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47. Prophylaxis of Malaria in Central and Southern Brazil.—Several anti-malarial campaigns have been carried on under the technical direction of our Institute, all of which have been crowned with the most complete success. They were undertaken in the following chronological order:—

- (1) In the construction of the Itatinga Railway, Santos.
- (2) In the work of damming the Rivers Xerem and Mantiquira, for the water-supply of the city of Rio de Janeiro.
- (3) At the time of the extension works of the Brazilian and Northern of Minas Railway.
- (4) During the survey work for the Bahia and Espirito Santo Railway.
- (5) During the construction of the North West of Brazil Railway.
- (6) In the suburbs of the city of Rio de Janeiro in connection with the prophylaxis of yellow fever.

The most important campaigns were conducted by Drs Carlos Chagas, Arthur Neiva and Gomes de Faria, Members of the Institute; and Dr Carlos Chagas (1906-1907-1908) had already written on some of them, he being among us the first to organise a scientific campaign against malaria.

The prophylactic formulae adopted by the Institute comprised the following:—

- (1) Prophylaxis by quinine exclusively, adopted when the treatment had to be applied to a moving population

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and one not remaining any length of time in a particular zone (railway construction).

- (2) Preventive administration of quinine, isolation of the persons infected with gametes, in infirmaries fitted with wire-gauze, and unrelaxing treatment of those infected. This system was adopted when the persons already infected had to reside for some time in the infected zone with healthy persons, and where the work was done more slowly.
- (3) The same measures as above, together with systematic sulphur disinfection of infected dwellings. Prophylaxis adopted when the staff remained for a longer period in the infected zone, and where it was not possible to carry out prophylaxis by means of larvicide.
- (4) Indirect prophylaxis by war on mosquitos.

Let us see more in detail how these prophylactic systems were carried out among us.

The first prophylactic formula.—This was put into execution with success in the surveys for the South of Bahia Railway, by Drs Mauricio de Abreu and F. Soledade, of the General Board of Public Health. The process consisted in the daily administration of 50 centigrammes of hydrochlorate of quinine. It was compulsory, and the medicine was administered by the doctors themselves, who saw that the patients swallowed the capsule. In this case, as the persons never remained long in the same place, the dose of quinine given was always prophylactic, which is not the case when the persons remain for a long time in the same infected places, as we shall see later. In the special case, the results were most complete; not one of the persons subjected to the *régime* fell sick, whereas others who accompanied the party, without belonging to it, and who would not submit to the same prophylaxis, were attacked by malaria.

The second prophylactic formula.—Here the process followed out included:—

- (1) The preventive administration of quinine, in the dose of 50 centigrammes every three days.
- (2) The isolation of the persons infected with gametes, in infirmaries protected by wire-gauze during the hours the *Anopheles* sting, being subjected to strict treatment until the gametes disappear.
- (3) Early and radical treatment of persons infected for the first time and not themselves infectious (this was done without isolation), in order to prevent them becoming infectious to mosquitos by the formation of gametes.

Dr Neiva, who was entrusted with the carrying out of the quinine prophylaxis on a large scale (among some 3,500 workmen at Xerem), observed that among those treated with quinine cases of first infection began to appear and increase rapidly. He was able to verify these positively by excluding the cases of reappearance noted after the beginning of the campaign. Satisfied that the dose of quinine was not sufficient to guarantee the prophylaxis, he proceeded to administer it at intervals of two days; after some time, fresh cases of first infection began to appear, and these were only really stopped when he commenced to administer the quinine in a daily dose of 50 centigrammes.

It is interesting to note that among the persons thus treated with quinine an outburst of malaria occurred when they discontinued the use of quinine, even though the practice had been continued *after leaving the infectious malarial zone*; and to prevent such attacks it became necessary to continue the use of quinine for a long time, and repeat treatment at intervals. Stranger still, persons who, after leaving the malarial zone, went to reside in places which were certainly not infected, where they continued the use of the quinine (50 centigrammes daily) for a month, as soon as they abandoned this preventive were attacked by malaria. Such persons had remained for fourteen months in the infected zone *without ever suffering any attack of fever*. When under the action of quinine they

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had no fever, but harboured plasmodia in the system. Dr Neiva, in view of his observations, admits that during the quinine prophylaxis the plasmodia become gradually accustomed to the quinine and immune *against this poison*, giving rise to a family able to resist the quinine, and similar to the families of trypanosoma which defy atoxyl. Subsequent to this interesting observation of Dr Neiva's (made in October 1907) several other authors have referred to analogous facts.¹

The occurrence of the new infections could not be attributed to the inefficient administration of the quinine. This was compulsory, and was administered by trustworthy persons, the infections being found to exist in persons who undoubtedly had taken the prescribed doses.

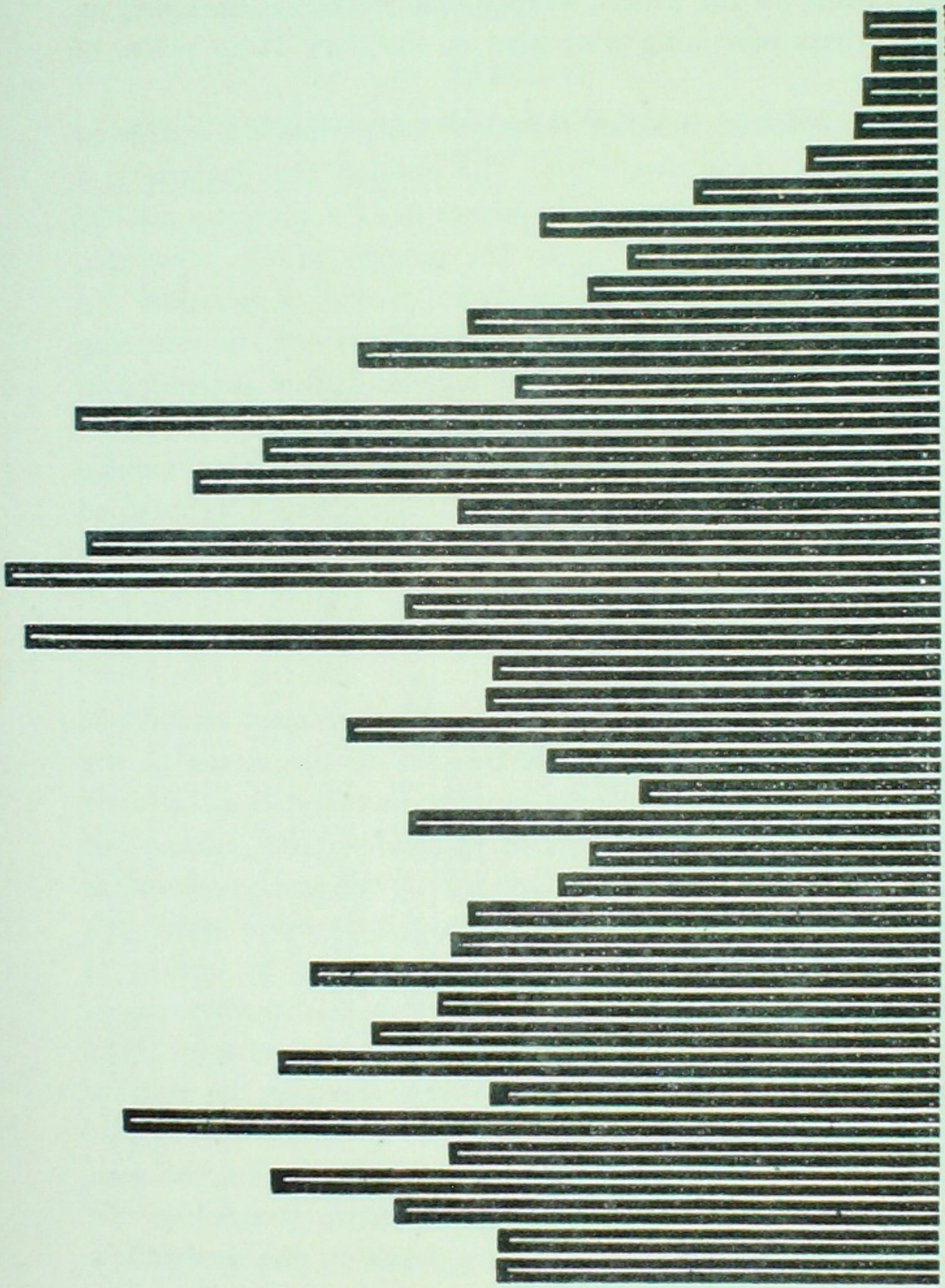
The second item of the prophylactic formula under consideration is intended to destroy the gametes in circulation, which prevents the infection of the mosquitos, which, as we know, can only occur when there are gametes in the periphery. This result was obtained by the daily and continuous administration of 50 centigrammes of quinine. It was proved by the microscope that after a time it was no longer possible to recognise the existence of gametes, whether of the benign or of the malignant (tropical) tertian. When the parthenogenesis of the gametes occurred, following on excessive work or heavy rains, 1 gramme of quinine was given daily, as a rule by intramuscular injection. It should be noted that no scabs appeared after the injections.

The above shows the necessity of carrying on the anti-malarial campaigns by persons capable of making the utmost use of the assistance furnished in such cases by the microscope.

The third prophylactic formula.—Dr Carlos Chagas, in his studies on the epidemiology of malaria, and on the biology of the *Anopheles* responsible for the transmission of the trouble within the zones, found that there were dwellings constituting regular hot-beds of malaria, and that such houses were invaded

¹ Incubation retarded by quinine is well known.—R. Ross.

TABLE I.



1864 1865 1866 1867 1868 1869 1870 1871 1872 1873 1874 1875 1876 1877 1878 1879 1880 1881 1882 1883 1884 1885 1886 1887 1888 1889 1890 1891 1892 1893 1894 1895 1896 1897 1898 1899 1900 1901 1902 1903 1904 1905 1906 1907 1908 1909 1910 1911

DESTRUCTION OF LARVAE

at night by the *Anopheles*, which stayed there till dawn, some withdrawing to the woods, whence they returned the following night, others remaining concealed in the dark damp places of the huts.

These infected mosquitos caused the permanently infected condition of these dwellings. The opinion that malaria is a disease commonly infectious in houses finds a perfectly feasible basis in arguments relating to the biology of the *Anopheles*, and in numerous facts arising from careful observation. In view of this Dr Chagas resolved to make systematic cleansing by sulphur vapours in such dwellings, and thus succeeded in sterilising these centres of infection.

These measures were always accompanied by quinine prophylaxis. But as an experiment Dr Chagas ascertained that the treatment of dwellings by sulphur was sufficient to prevent the infection of the persons who passed the night in such deadly centres of malaria, and who were not subjected to the action of quinine.

The fourth prophylactic formula.—This consists of indirect war against malaria by the destruction of the larvae of the *Anopheles*. This prophylactic system was tested at Rio de Janeiro, when the prophylaxis of yellow fever was carried out in the metropolis of Brazil. One part of the war on mosquitos was begun by drying up all temporary deposits of water, the destruction of the larvae in natural deposits by means of the cultivation of larvae-devouring fish (*Girardinus caudimaculatus*), by the protection of indoor water-cisterns from mosquitos, the petrolising of large sheets of water, the destruction of the *Bromelias epiphytes*, etc.

The results obtained were very favourable, as may be seen by an examination of Table No. 1, which we give below. In Table No. 2 is given the complete result of the anti-yellow fever campaign. The malaria figures do not show the same decrease as those for yellow fever, because in the table for malaria the cases existing in the urban hospitals, where

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patients were received from rural zones not influenced by the prophylactic campaign, appear.

TABLE II.

TABLE OF MORTALITY BY YELLOW FEVER IN RIO DE JANEIRO FROM
1872 TO 1909.

Years.	January.	February.	March.	April.	May.	June.	July.	August.	September.	October.	November.	December.	Total.
1872	1	1	3	1	...	1	8	16	71	102
1873	949	1,168	953	281	180	83	20	3	2	5	2	13	3,659
1874	16	51	168	297	165	69	25	5	4	6	10	13	829
1875	23	168	385	301	244	104	37	7	5	4	3	11	1,292
1876	122	319	1,405	1,019	395	147	41	12	6	4	4	2	3,476
1877	3	10	74	35	40	12	4	15	7	8	18	56	282
1878	156	420	331	130	60	23	18	4	8	10	3	13	1,176
1879	102	227	226	169	81	54	43	26	11	8	9	18	974
1880	138	496	471	273	115	58	18	9	5	5	13	24	1,625
1881	50	67	46	26	25	14	13	6	1	2	4	3	257
1882	3	13	23	27	12	8	1	1	1	89
1883	8	91	335	598	300	111	69	34	12	6	15	29	1,608
1884	79	208	253	210	68	15	12	6	2	...	6	4	863
1885	15	28	58	51	65	57	44	20	18	10	21	58	445
1886	201	351	483	304	74	23	9	2	...	1	...	1	1,449
1887	6	18	89	37	18	8	1	3	2	2	1	13	137
1888	30	39	29	128	116	89	50	18	15	16	49	108	747
1889	510	719	539	142	97	61	27	15	8	8	10	20	2,156
1890	57	103	187	169	109	38	22	6	4	5	9	10	719
1891	51	357	1,026	960	600	421	190	106	62	105	195	383	4,456
1892	1,006	1,290	1,404	410	147	35	14	1	1	1	2	1	4,312
1893	4	57	108	135	172	141	73	48	28	9	13	37	825
1894	371	1,351	1,978	695	305	114	14	12	3	2	...	7	4,852
1895	27	41	86	141	104	77	51	29	23	17	56	166	818
1896	524	731	1,002	445	136	37	20	9	4	4	9	8	2,929
1897	28	33	37	20	17	6	3	...	1	...	1	3	159
1898	22	90	255	287	186	78	65	34	19	13	8	21	1,078
1899	99	170	204	91	48	25	11	10	11	14	14	34	731
1900	42	64	78	61	36	28	9	7	5	6	4	4	344
1901	13	41	69	64	37	17	14	9	10	13	8	4	299
1902	32	64	165	178	154	131	79	50	27	10	18	76	984
1903	133	142	151	99	24	10	9	4	4	2	2	4	584
1904	2	7	7	8	10	4	4	1	1	...	3	1	48
1905	3	13	23	59	64	61	26	9	6	5	8	12	289
1906	6	9	6	8	2	1	2	...	1	3	1	3	42
1907	1	1	6	14	6	4	4	1	1	...	1	...	39
1908	1	3	4
1909	0

Table No. 3 shows the results obtained in the campaign undertaken at the time of the damming of the Rivers Xerem and Mantiquira for the water-supply of the city of Rio de Janeiro. The region through which canalisation work had to

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be extended was so devastated by malaria that 95% of the men employed in the work were attacked, the mortality being so heavy that the Government was obliged to abandon the first attempt. Work could not be resumed until the special prophylactic service for malaria had been organised, with the result that in a few months the works were completed and the city of Rio de Janeiro provided with an abundant supply of drinking water.

In the malarial zones of Brazil the following species of *Anopheles* are found:—*Cyclolepteron mediopunctatum* (Theob, Lutz), *Cyclolepteron intermedium* (Chagas), *Cellia argirotarsis* (Theob), *Cellia albimana* (Wied), and *Arribalzagaia pseudomaculipes* (Chagas).

These are undoubtedly the transmitters of malaria, as was experimentally shown by the characteristic forms of evolution of the plasmodium in them.

The following species are suspected of transmitting the malaria, so far as can be judged by epidemiological studies:—*Myzomyia lutzi* (Theob), *Cellia braziliensis* (Chagas), *Myzorhynchella lutzi* (Cruz), *Myzorhynchella parva* (Chagas).

As to the habits of the *Anopheles*, Dr Chagas noticed that as a rule they suck only at certain hours, at nightfall, when they come in swarms, or in the early hours of the morning. They disappear entirely during the day and night, at which time, therefore, there is no danger of men being infected by the contaminating mosquitos, or of the mosquitos being infected by sick persons with gametes. An exception to this rule is the *Cellia braziliensis* (Chagas), which attacks for preference during the day and in the sun, which fact shows the necessity of studying the *Anopheles* fauna of the region in which it is proposed to start an anti-malarial campaign.

Further details as to the Brazilian *Anopheles* and their relations with malaria may be found in the works of Dr A. Neiva, lately published (1909).

In dealing with the organisation of the systematic prophy-

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laxis against malaria a knowledge of the existence of the *Myzomyia lutzii* (Theob.) in the region is deserving of special attention.

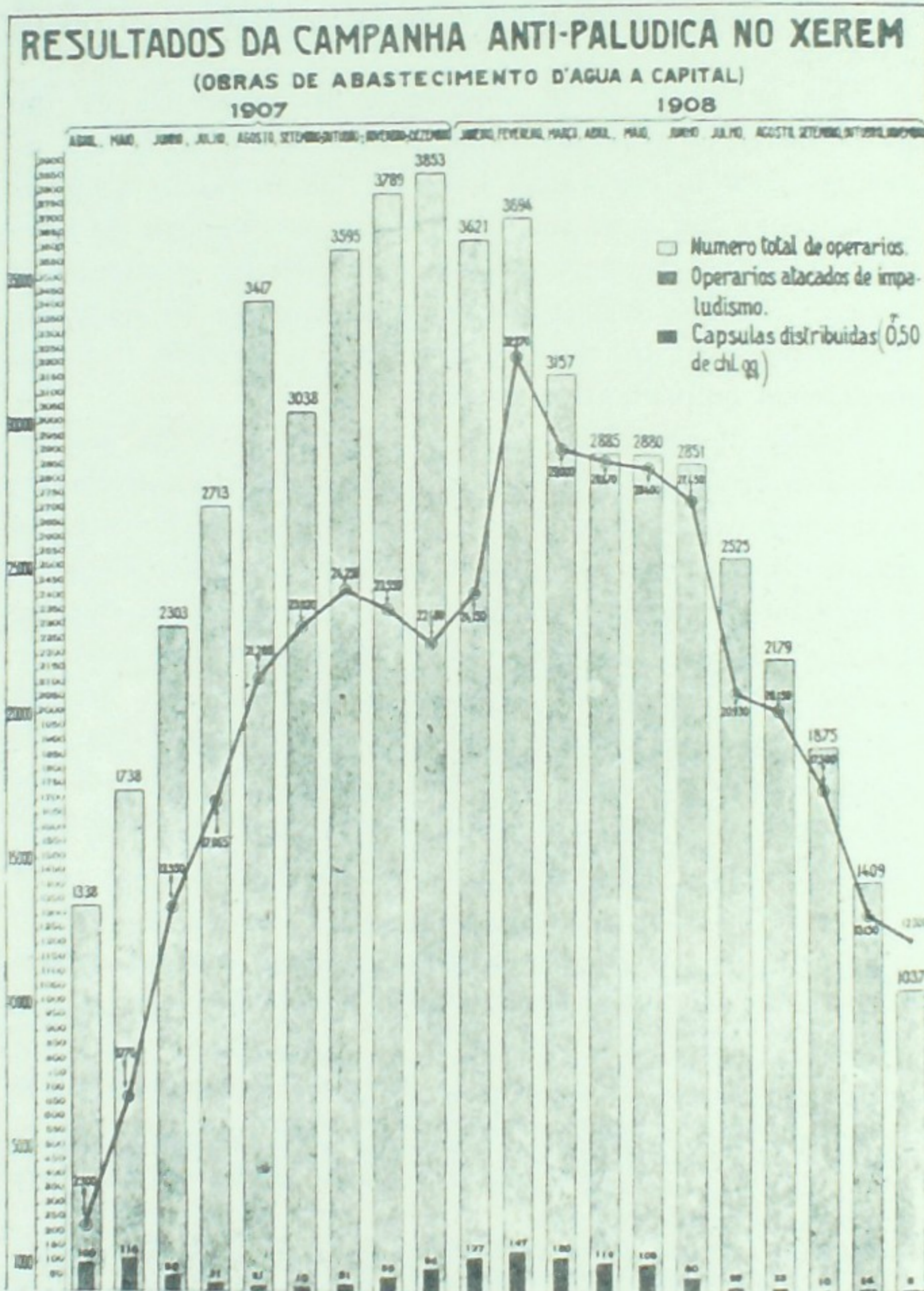
This mosquito, which appears to be responsible for the transmission of malaria in the regions where there are no swamps, lives in the waters found in the *Bromelias epiphytas* (Lutz, 1902), and is so small that it can pass through the wire-gauze of 1.5 mm. mesh, usually employed for protection of houses. For this further reason it is advisable to study the *Anopheles* fauna of the region before proceeding to instal mechanical prophylaxis of malaria.

Finally, it should be mentioned that the quinine prophylaxis has been carried out without the slightest inconvenience to the persons subjected thereto, there being a large number of people who have used daily 50 centigrammes of hydrochlorate of quinine for the last two years and ten months without showing the slightest bad effect from the employment of this medicine. Further, the phenomena of noises in the ears, etc., are not observed when the quinine is administered at meal times. No cases of hoemoglobinuria have been observed following on the administration of the quinine, and the few cases (8) of this morbid nature observed disappeared with the quinine treatment.

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TABLE 3.



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