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The Secretary of the Expert Committee on Malaria  
has the honour to communicate the following note on

## THE APPLICATION OF PYRIMETHAMINE IN RURAL AREAS

by

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It appears to be the general opinion that pyrimethamine is an excellent drug destined to be used for mass prophylaxis rather than treatment. Its major advantages are that it is tasteless and that only very small doses need be taken, which also makes it inexpensive in use.

1. We began in September 1951 to experiment with this drug in rural areas (VINCKE, 1952).<sup>1</sup> For a first series of experiments we chose a group of small villages, Kasongo and Mumema, about 70 kilometres to the north-east of Elizabethville and inhabited by about 200 people. These villages had not themselves been treated with DDT, but the area for a radius of 30 to 50 km had been disinfected. They were chosen on account of their very dense anopheles population.<sup>2</sup>

This first experiment showed us that after 15 weeks of more or less regular distribution the plasmodial index fell to zero.

The distribution was continued for 25 weeks in all, at the rate of 25 mg per week (see Table I) up to 18.2.52. We then - about the 20th of the month -

<sup>1</sup> VINCKE, I.H. Ann.Soc.Belge Méd.Trop. 1952, 32, 1. 91-99

<sup>2</sup> In another publication we mentioned that in the numerous observation posts where we noted the plasmodial index it was over 50% among the children in altitudes not higher than 1,100-1,200 m. Our figures are not very high in the case of Kasongo-Mumema but they correspond to those of the province as a whole.

tested the blood of children and adults. On 26 March, the index was still negative but from the month of April it began to rise again. Subsequently, some further distributions were made, but irregularly, since we ran short of the product on several occasions (see Table I). On 18 August the three villages were treated with DDT. A glance at Table I will show that, in spite of simultaneous treatment with DDT and Daraprim, after cessation of treatment the index reached a relatively high level again at the end of a few months. It is true that examinations were not very numerous, the zone having become more or less de-populated in the meantime. It is not easy to interpret the return to such a high plasmodial index: it is difficult to say whether it was caused by re-infection or relapse. It should be pointed out that from the month of April (cf April 1952 results) the sporozoite rate in mosquitos drops very considerably; transmission is still possible, however. It is surprising, nevertheless, to note that from the month of September 1952, the rate again fell to zero and that it rose again considerably at the end of two months in spite of the combined action of Daraprim and DDT. However, these villages were situated near the frontier and in view of the frequent population movement it was not possible to draw any definite conclusions.

We studied the sporozoite rate simultaneously with the plasmodial index. In the Upper Katanga as a rule the sporozoite rate varies according to the season: it increases from the month of September with respect to the two species A. gambiae and A. funestus and may reach a level of 10% to 14%, whereas it falls to zero during the colder months. After the administration of Daraprim, transmission fell rapidly to a negligible rate, particularly in comparison with a control area not very far from Kasongo-Mumema and also selected as a bush observation post on account of the very large anopheles population (Table V).

2. In October 1952 we chose another region, the Kundelungu plateau. This plateau, previously uninhabited, is at an altitude of 1,700 m and we have kept it under observation since 1949 without ever discovering a malaria vector of any kind. Since a company of livestock breeders has installed itself there, there has been an incessant and progressive immigration. The following procedure was adopted: all new arrivals were examined before and after a course of 20 Daraprim tablets, and subsequently every month (12.5 mg for children; 25 mg for adults). The experiment is

still proceeding but it can be seen (Table II) that two months after cessation of treatment the plasmodial index is still at 0, which was not the case at Kasongo-Mumema. A certain amount of malaria may be expected without concluding that there are relapses since the natives, even in this relatively isolated area, make constant journeys to the lower regions. We have, however, adopted every possible means to enable us to follow up the natives individually and we have also surrounded the plateau with a zone protected by DDT.

3. The Kundelungu zone constituted a kind of pilot zone for a larger-scale experiment which we undertook in the Baudouinville Territory. The Baudouinville Territories (Albertville and Nyunzu) have been treated with DDT since 1951. Since October 1952, pyrimethamine has been progressively distributed in the same doses in the Kundelungu district, once a week and to about 15,000 inhabitants and we expect to reach the figure of 20,000. It is obvious that an experiment on this scale could not be supervised as carefully as the previous ones and that it was necessary to persuade the natives to take their doses spontaneously. On the advice of the Administrator of the Territory, Mr. Bricot - to whom we owe a debt of gratitude in this connexion - we made the first distribution coincide with the DDT campaigns, and the vehicles of our agents bore the same distinguishing marks as the de-anophelization units. Thus, DDT - a very popular measure - publicized Daraprim and the idea was found to be very ingenious since the natives call Daraprim "the DDT medicine".

It could not be expected that all the natives of the region would cover long distances on foot, particularly in the rainy season, in order to collect their doses individually. The total dose was therefore collected by delegates from the villages, without coercion, and a distribution was then made in the villages themselves with relatively little surveillance. It would seem that the natives followed our instructions carefully for in February 1953, i.e. after a distribution of 15 to 16 Daraprim tablets, the index was practically zero. In fact, the only positive case detected seems to have been a native who had never taken Daraprim (Table III).

The results in this case must be compared with the indices in the Kirungu "chefferie" which is composed of a series of villages either right on the lakeside or on the plateau. The September 1949 index (70.7%) is an overall figure, i.e. it covers

the natives on the lakeside, where anophelism is certainly more intense, and those inhabiting the plateau at about 1,100 m, where the anopheles population is much smaller. The September 1951 index (46.3%) refers only to the plateau inhabitants, whereas the February 1953 index (0.82%) covers the inhabitants of the plain bordering on the lake.

4. Finally, a fourth experiment was carried out in the Kasenga region (see Table IV). Dr. Mac Call, medical officer of the region had informed us that certain acute cases had been resistant to Daraprim and we wondered whether there were resistant strains in that region; it was for this reason that we also commenced distribution of Daraprim under the direction of this colleague, and it will be seen that the results in the Chibambo region are as promising as elsewhere.

#### Summary and conclusion

The next months will provide a great deal of information, but already the results are very encouraging in so far as the plasmodial indices and sporozoite rates are concerned. We shall shortly know the periodicity which must be adopted in prophylactic treatment. The sporozoite rate has obviously not fallen completely to zero and a few infected A. funestus have always been found. But are these human sporozoites? We have reason to believe that there is a reservoir of non-human virus capable of maintaining a slightly positive sporozoite rate; it is not unlikely that A. funestus and A. gambiae are also infected from this reservoir.

The Kasongo-Mumema experiment made it possible to assess the effects of chemo-prophylaxis of malaria in man and in anopheles; on account of the geographical situation the experiment was not very conclusive as far as persistence of results was concerned. The experiments in the Kundelungu area and in the Kirungu "chefferie" provided data of another kind: in the Kundelungu district we are dealing with a carefully supervised population and there is no anophelism; in the Baudouinville Territory, DDT did not enable us to completely eliminate anophelism and we saw that it would be difficult to pursue this aim.

The effect of residual anophelism is compensated for by greater extent of the area treated and we believe that the two experiments are complementary; we shall not know for some months whether the combined effect of DDT application and chemo-prophylaxis permits us to hope that enduring eradication of malaria may be achieved in rural areas. Interesting conclusions may be drawn in connexion with the confidence placed in European medicine by the natives.

Finally, in these experiments there was no sign of poisoning or of intolerance.

I. PLASMODIAL INDICES FOR KASONGO-MUMEMA

Date Daraprim	Date examination	General total All ages			Total Children 4-11			Total Children		
		Ex.	+	%	Ex.	+	%	Ex.	+	%
	14. 4.51	53	35	66.04	28	18		53	35	66.3
	3. 9.51	183	40	21.86	51	23		77	29	37.66
	24. 9.51	172	11	6.4	49	4		75	5	6.66
	1.10.51	170	6	3.53	51	1		79	3	3.79
DARAPRIM	22.10.51	158	4	2.53	38	1		63	2	3.17
	19.11.51	149	2	1.34	37	1		67	1	1.49
	17.12.51	161	0	0	34	0		71	0	0
	21. 1.52	170	0	0	50	0		78	0	0
	26. 2.52	146	0	0	39	0		62	0	0

Total dose:  
25 tablets

	26. 3.52	146	0	0	36	0		62	0	0
	April 52	138	24	17.4	39	11	28.2	62	17	27.4
	May 52	135	17	12.59	37	6	16.21	62	11	17.74
	June 52	115	38	33.04	29	13	44.82	49	24	48.97
29/7 to 18/8/52	July 52	127	33	25.98	33	14	42.4	43	18	41.86
	August 52	49	4	8.16	13	1	7.69	20	2	10.-
DDT	9.52	99	0	0	26	0	0	38	0	0
7/10 to 4/11/52	10.52	112	1	0.89	30	0	0	48	1	2.08
	2.12.52	104	2	1.92	23	0	0	38	2	5.26
	4.53	90	18	20.-	22	9	40.90	36	14	38.8

II. KUNDELUNGU

Date Daraprim	Date examination	General total All ages			Total Children 4-11			Total Children		
		Ex.	+	%	Ex.	+	%	Ex.	+	%
New arrivals		429	97	0	35	16		133	63	47.44
End of Daraprim		178	0	0	7	0	0	40	0	0
1 month after		133	0	0	7	0	0	30	0	0
2 months after		95	0	0	7	0	0	22	0	0

Total dose = 20 tablets

III. "CHEFFERIE" OF KIRUNGU BAUDOINVILLE (MOBA)

(Territorios treated with DDT since 1951)

	Sept. 49				208	147	70.7			
	Sept. 51				173	81	46.8			
<u>After Daraprim</u>	Feb. 53	150	1		121	1	0.82	150	1	

Total dose = 15-16 tablets

IV. CHIBAMBO (KASENGA)

	July 52				192	126	65.6			
	Nov..52				312	190	60.9			
<u>After Daraprim</u>	June 53				194	1	0.51			

Total dose = 6-7 tablets

V. SPOROZOITE RATE

	KAIJULU - DEMONS. AREA						KASONGO-MUTEMA - ZONE DARAPRIM FROM 3 SEPT. 51 TO 18 FEB. 52					
	A. funestus			A. gambiae			A. funestus			A. gambiae		
	Ex.	+	%	Ex.	+	%	Ex.	+	%	Ex.	+	%
April 1951	-	-	-	-	-	-	56	4	7.14	2	0	-
September - December 1951	-	-	-	-	-	-	486	4	0.82	51	0	0
November - December 1951	329	11	3.34	44	0	-	-	-	-	-	-	-
January 1952	249	4	1.6	82	4	4.87	495	1	0.2	282	0	0
February 1952	356	8	2.24	86	4	4.65	440	0	0	239	0	0
March 1952	353	13	3.68	139	6	4.31	1419	2	0.14	279	0	0
4 April 1952	79	2	2.53	26	3	11.53	143	0	0	82	0	0
Total	1366	38	2.78	377	17	4.5	2983	7	0.23	933	0	0
		Ex.	+	%			Ex. <sup>1</sup>	+	%			
Total anopheles		1743		55		3.15	3916		7			0.17

<sup>1</sup> After Daraprim

(The original manuscript shows, for Tables I and II, classification of haematological examinations by age-group. This has been omitted here in order to make the two Tables easier to read. Ed.)