A SEVENTH YEAR'S OBSERVATIONS ON MALARIA IN PANAMA¹

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The observations here reported have been in progress over a period of seven years. Our previous reports on the subject (1, 2, 3, 4, 5, and 6) should be referred to for details regarding the location and topography of the area under observation, the type of inhabitants, the conditions under which they live, and other pertinent data. The object of our continued observations has been to devise a method of malaria control suitable for use by commercial organizations operating in tropical lowlands of the Americas, which may not be able to use anti-mosquito measures, because of their high cost. Our goal was to find a method whereby labor efficiency might be increased and labor forces stabilized, by controlling malaria, which is one large factor reducing such efficiency in the tropics.

Our original plan envisaged an attack upon the "seed-bed" of malaria infection, which exists in the young children and adolescents among the population. We had thought to destroy this "seed-bed" by the use of anti-malarial drugs, and in such an attempt quinine sulphate, atabrine, and plasmochin have been used. 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.

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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 numerous. Our experience during the winter of 1935, when an epidemic of malaria occurred in all the 6 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.

The present report contains no new conclusions, as it is merely a progress report based on a similar series of monthly blood surveys made in the same groups of people, under the same conditions as existed in previous years. One small village, called Agua Clara, was added to the six villages under observation in previous years. This contained only 40 people, all of the same general type as those living in the original six villages. The malaria rate in these people closely approximated that found in the other villages under atabrine-plasmochin treatment. The inhabitants of the seven villages under observation were divided into three groups; 5 villages on the banks of the Chagres River, below Madden Dam, just outisde of the Canal Zone boundary, were considered as one unit, and were treated with atabrine and plasmochin. The inhabitants of another large village were treated as one unit, with quinine sulphate and plasmochin. The third group, inhabiting a number of villages scattered along the Madden Highway, some 5 or 6 miles from the atabrine-treated villages, was used as acontrol, quinine sulphate being used here, without supervision of treatment.

DESCRIPTION OF THE THREE GROUPS

The first group, consisting of approximately 400 persons, lives in five villages on or near the banks of the Chagres River, between the Madden Dam and the eastern boundary of the Panama Canal Zone. The villages are Santa Rosa, Guayabalito, Gatuncillo, and Las Guacas, on the river banks, and Agua Clara (40 persons) some distance away from the river. The persons found positive for malaria parasites in regular monthly surveys in this group were 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.

The second group consisted of approximately 400 people living in the village of San Juan, which is located on the banks of the Gatuncillo River, a tributary of the Chagres, about 2 miles from the Chagres basin. Here quinine sulphate, 15 grains daily for 5 days, is administered by two native women, to all parasite positives who can be reached. During the following week, plasmochin simplex, 0.01 gram twice a day for 5 days, is administered under the observation of a "supervisor," an intelligent native man who has assisted us in the work for the past five years. One of us also visits this village one day a week, during the period of plasmochin administration. This village of San Juan is somewhat scattered, making access to the positive cases rather difficult, and cooperation and supervision are not as good as in the atabrine-treated towns, which are under better control. We believe that this fact accounts for the higher percentage of positives found here, as compared with the atabrine-treated group.

The third group consists of the inhabitants of a number of villages located on the southern slope of the Chagres valley, some 5 miles from the river, along the concrete highway leading from Madden Dam to Panama City. There is a great deal of moving about among these people, and the proportion of transients surveyed monthly is high. For this reason, the group is not as satisfactory a control as we would like. But it is at present the most available control group we have; treatment is unsupervised, as quinine sulphate in capsules, with a name-list of all positives is left with the local village officer of Chilbre, one of the towns. Those desiring treatment receive sufficient quinine sulphate from him for a course of 15 grains daily for 5 days, and take it as they please. No one of our staff visits this area except the tech-

nician who makes the monthly blood survey. Treatment is entirely voluntary in this group. The proportion of children examined in the monthly surveys in this group drops off sharply during the dry-season months of February, March, and April, as the local school is closed during this period.

SURVEY METHOD

A monthly survey of all persons who can be reached, who live in these three areas, the Chagres River group, the New San Juan group, and the Madden Highway group, is made near the middle of each month. The thick-film technique of Barber and Komp (7) has been used in all the surveys since beginning our work, and the staining and examination is done by experienced technicians, many of whom have been doing this work since its inception.

RESULTS OF MALARIA SURVEYS IN 1936-37

Table I shows the monthly malaria parasite rate, compared with the rainfall as recorded at Madden Dam, located in the same general area. Totals for three previous years are given at the bottom of this table. The rates show no seasonal variation which can be attributed to decreased rainfall during the dry season, from December to April. The apparent decrease in rate in the Madden Highway group is due to the smaller number of children examined during the months of February, March, and April, as mentioned above. Mosquito production is not dependent upon annual rainfall, as most of the Anopheles breeding is found in the lagoons and backwaters of the Chagres River, which is at a more or less constant level throughout the year, especially since the completion of Madden Dam.

A total number of 1,898 examinations were made during the year, parasites being found in 682 cases, a rate of 35.8 per cent, just slightly lower than the rate of 36.1 per cent obtained in 2,248 examinations made during the previous year. Many of the persons examined were transients, who were examined only once or twice during the entire year.

Table 2 shows the parasite rate for 1,898 persons forming the average number of permanent inhabitants in the 3 groups.

These persons are shown in two groups, adults and children; the rates are cumulative for the year.

TABLE 1

Monthly malaria parasite-index compared with Madden Dam rainfall

MONTHS	CHAGRES VILLAGES	NEW SAN JUAN	MADDEN HIGHWAY	MADDEN DAM RAINFALL
1986				inches
September	5.7	17.1	19.4	15.62
October	6.1	14.7	15.5	14.03
November	2.6	14.8	14.2	9.99
December	4.9	22.2	18.6	0.63
1987		100		
January	8.2	17.8	19.7	1.52
February	9.9	20.4	9.3*	0.23
March	8.2	12.5	10.2*	0.13
April	8.7	10.8	5.2*	0.90
May	6.9	8.0	17.9	10.98
June	11.1	9.7	18.3	10.39
July	6.3	7.9	13.4	9.48
August	9.7	14.4	21.7	14.43
Totals	7.4	14.4	16.2	88.33

^{*} During February, March and April schoolchildren are on vacation, and hence are not available for examination; this accounts for the lowering of parasite rates during this period.

TABLE 2

Parasite-index. Adults (over 15 years) versus children (15 years and under).

Cumulative result for the year

and the second second		ADULTS		CHILDREN			
LOCATIONS	Exam- ined	Positive	Per cent	Exam- ined	Positive	Per cent	
Chagres	357	113	31.6	282	110	39.0	
New San Juan	324	94	29.0	276	128	46.4	
Madden Highway	160	37	23.1	499	200	40.1	
Totals	841	244	29.0	1,057	438	41.4	
Totals for 1935-36	1,063	292	27.4	1,185	519	43.8	

If the total number of examinations, 1,898, are grouped according to the number of times each person was examined, an interesting relation is brought out. In table 3 is shown the number of

those examined in the monthly surveys 1 to 5 times; those examined in the regular surveys 6 to 11 times; and those examined at every one of the 12 consecutive monthly surveys. It will be noted that only one person in the Madden Highway group was examined at every survey, which is a further indication of the great numbers of transients found in this group. From this table, it will be seen that the number of times an individual is found positive is closely related to the number of times that person is examined. Omitting the Madden Highway group, it will be seen that the per cent found positive in 1 to 5 monthly surveys is only half that of the group examined 12 times during the year 1936–1937.

TABLE 3

Parasite-index. Three survey groups. All areas

	1-5 survers			6-11 surveys			12 COMPLETE SURVEYS		
LOCATIONS	Examined	Positive	Per cent positive	Examined	Positive	Per cent positive	Examined	Positive	Per cent positive
Chagres	274	55	20.1	221	111	50.2	144	57	39.6
New San Juan	349	78	22.3	205	119	58.0	46	25	54.3
Madden Highway	424	112	26.4	234	124	53.0	1	1	100.0
Totals	1,047	245	23.4	660	354	53.6	191	83	43.5
Totals (1935-36)	1,383	333	24.1	606	323	53.3	259	155	59.8

Table 3 also shows that the past year was a time of low malaria incidence, which has a definite relation to the conclusions deduced from this study.

In table 4 is presented the cumulative incidence of malaria by age-groups. The total number of persons examined, even if examined only once, is included in this table, the grand total of all groups, treated and untreated, being 1,898.

It is interesting to note how similar the rates are for the past year, and the year preceding. This similarity is a further indication that the year 1936–1937 was a year of low incidence.

Further evidence that this is so is contained in the low rates

for the age-group 0 to 5 years. This is the group which usually suffers considerably during periods of high incidence. In the past year, and in the year preceding it, the highest malaria rate

TABLE 4
Cumulative incidence of malaria by age groups. All groups of table 3 combined

	c	HAGRE	8	NEW	SAN J	UAN	MADDEN HIGHWAY			TOTAL		
AGE	Examined	Positive	Per cent positive	Examined	Positive	Per cent positive	Examined	Positive	Per cent positive	Examined	Positive	Per cent positive
years												
0-5	120	32	26.6	137	53	38.7	56	11	19.6	313	96	30.7
5-10	92	45	48.9	69	41	59.4	239	96	40.2	400	182	45.5
10-20	135	62	45.9	130	63	48.4	247	109	44.1	512	234	45.7
20-40	163	41	25.1	158	40	25.3	69	13	18.8	390	94	24.1
40-60	102	33	32.4	75	20	26.7	38	7	18.4	215	60	27.9
Over 60	27	10	37.0	31	5	16.1	10	1	10.0	68	16	23.5
Totals	639	223	35.0	600	222	37.0	659	237	36.0	1,898	682	35.9
Totals for	A	MES IS		100000	200200					onesi.	00000	773555
1935-36	688	244	35.4	710	239	33.6	850	328	38.6	2,248	811	36.1

TABLE 5
Incidence of malaria by age groups. Limited to people examined in 12 consecutive monthly surveys

AGE GROUPS	NUMBER EXAMINED	NUMBER POSITIVE	PER CENT POSITIVE
0- 5	53	16	30.2
5-10	46	23	50.0
10-20	32	20	62.5
20-40	30	11	36.7
40-60	22	9	40.9
Over 60	8	4	50.0
Totals	191	83	43.5
Totals for 1935-36	259	155	59.9

was in the age-group from 5 to 20 years. However, this apparent difference may be due to the fact that nearly half of those examined in 12 consecutive monthly surveys were in this age-group.

Again the high rate of incidence in persons over 40 is notable;

it compares well with the rate for the same group in 1935–1936, as in that year it was 26.0 per cent, while in 1936–1937 it was 26.8 per cent. This is a rather high infection rate for persons who have lived all their lives in an endemic area. As usual in this group, however, we have found exceedingly few clinical cases, showing that tolerance is very high.

Table 5 presents the cumulative malaria rate in those persons in all the groups, treated and untreated, who were examined in 12 consecutive monthly surveys. The data are presented by age-groups.

It will be noted that only a very small percentage, 191 persons out of a total of 1,898, or 10.6 per cent, were examined 12 times during the year. If table 3 is referred to, it will be seen that only 1 person among the 659 inhabitants of the Madden Highway control group was examined at every monthly survey. This is further evidence that, as a control group, the people of this area are rather unsatisfactory, because of their migratory habits.

THE RELATIVE IMPORTANCE OF RELAPSE AND REINFECTION ON THE MALARIA RATE FOR THE YEAR

There is no known method of distinguishing a relapse of a malaria infection from a new infection, except in the case of infants under one year of age, who have never had an opportunity to be previously infected. This difficulty in distinguishing relapse from reinfection is increased in an area of endemicity, where a large proportion of the population doubtless harbors parasites from year to year. We believe that a large proportion of those found positive over a number of months are relapses of old infections, and that the proportion of new infections is rather slight, except in epidemic years. If we take those individuals who were examined at each consecutive monthly survey, and note the number of times each was positive at these surveys during the year, we can form some idea of the relative importance of relapse in keeping up the malaria rate. Those persons found positive from 2 to 5 times in 12 consecutive surveys are those who have been positive at intervals, more or less lengthy, for years past, in spite of repeated treatments. Previous records over a period of several years, show that these persons exhibit the same tendency to remain positive, while other persons in the same group either remain free of infection, or are apparently easily cured. Table 6 shows the number of times 83 persons, examined in 12 consecutive monthly surveys, and found positive at least once, were found with parasites during the course of these 12 surveys.

TABLE 6
Individuals (83) showing malaria who were surveyed regularly for 12
consecutive months

NUMBER OF TIMES	NUMBER OF CASES							
FOUND POSITIVE	Chagres	New San Juan	Madden Highway	Grand total				
1	36	10	1	47				
2	15	9	0	24				
3	3	2	0	5				
4	2	2	0	4				
5	0	2	0	2				
6	0	0	0	0				
7	0	1	0	1				
Totals	56	26	1	83				

TABLE 7

Positive cases found positive 2 or more times in 12 consecutive monthly surveys

GROUPS	NUMBER POSITIVE	NUMBER POSITIVE MORE THAN ONCE	PER CENT POSITIVE MORE THAN ONCE	AVERAGE NUMBER POSITIVE EXAMINA- TIONS PER PERSON
Chagres River (atabrine and plasmochin).	56	20	35.7	1.48
San Juan (atabrine and plasmochin)	26	16	61.5	2.27
Madden Highway (control, quinine)	1	0	0.0	1.00
Totals	83	36	43.4	1.72

It will be noted that the number of persons found positive more than once falls off rapidly in the Chagres River group, which was atabrine-treated, and well supervised.

This can be shown more graphically if the average number of positive examinations per person, in the same group of 83 persons, is stated. Table 7 gives this information.

Here it is shown that there were 35 per cent more positive examinations in the less well supervised New San Juan group. In the Chagres River group, 36 of the 56 were positive only once; in the New San Juan group, 10 of the 26 were positive only once, giving relative percentages of 65.4 and 38.5 respectively. This is also good evidence that adequate supervision of treatment was of importance in reducing the number of positives.

OBSERVATIONS OF TYPES OF MALARIA PARASITES, CRESCENT INCIDENCE, INTENSITY OF INFECTIONS, AND MOSQUITO INFECTION RATES

Table 8 shows the incidence of malaria parasite species in 682 positive examinations.

TABLE 8
Incidence of parasite species in 682 cases. Cumulative for the year

SPECIES OF PARASITE		CHAGRES RIVER		SAN JUAN		MADDEN HIGHWAY		TOTALS	
		Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	
P. falciparum	169	75.8	178	80.2	152	64.1	499	73.2	
P. vivax	35	15.7	20	9.0	40	16.8	95	13.9	
P. malariae	2	0.9	0	0.0	8	3.4	10	1.5	
Falciparum and vivax	14	6.4	24	10.8	27	11.4	65	9.5	
Falciparum and malariae	1	0.4	0	0.0	3	1.3	4	0.6	
Vivax and malariae		0.4	0	0.0	3	1.3	4	0.6	
Falciparum, vivax and malariae		0.4	0	0.0	4	1.7	5	0.7	

In the year 1935–1936, 811 cases showed P. falciparum in 607, or 74.8 per cent; P. vivax in 102, or 12.6 per cent; P. malariae in 5, or 0.6 per cent. These rates are very similar to those of the present year. In the epidemic year of 1934–1935, a slight increase of estivo-autumnal cases was observed, the number of P. falciparum infections in 1,820 cases being 1,507, or 82.2 per cent. This predominance of P. falciparum infections has been present throughout the period of our observations in this region, and is a reflection of the preponderant negroid strain in the population we deal with.

The crescent carrier rate for the year is shown in table 9. It is interesting to note that the incidence of crescents was

higher in the group treated with atabrine and plasmochin than in the unsupervised control group, which received quinine only. This may be explained by the rates in the next table, which shows the incidence of heavy infections. A heavy infection is one in which 1 or more parasites are present in each thick-film microscope field. Table 10 gives these figures.

This table shows that there were fewer heavy infections noted in the relatively untreated control group, than in the well-treated, well-supervised atabrine-plasmochin group.

TABLE 9

Crescent rate in P. falciparum cases (individual crescent carriers counted only once per year)

FOCATITA	NUMBER OF P. FALCIPARUM CASES	NUMBER OF CRESCENT CARRIERS	PER CENT CRESCENT CARRIERS
Chagres River	185	78	42.1
San Juan	202	76	37.6
Madden Highway	186	59	31.7
Totals	573	213	37.2

TABLE 10

Heavy infections found in surveys (not necessarily clinical cases)

LOCALITY	NUMBER OF POSITIVE CASES	NUMBER OF HEAVY INFEC- TIONS	PER CENT OF HEAVY INFEC- TIONS
Chagres River	223	31	13.9
San Juan	222	55	24.8
Madden Highway	237	25	10.5
Totals	682	111	16.3

INFECTIONS IN INFANTS

During the year we examined 59 infants under one year of age, and ranging from 2 months to 12 months. Of these, 8 were found positive for malaria parasites, giving a rate of 13.5 per cent. It was not always possible to examine these infants during consecutive months. It is interesting to note that none of the 23 infants living in the four villages (Santa Rosa, Guayabalito, Las Guacas, and Gatuncillo) along the Chagres banks, in which

treatment with atabrine-plasmochin was used, and in which malaria parasite rates were lowest, was found infected. The only infant found positive in the Chagres River towns lived in Agua Clara. This child was 7 months old when found positive for P. vivax.

Only 7 infants were examined, each one at only one examination, in the control group of Chilibre. None of these were found positive.

Infants found positive in New San Juan were as follows:

NUM	BEB	CHECK NUMBER	AGE	SPECIES OF PARASITE FOUND
		The second second second	months	TE THE THE
		323	2	P. falciparum
2	2	599	3	P. falciparum
2	3	231	4	P. vivax
4	1	231	10	P. falciparum
	5	374	5	P. falciparum
(5	498	10	P. falciparum
7	7	498	11	P. falciparum
	3	230	10	P. falciparum
()	251	12	P. falciparum

Note: Nos. 231 and 498 were positive twice during the year, the first with P. vivax and later with P. falciparum. No. 498 was positive for P. falciparum for two successive months. Nos. 230 and 231 are twins.

OBSERVATIONS OF MOSQUITO INFECTION RATE

Our second year's work (2) was mainly an attempt to sterilize gametocyte carriers with plasmochin simplex, quinine being given for the relief of clinical symptoms. As reported, 832 Anopheles albimanus caught in houses in the four towns in which plasmochin simplex was administered, were dissected. Stomach infections were found in 4 specimens, giving a rate of 0.48 per cent infected. During the past year, 355 Anopheles albimanus caught in houses in the village of Santa Rosa, which was under combined atabrine-plasmochin treatment, were dissected. Stomach infections were found in 4 specimens, giving a rate of 1.1 per cent. This is a discouragingly high incidence of mosquito infection, and is all the more remarkable when the low parasite

rates for the year are considered. During the second year's observations, when a rate of 0.48 per cent was found, the general parasite rate in 5,637 examinations was 16.8 per cent. During the past year, the general parasite rate was 7.4 per cent, in the same town surveyed in 1931–1932. The data apparently show that a relatively high mosquito infection rate can exist even in the presence of a low malaria rate. However, too many variable factors are present in determining the mosquito infection rate for us to draw any very hard and fast conclusions from the results of such a small number of dissections in both instances, so the data are given for what they are worth.

It is interesting to note that in spite of the difference in crude parasite rates, 13.2 per cent crescent carriers were found in 821 cases of falciparum infections in 1931–32, compared with 39.1 per cent crescent carriers in 387 cases of falciparum infections in 1936–37. Yet mosquito infection rates were higher in the year with the lower carrier rate. This result does not speak well for the efficacy of plasmochin as a gametocide, when given under the conditions of our studies.

SUMMARY

A seventh year's observations on malaria in an unsanitated area in the Republic of Panama are reported. It is hoped to continue these observations for a period of ten years, at least. We feel that such a period is required in order to obtain sufficient data of worth from which to draw conclusions as to the most practicable method of controlling malaria under our conditions. Such a period of time will also enable us to prove or disprove various theses advanced in previous papers concerning the natural history of malaria, both in treated and untreated groups.

The period herein reported upon was a period of low incidence, as was the year preceding. If our thesis concerning the cyclical nature of malaria incidence in Panama is correct, the time should not be far distant when another epidemic outbreak is to be expected.

The methods used during the period reported upon were the

same as have been in use for some years past. The monthly blood-parasite rates in groups treated with atabrine-plasmochin, quinine-plasmochin, both under adequate supervision, and with quinine sulphate under no supervision, are respectively 7.4, 14.4, and 16.2 per cent. As in past years, the rates showed no correlation with monthly rainfall.

The blood-parasite rate, cumulative for 12 months, in those persons examined at every monthly survey, shows that slightly less than half (43.5 per cent) had parasites in the blood during the year (table 5). The same table shows that a rather high annual rate can exist in all age-groups of a relatively tolerant population.

The blood-parasite rates during the period are the lowest so far recorded, and show that adequate treatment can reduce this rate to negligible proportions, during an inter-epidemic period.

A record of 83 persons examined in 12 consecutive monthly surveys, who were found positive, is given in table 6. The figures in this table indicate the efficacy of supervised treatment. Table 7 presents the same data in a different manner.

Table 8 shows the incidence of species of malaria parasite found in the 682 positives discovered during the year. As in previous years, heavy infections were somewhat more numerous in the two treated groups than in the control group.

The malaria rate in infants showed that transmission was not active during the period, as only 8 of the 59 infants examined at least once, showed parasites, giving an annual rate of 13.5 per cent. In the 1935–36 period, this rate among 66 infants was 9.1 per cent.

Mosquito infection rates were higher in 355 Anopheles albimanus dissected during the year, than during 1932, when 832 A. albimanus were dissected. The rate for 1936–1937 was 1.1 per cent, while for 1932 it was 0.48 per cent. The rate obtained for the year just past was relatively high, but the number of mosquitoes dissected was small. So many variables enter into the problem that the only safe conclusion that may be drawn is that enough human reservoirs (probably transients) escaped treatment, to permit mosquito infection.

The immediate results of the treatment work are well summarized as follows (8):

Our human parasite-index has fallen tremendously, and the physical condition of the inhabitants is good, but the mosquito-parasite index has not fallen with the human parasite rate. . . . The general physical condition of the people in the treated areas is improved; from the standpoint of an industrial organization this is a good result. . . . The disturbing feature of our work is the number of relapses that occur. Apparently we only suppress the malarial infections, and do not eradicate them by any form or length of drug administration. The parasite index for age-groups is the same this year as last.

To which may be added that malaria control by means of drugs, without any attempt to control the Anopheline vector, may be a two-edged sword. Excellent results in controlling clinical illness may be obtained during an inter-epidemic period, such as we have just passed through. But we fear that clinical rates will be much higher, and that more serious cases of malaria may occur among the well-treated groups during an epidemic period, than in groups living in the same locality who have had little treatment, and who therefore have retained a certain degree of tolerance.

We believe that the ideal method of malaria control is the elimination of Anopheles, but where this is impossible, as under our conditions, immediate treatment of clinical cases is a most useful measure. Such treatment can be given most economically by non-medical personnel in the field. Such personnel should be supervised by a medical officer, who should make weekly inspection visits. By this method, low-grade infections will not be treated, and there will be little interference with the acquirement of natural immunity.

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Fig. 1. Town of Santa Rosa Chagres River in middle ground of photograph

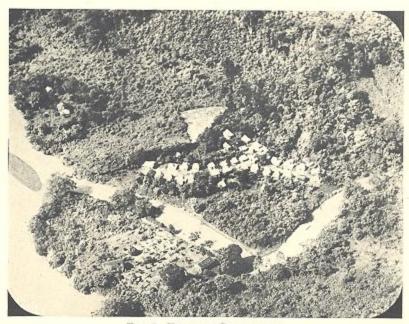


Fig. 2. Town of Gatuncillo
Chagres River to extreme left, and Gatuncillo River, forming the bend, in
foreground



Fig. 3. Town of Las Guacas in Middle Foreground Chagres River in middle distance, with a few huts of the village of Santa Rosa to extreme left