parasites in the course of November. She promised to provide us with a most beautiful natural repetition of our experiments on long incubation *, but she disappointed us: the child had no malaria in 1935. We are quite sure about this, because we engaged the family-physician’s interest in the case, and nothing of the slightest moment could happen without his knowing it. In 1935 and 1936 the girl continued as a parasite-carrier and infected anophelae were found in her house during the autumn of these years. Finally, in June 1937, she had an attack of malaria, two years too late. All that time the house had been listed as an example of the presence of infected anophelae not being followed by human malaria.

Asymptomatic vivax malaria without prior exposure
Relapse

Hence, the relapse-rate over one year was thirty-five per cent in Wormerveer after a seven days' treatment with atebrin, and thirty-seven per cent in Uitgeest after an eight days' treatment with sulfate of hydroquinine. The difference is so slight as to be practically of no account.

36%
Malariatherapy
Proceedings of a Meeting of the Society held on Thursday, 15th May, 1924, at 8.15 p.m., at 11, Chandos Street, Cavendish Square, W. 1, Dr. A. G. Bagshawe, C.M.G. (Vice-President), in the Chair.

The Chairman said he had received a letter from the President, Sir Percy Bassett-Smith, who wished the meeting to be informed how sorry he was he could not occupy the Chair, but he hoped to be able to do so at the next meeting.

OBSERVATIONS ON MALARIA MADE DURING TREATMENT OF GENERAL PARALYSIS.

BY

Warrington Yorke, M.D., and J. W. S. Macfie, D.Sc., M.B., Ch.B.

Malignant Tertian Malaria.—At the very beginning of our work one case was inoculated with the blood from a patient suffering from malignant tertian malaria. The infection which resulted was of a fulminating character and the disease terminated fatally.
Blood inoculation:
4-18 months follow up following quinine treatment
1/61 recrudescence
(XXX grains/day 2-4 days)

Mosquito inoculation
2-6 months follow up following quinine treatment
4/31 relapsed; Intervals (days)
1. 24, 19
2. 24, 31
3. 11, 18, 33, 40
4. 25, 42
Blood inoculation:
18-24 months follow up following quinine treatment
2/100 recrudescence
(XXX grains/day 2-4 days)

Mosquito inoculation
21/34 relapsed!; median 168 (range)20-331 days
Relapse

In mosquito-borne malaria the case is different. It is likewise amenable to quinine taken in doses as quoted above. But relapses occur in a certain proportion of the cases. They are not so numerous, however, as in spontaneous malaria. Out of 58 patients, suffering from mosquito-borne malaria and subsequently treated with a daily dose of 15 grains of sulfate of quinine for five consecutive days, nine had a relapse within the next eighteen to twenty-four months: a relapse-rate of fifteen per cent. Out of 81 similar patients, treated with quinoplasmine (fourteen grains of quinine and half a grain of plasmoquine daily) for one or two weeks, nine relapsed within the same period: a relapse-rate of eleven per cent.

15% (artificial) vs 36% (natural)
Relapse

In general practice about fifty per cent of the malaria patients, treated with quinine for seven days, are reported to relapse during the year they were treated and the next year. Our patients were much better observed than they ever can be in general practice. Nevertheless, their relapse-rate was less than one third of the above.

15% (artificial) vs 50% (natural)
Medicine. — Report on a small experimental epidemic of benign tertian malaria started in September 1931 and followed up till January 1933. By N. H. Swellengrebel. (Communicated by Prof. W. A. Schüffner.)

(Communicated at the meeting of February 25, 1933.)

Korteweg
N=30
Malaria cases

Month

A.atroparvus

Delayed primary illness

Relapse and early primary illness

[Graph showing malaria cases over months with a peak in August and a secondary peak in February]
The foregoing is a rough outline of the history of malaria and its control until about 1920-22.

At that time, the sexual life cycle of malaria plasmodia in the mosquito had already been elucidated. On the other hand, knowledge of the course of the asexual cycle in the vertebrate host was still fragmentary.

Two questions that remained completely unanswered were:

(1) What is the fate of the sporozoite after its entry into the body of the vertebrate host?

(2) How do relapses, with fever and parasitaemia, develop after a more or less long interval, even when the treatment of an acute infection has apparently been successful?
Fig. 1. The two charts display the recrudescence and relapse patterns of *P. falciparum* on the one hand and those of the long term relapse Madagascar strain of *P. vivax* on the other. (From James, S. P., Nicol, W. D. and Shute, P. G., 1936. *Proc. Roy. Soc. Med.*, 29, 879.)
THE MADAGASCAR STRAIN OF PLASMODIUM VIVAX

by

the late P. C. SHUTE, P. C. C. CARNHAM and Mary MARYON

directly derived from the sporozoite) in the liver. In a series of cases, James, Nicol and Shute (1936) recorded the time of the relapse and showed that the relapses occurred between 189 and 273 days after the primary attack.
Differences between the Madagascar and Netherlands “strains” of *P. vivax*

Induced benign tertian malaria

The two strains of *Plasmodium vivax* employed to induce malaria for therapeutic purposes. — We shall have to refer to these strains more than once and so we begin by saying what they are. One is called the home-strain, indigenous in North-Holland and Friesland. No difference can be detected between parasites from these provinces. The other is James’ *Madagascar strain*. They differ in regard of the period of incubation, the tendency to lapse into latency, the type of fever they cause, their susceptibility to neosalvarsan, and by an incomplete reciprocal immunity.

This put us in a position accurately to fix the length of the period of incubation. In the Madagascar strain it proved to be twelve days; on an average, whereas it was twenty-one days in our home-strain. This difference is apparent in mosquito-transmitted malaria only. After subcutaneous inoculation the incubation lasts for nine days in both strains.
Case-fatality. — The Amsterdam mental hospitals always see to it that every patient who is to be subjected to treatment with malaria is thoroughly examined by a specialist, to make sure that he is fit for this treatment. Nevertheless, sixty-two out of eight hundred and seven patients, in whom benign tertian malaria had been induced for therapeutic purposes, died during the period of incubation, during the treatment, or within a week after its cessation. That represents a case-fatality approximating eight per cent. As a rule, the patients died notwithstanding the parasites in their blood proved perfectly amenable to quinine treatment.

This case-fatality is to be accounted for by the circumstance that a series of twelve paroxysms affects much more seriously an individual weakened by general paralysis (usually aggravated by syphilitic vascular lesions, an incipient ataxia, and other morbid symptoms) than an otherwise healthy person.

In some instances autopsy clearly revealed other causes of death, like pneumonia, septic conditions following bed-sore, syphilitic aortitis, or myocarditis. There can be no doubt, however, that malaria is a contributory cause of the death of many patients. There is little use in minutely scrutinizing this death-roll to exonerate the therapy of induced malaria. It is better to face the truth that this method of treatment carries with it grave risks to the patient who is to profit by it. At the same time we ought to bear in mind that it is amply justified by the absence of any other means to stop the insidious progress of general paralysis.
Complications and case-fatality. — Quartan is occasionally blamed for causing “nephrosis”, a renal condition characterized by albuminuria and oedema, in the absence of urea retention and of hypertension. We have never met with it in our hundred and thirteen patients treated with quartan malaria. A few of them developed a slight and transient albuminuria; that is the nearest approach to the above named condition we ever came across.

Eleven of our patients died: a case-fatality of ten per cent, slightly higher than in patients treated with tertian malaria in whom it approximated eight per cent.