

AN EIGHTH YEAR'S OBSERVATIONS ON MALARIA IN PANAMA

H. C. CLARK AND W. H. W. KOMP

From The Gorgas Memorial Laboratory, Panamá, R. de Panamá

The observations made during the past year (September, 1937 to August, 1938) are a continuation of those begun in 1930, and carried on uninterruptedly since that time. Our previous reports (1-7) contain the details of the location, terrain, type of population involved, their living-conditions, and the observations on malaria as it occurs in this group in Panama. The primary object of our studies has been to evolve a method of malaria control applicable to a native population inhabiting the tropical lowlands of the Americas, where conditions are such that antimosquito measures cannot be used. Such a method, if feasible, could be applied by commercial organizations operating in the American tropics, which are dependent upon a local source for their labor-supply.

We first proceeded upon the supposition that it was possible to reduce malaria by an attack on the gametocyte-carriers, which are most numerous in young children and adolescents, and which constitute the "seed-bed" from which new infections might be spread to the rest of the population. In this attack on the "seed-bed" we used several drugs and combinations of drugs, such as quinine sulphate, atabrine, and plasmochin. "Our experience over several years forced us to conclude that there is little hope of destroying this "seed-bed." Two factors combine in causing this failure. The first is that not all carriers of the disease can be reached and treated adequately. Some are missed at every survey, and these are apparently sufficient in number to keep up malaria transmission. The other factor is the relative inefficacy of the drugs used; none of them, alone or in combination, is able to destroy completely malaria

infection in large numbers of cases, so that relapses are common. Our experience during the winter of 1935, when an epidemic of malaria occurred in all the six towns under observation, after 5 of them had been under intensive treatment with atabrine for two years, led us to conclude that malaria exhibited cyclical variations in intensity in Panama, and that drug control methods were hopeless in attempting to control such variations. We also concluded that we had destroyed a certain amount of natural immunity by treating all subclinical cases, thereby causing an increased number of clinical cases in the treated groups, when an epidemic later occurred" (7).

The observations contained in this present report are a continuation of those previously reported, and no new evidence has arisen to alter our conclusions; the present report is merely a progress report based on the results of the same procedure in examination and treatment as we have used during the past several years.

It was found impracticable to continue the blood-surveys in the group formerly used as a control, on which quinine sulphate was provided for treatment, but in which no attempt at supervision of treatment was made. Our records showed that consecutive monthly examinations of this group were increasingly hard to obtain, and also that a very large proportion of those examined were transients. Data from such a group were almost valueless for our purposes, so that the group was abandoned as a control. During the past year, one large town, New San Juan, of about 500 people, was treated under supervision with quinine sulphate in capsules, followed by a 5-day course of plasmochin simplex; the other group, consisting of the inhabitants of five villages along the banks of the Chagres River, were treated under supervision with atabrine and plasmochin. As a check on the rates in the treated areas, one survey was made in July of about 200 school children in the former control area of Chilibre.

SURVEY METHOD

All the inhabitants of the two areas who can be reached, are surveyed every month, using the thick-film technique of Barber

and Komp (8). The staining and examining of the films is done by experienced technicians, many of whom have been doing this work since the beginning of the observations.

TREATMENT METHODS

The population of the area under observation was divided into two groups. The first, living in the towns of Agua Clara, Santa Rosa, Guayabalito, Las Guacas, and Gatuncillo, and comprising about 700 "regular" inhabitants, was treated with atabrine 0.1 gram three times a day for a period of five days, followed by plasmochin simplex 0.01 gram twice a day over a succeeding period of five days. This treatment was administered to all those found positive in the monthly surveys. The second group consisted of approximately 550 inhabitants of the village of New San Juan, situated on a small tributary of the Chagres, about 2 miles from the nearest Chagres River village. Here quinine sulphate, 15 grains daily for 5 days, is administered by two native women to all the positives found during the monthly surveys. During the following week, plasmochin simplex, 0.01 gram twice a day for 5 days, is administered by a "supervisor," an intelligent native man who has been doing the same work for a number of years past. One of us visits all the towns one day a week, during the period of plasmochin administration.

The villages under atabrine treatment are all relatively easy of access, with the exception of Agua Clara, a town of about 100 people. The village of New San Juan is rather scattered, and coöperation and supervision are not as good as in the atabrine-treated towns. In spite of this fact, the annual rate in New San Juan, 6.6, is slightly better than the rate of 6.7 in the atabrine-treated towns. The principal difference between the two groups lies in the number of persons repeatedly positive after they are presumed to have taken treatment. In the atabrine-treated group only 14 persons out of 203 who were positive in one survey, were positive during the succeeding month, a percentage of 7.0. In New San Juan, 17 persons out of 116 who were positive in one survey, were positive during the succeeding month, a percentage of 20.6. We believe that this greater percentage of

persons who were positive for two successive months is due to poorer coöperation and less supervision, rather than to any superiority of atabrine over quinine in ridding the blood of parasites.

RESULTS OF MALARIA SURVEYS IN 1937-38

Table 1 shows the monthly malaria parasite rate, compared with the rainfall as recorded at Madden Dam, a few miles north-east of the area in which our villages are located. Totals for

TABLE 1

Monthly malaria parasite rates compared with rainfall at Madden Dam

MONTH	CHAGRES VILLAGES	NEW SAN JUAN	MADDEN HIGHWAY	RAINFALL AT MADDEN DAM
				<i>inches</i>
September, 1937.....	6.8	8.5		10.87
October, 1937.....	6.5	7.5		13.51
November, 1937.....	5.0	8.9		17.53
December, 1937.....	5.7	4.5		18.51
January, 1938.....	4.8	11.7		0.20
February, 1938.....	7.2	9.1		0.06
March, 1938.....	6.9	4.8		0.63
April, 1938.....	4.3	3.4		3.87
May, 1938.....	5.9	6.7		13.26
June, 1938.....	8.6	6.8		15.92
July, 1938.....	9.1	3.2	16.4*	7.97
August, 1938.....	11.3	4.8		9.80
Totals.....	6.7	6.6	16.4	112.13
Totals, 1936-37.....	7.4	14.4	16.2	88.33
Totals, 1935-36.....	9.1	12.3	18.5	110.13

* One survey of school children from former control area of Chilibre.

three previous years are given at the bottom of this table. As before, no seasonal variation occurred during the past year, which could be correlated with the seasonal rainfall. It is of interest to note that the rainfall was greater during the past year than it was during 1936-37, while the malaria rate as a whole was considerably lower. As stated previously, mosquito production is not dependent on rainfall in our areas, as most of the breeding occurs in the vegetation-covered lagoons and backwaters of the Chagres River, which are full the year round.

A total number of 1557 examinations were made during the year, parasites being found in 366 cases, a rate of 23.5 per cent, which is considerably lower than the rate of 35.8 per cent found during the year 1936-37.

Table 2 shows the parasite rate for 1270 persons forming the average number of permanent inhabitants in the two treated groups. The Chagres group received atabrine and plasmochin, and the inhabitants of New San Juan received quinine sulphate and plasmochin. These two groups are divided into adults and children, and the rates are cumulative for the year. The results of the single survey of the school children in the former control group are also included for purposes of comparison, but the number examined is not included in the total of 1270.

TABLE 2

*Parasite index. Adults (over 15 years) versus children (15 years and under).
Cumulative result for the year*

LOCATIONS	ADULTS			CHILDREN		
	Exam-ined	Positive	Per cent	Exam-ined	Positive	Per cent
Chagres Villages (5).....	399	104	26.3	310	99	31.9
New San Juan.....	303	49	16.1	258	67	25.9
Madden Highway school children*.....	18	3	16.6	269	44	16.3

* A single survey of school children from former control area.

Table 3 shows the number of persons examined in the monthly surveys 1 to 5 times; those examined in the surveys 6 to 11 times, and those examined at all 12 of the consecutive monthly surveys during the year. As might be expected in a native population continuously exposed to malaria infection, the more times an individual is examined, the more times he is likely to be found positive. Table 3 well indicates that the year just past was a continuation of the period of low incidence, the downswing of the cyclical curve, which had begun in the spring of 1935, and has continued to the end of the present year.

In table 4 the cumulative malaria rate by age-groups is given. The total number of persons examined, even if only surveyed at one monthly examination, is given, the grand total, including

the July survey of the untreated Chilibre school children, being 1,557.

The striking similarity in rates for the past three years, as shown at the bottom of table 4, is further evidence, if such be needed, of the fact that we are now in a period of low incidence.

TABLE 3
Parasite index. Three survey groups. All areas

LOCATIONS	1 TO 5 SURVEYS			6 TO 11 SURVEYS			12 COMPLETE SURVEYS		
	Exam-ined	Posi-tive	Per cent	Exam-ined	Posi-tive	Per cent	Exam-ined	Posi-tive	Per cent
Chagres Villages...	341	56	16.4	276	112	40.6	92	35	38.0
New San Juan.....	348	44	12.6	134	44	32.8	79	28	35.4
Madden Highway*	287	47	16.4						
Totals.....	976	147	15.1	410	156	38.0	171	63	36.8

* One survey of school children in former control area.

TABLE 4
Cumulative incidence of malaria by age-groups. All groups combined

AGE-GROUP	CHAGRES			NEW SAN JUAN			MADDEN HIGHWAY*			TOTALS		
	Exam-ined	Posi-tive	Per cent	Exam-ined	Posi-tive	Per cent	Exam-ined	Posi-tive	Per cent	Exam-ined	Posi-tive	Per cent
0-5	143	31	21.6	129	32	24.8	2	1	50.0	274	64	23.3
5-10	107	40	37.4	80	15	18.8	141	22	15.6	328	77	23.4
10-20	151	58	38.4	108	39	36.1	139	24	17.2	398	121	30.4
20-40	185	47	25.4	149	25	16.7	5	0	0.0	339	72	21.2
40-60	94	21	22.3	66	4	6.1	0	0	0.0	160	25	15.6
Over 60	29	6	20.7	29	1	3.4	0	0	0.0	58	7	12.1
Totals.....	709	203	28.6	561	116	20.7	287	47	16.4	1,557	366	23.5

* One survey of school children from former control area.

Total for 1936-37..... 639 223 35.0 600 222 37.0

Total for 1935-36..... 688 244 35.4 710 239 33.6

The low rates obtained in the age-group 0 to 5 years is further evidence of this, for the young children usually suffer greatly during periods of high incidence.

Table 5 shows the cumulative malaria rate in all persons who were examined in 12 consecutive monthly surveys. The data are presented by age-groups. The percentage of persons ex-

amined 12 times during the year was slightly lower than it was during the previous year.

It is interesting to observe that of the 171 persons examined at every monthly survey, there were 108, or 63.2 per cent, who were negative for parasites at every examination. This is a remarkable showing, when compared with some of the rates obtained in a similar group in the early days of our work.

The highest incidence of parasites in the individuals examined at every monthly survey was among the age-group between 10 and 20 years. The same distribution was noted during the year 1936-1937. The per cent positive in the age-group 0 to 5

TABLE 5

Individuals surveyed 12 consecutive months. Entered by age-groups

AGE-GROUPS	NEW SAN JUAN		CHAGRES		TOTALS		
	Examined	Positive	Examined	Positive	Examined	Positive	Per cent
0-5	40	14	27	7	67	21	31.3
5-10	18	7	30	12	48	19	39.5
10-20	9	5	10	5	19	10	52.6
20-40	6	1	15	7	21	8	38.1
40-60	4	1	7	3	11	4	36.3
Over 60	2	0	3	1	5	1	20.0
Totals.....	79	28	92	35	171	63	36.8

years was approximately the same as in 1936-1937, when it was 30.2 per cent.

As has been stated in our previous reports, we cannot distinguish between new infections and relapses in recording the individuals found parasite-positive. However, we continue to find malaria parasites slightly more frequent in certain individuals, who are known to us from their past histories as more or less continuing to harbor parasites, in spite of treatment. Table 6 shows the number of times 63 persons, examined in 12 consecutive surveys, and found positive at least once, were found with parasites during the course of these 12 surveys. In this table all persons, whether in the quinine-treated or the atabrine-treated group, are included.

In addition, there were 108 individuals examined at all 12 surveys, who were consistently negative throughout.

The fact that such a number of individuals were repeatedly positive is an indication that many parasite positives are cases of relapse, and not of new infections.

TABLE 6

Individuals (63) showing malaria who were surveyed in 12 consecutive monthly surveys

Number of cases

NUMBER OF TIMES POSITIVE	CHAGRES VILLAGES (ATABRINE-PLASMOCHIN)	NEW SAN JUAN (QUININE-PLASMOCHIN)	TOTALS
1	26	14	40
2	5	5	10
3	3	4	7
4	1	3	4
5	0	2	2
Totals.....	35	28	63

TABLE 7

Individuals (106) examined in 10 monthly surveys

NUMBER OF TIMES POSITIVE	CHAGRES VILLAGES (ATABRINE-PLASMOCHIN)	NEW SAN JUAN (QUININE-PLASMOCHIN)	TOTALS
1	40	24	64
2	12	6	18
3	9	7	16
4	2	2	4
5	1	3	4
Totals.....	64	42	106

If the individuals examined in 10 of the 12 surveys are tabulated, the number repeatedly positive is even more evident. This is shown in table 7.

In addition, there were 162 persons who were consistently negative in the 10 monthly surveys at which they were examined.

The percentages found positive more than once were 37.6 for the Chagres villages, and 42.9 per cent for the village of New San Juan.

OBSERVATIONS ON TYPES OF MALARIA PARASITES, CRESCENT INCIDENCE, AND INTENSITY OF INFECTIONS

There has been a slight change in the presentation of the material dealing with the type of malaria parasite found in the surveys. Instead of counting each positive slide found, the results are based on the number of individuals found positive. Table 8 shows the species of parasites encountered during the surveys.

TABLE 8

Species of malaria parasite found in individuals during the year

SPECIES OF PARASITE	CHAGRES VILLAGES	NEW SAN JUAN	TOTALS
<i>P. falciparum</i>	144	83	227
<i>P. vivax</i>	33	16	49
<i>P. malariae</i>	4	6	10
<i>P. falciparum</i> and <i>P. vivax</i>	19	7	26
<i>P. falciparum</i> and <i>P. malariae</i>	3	3	6
<i>P. vivax</i> and <i>P. malariae</i>	0	1	1
Total.....	203	116	319

TABLE 9

Incidence of each species taken separately

SPECIES	NUMBER	PER CENT OF TOTAL
<i>P. falciparum</i>	259	73.6
<i>P. vivax</i>	76	21.6
<i>P. malariae</i>	17	4.8
Total.....	352	100.0

The incidence of each species, whether or not it occurred mixed with another, is shown in table 9.

The percentage of *P. falciparum* infections has remained quite stable at slightly less than 75 per cent, since the year 1935-1936. There was a slight relative increase in *falciparum* infections during the epidemic of 1935. The predominance of *falciparum* infections is doubtless owing to the strong negroid strain in the population under observation.

The crescent rate in *falciparum* infections has also remained relatively stable over these years, varying from 22 to 44 per cent. The rate was somewhat higher in the quinine-plasmochin treated town of New San Juan during the past year. This cannot be explained on the basis that more heavy infections occurred in this town, as a later table will show that the percentages of such infections were nearly equal in the two groups.

Table 10 shows the crescent rate in the two groups. Crescents were counted once whenever they appeared in a positive blood-

TABLE 10
Crescent rate in P. falciparum cases

LOCALITY	NUMBER OF FALCIPARUM CASES	NUMBER OF CRESCENT CARRIERS	PER CENT OF CRESCENT CARRIERS
Chagres Villages.....	93	34	36.6
New San Juan.....	166	80	48.2
Totals.....	259	114	44.0

TABLE 11
Heavy infections found in surveys

LOCALITY	NUMBER OF INFECTIONS FOUND	NUMBER OF HEAVY INFECTIONS	PER CENT OF HEAVY INFECTIONS
Chagres Villages.....	203	32	15.7
New San Juan.....	116	23	19.8
Totals.....	319	55	17.3

film, regardless of whether the individual was positive for crescents more than once.

Table 11 gives the incidence of "heavy" infections found in the surveys. A "heavy" infection is one in which one or more parasites are present in each thick-film microscope field. The rate is approximately the same as that found last year, which was 16.3 per cent.

INFECTIONS IN INFANTS

Additional evidence that the year just past was a season of low transmission was obtained by the examination of 53 infants,

all under one year of age. Only 1 of these, a child of 4 months, was found infected with *P. falciparum*. Not all of these infants were surveyed during every month, but it is believed that few positives were missed, as the mothers usually call our attention to any children who are ill; these are then examined immediately. The rate of infection found in these infants, 1.9 per cent, is the lowest found during the past eight years, and is a reflection of the general low parasite rate found in the whole region during the past year.

EVIDENCE FOR AND AGAINST CYCLICAL VARIATIONS IN MALARIA INCIDENCE IN PANAMA

One of the purposes in continuing our observations along the present lines is to secure evidence regarding the malaria cycle in Panama. The period between peaks of malaria incidence in the past has been about two or three years. However, since the last peak of the epidemic in the winter of 1935, the incidence of the disease has decreased steadily, and no epidemic has occurred. In this connection, it may be of interest to note that several scattered observations made in the Panama Canal Zone all show that the general malaria rate has been exceedingly low during the past year. The hospital admission rate of Panama Canal employees for the first eight months of 1938 was 12.2 per thousand, the lowest rate since 1930. A recent survey of natives living along the Chiva-Chiva Trail, in the Canal Zone, showed no infections among 184 examined. During the year from August, 1937 to July, 1938 inclusive, 1,069 examinations were made on an average of 89 persons living in two small unsanitated settlements on the Atlantic coast of the Canal Zone. These monthly surveys showed rates ranging from zero to 8.0 per cent, with a yearly average of 3.2 per cent. Seven years ago the surveys in these same localities showed rates averaging 45 per cent. A single survey of the school children living in our former control area showed their rate, 16.6 per cent, to be the same as for the group in the Chagres villages that was examined 1 to 5 times during the year, and to be the same as for the control group during 1936-1937 (see table 3). All these facts are evidence that we are still experiencing the downswing

of the malaria cycle. That an increase may be expected seems inevitable, as new strains of the parasite are being introduced into our areas continually, and there has been no change in the mosquito fauna or the living-habits of the inhabitants of our towns.

Evidence against the theory of a definite cyclical variation in malaria, operative over a wide area, is contained in the results of two surveys made during the past year in two widely separated localities in Panama. The first survey, made in March 1938, was of the personnel of the Santa Maria Lumber Company, living in sea-coast towns and camps about 220 miles west of Panama City, on the Pacific. In this locality, 338 persons were examined, of which 109 were found positive, a rate of 32.2 per cent. This is somewhat above the normal rate usually found in such aggregations of people in Panama.

In July, 1938, the inhabitants of six villages along the banks of the Tuira River, in the Province of Darien, were examined for malaria. At this time, 496 persons were examined, of whom 108 were found positive, a rate of 21.8 per cent. These villages are very similar, as regards the surrounding topography and other circumstances, to the Chagres River villages. The rather high malaria rate is evidence that not all of the reduction noted in our Chagres River malaria rates is due to a natural decline alone.

It seems quite probable, however, that the continuous treatment of the positives found in our surveys has served to accelerate the rate of any natural decline, and hence to lower the rate beyond the point to which it would normally have reached, unaided. At present we have very little clinical malaria among our villagers, the disease having declined to such an extent that it causes them little inconvenience. That we can restrain the disease within present limits when the normal upswing of the curve occurs is, however, extremely unlikely. We fear that the long period of comparative freedom from infection may have rendered the population less able to resist the effects of an epidemic, and we expect a rise in clinical malaria, as well as in general infection rate, when the next peak of the disease occurs.

SUMMARY

As mentioned in our seventh report "the time should not be far distant when another epidemic outbreak is to be expected." However, another year has passed since these words were written, and the curve has continued to descend. Therefore the methods used during the past year were practically the same as those in force during the past three seasons, and it is proposed to continue them during the next year of observation. However, we have had to abandon one group of people formerly used as a control, for the reasons cited in this report. The two groups used during the past year were treated with atabrine and plasmochin, and with quinine and plasmochin. The results, as shown in percentages of infection, did not favor either combination. More adequate supervision of the atabrine-plasmochin group undoubtedly accounts for the somewhat better results of treatment obtained.

As in past years, no correlation with rainfall is shown in our monthly parasite rates. The blood-parasite rate, cumulative for the 12 months, shows that slightly fewer individuals examined at every monthly survey had parasites in their blood during the past year (36.8 per cent) than in a similar group in 1936-1937 (43.5 per cent) (see table 3).

The parasite rates during the past year are the lowest so far recorded. These low rates are believed to be caused by a combination of the normal decline in rates, and treatment of all positives.

The incidence of the various species of parasites found in the positives was nearly the same as in previous years, with *P. falciparum* constituting nearly 75 per cent of all types found.

Transmission, as might be expected, was not active during the past year, as is shown by the fact that only 1 infant under a year of age was found infected, of a total of 53 infants examined. No toxic results have followed the use of atabrine during the year or in any previous year of our work.

Under our present conditions, the method of control we have adopted has been successful in reducing to the vanishing point

clinical illness from malaria. However, we have not been successful in completely eradicating the disease, and it is extremely doubtful whether under our conditions such a result will be possible. The ever-present mosquito, the newly-arrived carrier, the year-long transmission season, all conspire to prevent complete success, but undoubtedly much has been accomplished in reducing the ravages of the disease, and doubtless our methods would have wide applicability under similar conditions.

REFERENCES

- (1) CLARK, H. C. AND KOMP, W. H. W.: Observations on malaria incidence in some unsanitated river villages in the Republic of Panama with special reference to proposed construction projects in the canal zone. *So. Med. Jour.*, **25**, 642-647, 1932.
- (2) CLARK, H. C. AND KOMP, W. H. W.: A second year's observation on malaria in some unsanitated Chagres River villages with special reference to the use of quinine and plasmochin. Privately printed by Gorgas Memorial Laboratory, Panama, R. de P. 1932.
- (3) KOMP, W. H. W. AND CLARK, H. C.: A third year's observation on malaria in Panama with special reference to control with atebtrin. *Amer. Journal Trop. Med.*, **14**, 381-406, 1934.
- (4) KOMP, W. H. W. AND CLARK, H. C.: A fourth year's observation on malaria in Panama with special reference to control with atebtrin and plasmochin. *Amer. Jour. Trop. Med.*, **15**, 131-154, 1935.
- (5) KOMP, W. H. W. AND CLARK, H. C.: A fifth year's observation on malaria in Panama with reference to the failure of atebtrin to control an epidemic. *Amer. Jour. Trop. Med.*, **16**, 109-131, 1936.
- (6) CLARK, H. C. AND KOMP, W. H. W.: A sixth year's report on malaria in Panama (Chagres Valley) with reference to drug control. *Amer. Jour. Trop. Med.*, **17**, 59-77, 1937.
- (7) CLARK, H. C. AND KOMP, W. H. W.: A seventh year's observation on malaria in Panama. *Amer. Jour. Trop. Med.*, **18**, no. 3, pp. 271-288, 1938.
- (8) BARBER, M. A. AND KOMP, W. H. W.: Method of preparing and examining thick blood films for the diagnosis of malaria. *Public Health Reports*, **44**, 2230-2341, 1929.