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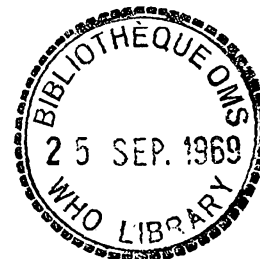
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THE SEROLOGY OF MALARIA

RECENT APPLICATIONS

by

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1. Introduction

The serology of malaria has a long and varied history. Only in the last decade have new serological techniques, such as the indirect fluorescent antibody and haemagglutination tests, been explored for use in solving problems associated with epidemiology, speciation and diagnosis. In our laboratory, studies on the serology of malaria have been devoted to the evaluation of the indirect haemagglutination (IHA) test as an epidemiological tool. We believe that malariometric techniques currently being employed for the assessment and eradication of malaria are not adequate and that new methods require evaluation. This is especially true in the undeveloped areas of the world where trained manpower to conduct various aspects of case finding, fever and spleen surveys, and slide examination are lacking. We are also studying the indirect fluorescent antibody technique (IFA) with emphasis on its evaluation as a diagnostic method. Some of the accomplishments of this programme are discussed.

2. Indirect haemagglutination studies

Desowitz & Stein (1962) and Stein & Desowitz (1964) described an indirect haemagglutination (IHA) test utilizing formalin and tannic acid treated sheep red cells sensitized with antigens from Plasmodium cynomolgi and P. coatneyi. This test was later used in a field study of malaria immunity in Australian New Guinea (Desowitz & Saave, 1965, Desowitz et al., 1966). Bray & El-Nahal (1966a) and (1966b) reported difficulties with this test system and recommended using fresh sheep red cells treated with tannic acid. Mahoney et al. (1966) fractionated antigens prepared from the plasmodia of P. knowlesi following disruption of the parasites in a French press.

Since the IHA test has proven to be useful in sero-epidemiologic studies on toxoplasmosis (Wells et al., 1967, Wells & Kagan, 1967) and other parasitic diseases (Cuadrado & Kagan, 1967) we attempted to standardize and evaluate the test for malaria (Rogers et al., 1968). Antigen

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is prepared from lysing mature schizonts from splenectomized rhesus monkeys infected with the Anopheles hackeri strain of P. knowlesi.¹ The infected cells are washed and lysed by adding at least 10 volumes of distilled water. The freed plasmodia were washed by centrifugation and stored at -70°C. Blood from a 3-kilogram monkey could be processed in four hours to yield five to 20 ml of plasmodial sediment. The plasmodia are disrupted by using a cooled French pressure cell,² operated at 20 000 lb/m² (1400 kg/cm²). The antigen is quite labile and cannot be stored for long periods. Methods for stabilizing the antigen are currently under study.

The IHA test is carried out with human group O erythrocytes that have been tanned with 1:20 000 tannic acid solution and sensitized with malaria antigen. A microtitration method employing 0.05 ml dilutions of serum is used for antibody titration.

To facilitate the collection of blood, samples obtained on filter paper by finger prick were compared with sera collected by venipuncture. These studies indicate that a finger prick filter paper technique yields comparable results and thus can be used to collect specimens in the field. The filter paper³ which met most of the requirements was cut in 1-x-3 in (2.5 x 7.6 cm) rectangles and imprinted with two circles, each 14 mm in diameter. For field studies, the paper rectangles were returned to the diagnostic laboratory in plastic bags with glassine interleaves and a dessicant.

In the laboratory, a 13/32-in (11.7 mm) disc was punched from within the filled circle. The disc was immersed in 0.2 ml of phosphate buffered saline solution (PBSS) and agitated twice during the 30-minute soaking period. The disc was removed with a rod, which was rolled over it to express some of the eluate. Approximately 0.13 ml of eluate could be obtained in this manner. The amount is approximately a 1:16 dilution of the original serum sample.

To evaluate the test for specificity, sera from 61 residents of St Lawrence Island, Alaska, 11 chronic tuberculosis patients from Atlanta, Georgia, and 43 syphilis patients from throughout the United States of America were assumed to be from malaria-free areas. A parasitology diagnostic battery of 166 sera were also tested. The sera contained 12 subgroups of specimens known to be serologically positive for echinococcosis, filariasis, schistosomiasis, trichinosis, or other non-malarious diseases, or negative for all these diseases. Titres of 1:16 and greater were uncommon (0.9%) in sera assumed to be free of antibody against malaria (Table 1). In the parasitology diagnostic battery, sera with titres of 1:16 or greater (6%) may represent true positives because they were collected from individuals living in areas where malaria may be endemic.

To evaluate the test for sensitivity, specimens from patients with proven infections were evaluated. Sera from 17 cases of P. falciparum infection primarily represented United States citizens who contracted malaria in a country with known endemic malaria. The sera from 130 persons with P. vivax infection were collected in a hyperendemic focus of malaria in Honduras.

Testing sera from persons with malaria diagnosed by blood film examination revealed a sensitivity of 96% when a titre of 1:16 or greater was considered a positive reaction (Table 2). Sera were collected and stored at -20°C over a 12-month period without a change of titre.

¹ Laboratory of Parasite Chemotherapy, NIH, Chamblee, Georgia, United States of America.

² American Instrument Company, Inc., Silver Spring, Maryland, United States of America (Use of trade names is for identification only and does not constitute endorsement).

³ ROPACO 1023.038, Rochester Paper Company, Rochester, Michigan.

To evaluate the test for seroepidemiological studies, 10 956 serum specimens representing four collections of military recruit sera were tested. The subjects were males varying in age from 18-22 years. The collections consisted of 2237 sera from the United States, 2681 sera from Brazil, 2961 sera from Colombia, and 3077 sera from Argentina. Table 3 lists the titres obtained with the military recruit sera. Although for diagnostic purposes a titre of 1:16 or greater was considered positive, it was decided based on the frequency distribution of the titres in each collection obtained from the military recruit study as shown in Fig. 1 that for epidemiological purposes, a titre of 1:8 or greater should be considered as positive. On this basis, the following prevalence of positive reactors was obtained: United States, 20 (1%) specimens positive; Brazil, 558 (21%) specimens positive; Colombia, 629 (21%) specimens positive; and Argentina, 142 (4.6%) specimens positive. The similar frequency distribution of titres obtained in Brazil and Colombia where malaria is widely endemic and the lower frequency distribution in Argentina where malaria endemicity occurs at a low level in limited parts of the country suggests that the test is measuring specific malaria antibody.

The sera positivity rate differs markedly from the rate of malaria positivity obtained by blood film examination in countries where malaria is endemic. In the United States collection, 99% of the sera examined were negative. This finding attests to the high specificity of the test in confirming the absence of malaria in this country. In Brazil and Colombia, the serologic prevalence rate was 21% but the slide positivity rates for these countries varied from 3 to 5%. The discrepancy in the two methods is probably due to the fact that the IHA test can detect antibody in the blood of an individual many years after infection, whereas the slide method only detects parasites present at the moment the blood is taken for examination. Comparison of serological and blood slide results from states in Brazil from which both data were available (Table 4) indicates that eight of the 10 states with the highest serological prevalence rates were also among the 10 states with the highest slide-positive rates. The same correlation was found in Colombia. The high correlation suggests that both methods are measuring malaria prevalence.

The persistence of the haemagglutination antibody can best be studied in areas where malaria has been eradicated or in individuals who have received radical curative treatment and do not live in endemic areas. A study in an area where malaria has been eradicated was made in Tobago. The last case of autochthonous malaria was reported in Tobago in 1953 and, except for a small introduced outbreak of *P. malariae* in 1966, the island has remained malaria free. Through the courtesy of Dr Wilbur Downs, 84 sera collected in 1955 in Tobago were titrated for malaria antibody. In 1969, a second collection was made and 40 of the individuals whose sera were collected in 1955 were bled again. Twenty-three sera were obtained by venipuncture and 13 by filter paper method. The prevalence for the 40 individuals fell from 84% to 10% and the geometric mean reciprocal titre from 52.5 to 3.3. None of these individuals was part of the malaria outbreak in 1966, or lived in the communities associated with the outbreak. Because the minimal detectable titre with filter paper is 1:16, all negative sera are considered 1:2 dilutions for calculating the geometric mean reciprocal titre. The four positive individuals were the oldest people in the sample and their titres were 1:128, 1:64, 1:16, and 1:16. The prevalence of malaria antibody in the 943 individuals sampled from five areas in the island was 1.52% and the geometric mean reciprocal titre was 2.1. These low rates indicate that malaria has indeed been eradicated in Tobago and that antibodies can persist in some individuals for at least 14 years.

A potential use of the serological method is to delineate the extent of malaria transmission. However for assessment of the results, it is essential that an individual history is taken of the movements of the people from which the sera were obtained. The question of whether malaria is being transmitted in Nepal above an elevation of 4000 ft (1500 m) was studied. In a collection of 163 individuals living in villages above this altitude, 22 (13.5%) were positive. Of the 22 positive, 19 were males with a history of travel to areas below 4000 ft (1500 m) which contrasted with a prevalence of 40% for 502

samples in an endemic area below this altitude. In Ethiopia, only 23% of 92 sera collected from individuals living above 6000 ft (1800 m) were positive compared to 58% of 122 samples collected below 6000 ft (1800 m).

The IHA test may also be useful in detecting focal outbreaks of malaria in an endemic area. In a Philippine study, in the province of Cotabato, the prevalence of malarial IHA antibody ranged from 10 to 56%. Two villages with positive serological rates of 30 and 56% and high geometric mean reciprocal titers were found in a geographical cluster of villages with rates ranging from 10 to 15% and low mean titres (Fig. 2). These data suggest that in the two villages with high serological prevalence, active transmission may be taking place. These malaria "hot spots" can be readily detected with such a survey method.

In Ethiopia serum samples taken in two locations in both wet and dry seasons showed that the positivity rate and the mean titre increased markedly in the wet season, the time of peak transmission. This finding indicates the potential use of the IHA test in monitoring seasonal changes in malaria transmission (Table 5).

A correlation between the mean geometric reciprocal titre for a survey population and the endemicity of malaria is apparent. To date, approximately 20 000 sera, representing collections from the Western Hemisphere, Africa, and Asia, have been titrated. These were not unbiased samples, though representing many types of populations and epidemiological situations. With the large number involved, some of the biases may have been cancelled out, however, matched populations will be studied.

When one plots, on a logarithmic scale, the geometric mean titre versus the per cent. positive in the collection, a straight line relationship appears (Fig. 3). Serial specimens drawn from a single area but under differing epidemiological situations move along this line in a predictable manner. This suggests that if a large number of samples are collected from an area, one may readily characterize the endemicity of malaria as hypoendemic, mesoendemic or holoendemic. Specimens collected at various intervals will make it possible to assess changes in malaria incidence in an area. This assessment can be made rapidly because a collection of several thousand sera can be titrated in a few days by the microtitration method.

In summary, the IHA test may have specialized applications in assessing the prevalence of malaria. Because of the long duration of malarial antibody in a person who has been infected, recent outbreaks of malaria can be detected only by testing young children or by noting a rise in the geometric mean titre over a given period. Since the mean geometric titre and per cent. positive of a carefully selected cross section of the population reflects the endemicity of malaria, small surveys in selected areas will readily detect focal outbreaks or a change in the epidemiology of the infection. The technique could be used to delineate the extent of malaria in a country. Other more practical applications, such as monitoring the effect of eradication, or a chemoprophylaxis programme in endemic areas, are under study.

3. Fluorescent antibody studies

The fluorescent antibody (FA) test for malaria was initially introduced by Tobie & Coatney (1961) and Voller & Bray (1962). In the last few years, a number of workers have made important contributions with this method as for example Kuvin et al. (1962a), (1962b), Garnham et al. (1963), Tobie (1964), Corradetti et al. (1964), Voller (1964), Collins et al. (1965), (1966), (1967), Lunn et al. (1966) and Voller & Bruce-Chwatt (1968). The FA test is the serological technique most widely used for the diagnosis of malaria at the present time. Reports by McGregor et al. (1963 and 1965) in Gambia, West Africa, on the use of the fluorescent antibody technique to measure the status of immunity in a population residing in an endemic area have shown that serological methods may be used to good advantage in the epidemiological assessment of malaria endemicity.

The FA test, because of technical problems, does not lend itself to mass screening methods. Nonetheless, epidemiological surveys on relatively large groups of individuals have been made in Nigeria by Collins et al. (1967) and Voller & Bruce-Chwatt (1968).

Use of a soluble antigen fluorescent antibody test with P. falciparum and chimpanzee erythrocyte lysates from experimental infections in chimpanzees as antigens adsorbed to cellulose acetate discs may be a more rapid means of performing the fluorescent antibody technique (Sadun & Gore, 1968). A stable antigen fractionated by sequential elution with chromatography from a DEAE Sephadex A 25 column gave fractions that were very active in this test. Approximately 50 000 tests can be performed with the amount of antigen normally collected from one infected chimpanzee. This technique is very promising and merits further study because fluorescence is read by a flurometer and objective criteria of positive and negative reactions are possible.

We have used a washed-cell thick-smear antigen in all our indirect fluorescent antibody studies (Sulzer & Wilson, 1967). Washing the parasitized cells removes soluble serum components, especially gamma globulin which may contain malaria antibody and thus may interfere in the test. When such a washed antigen is prepared as a thick smear, the number of plasmodia per field can be controlled. This greatly facilitates the reading of the test results (Sulzer et al., 1969).

The sensitivity and specificity of the test are very high. These parameters were evaluated with a battery of 232 sera, of which 184 were from persons never exposed to malaria and 49 from persons with patent plasmodial infections. All sera were randomized, coded, and tested with antigens prepared from Plasmodium vivax, P. falciparum, and P. brasilianum, the latter being used as a substitute for P. malariae. As seen in Table 6, only one of the sera from the non exposed group had a positive reaction at 1:16 with the P. falciparum antigen. Specificity is, therefore, greater than 99%. The false positive rates with the P. brasilianum and P. vivax antigens at the 1:4 dilution were less than 3%, but 14% of the sera reacted with the P. falciparum antigen. For this reason, a positive reaction at 1:4 with any antigen species is regarded as a questionable positive, and the lowest acceptable diagnostic titre for malaria is 1:16 (Sulzer et al., 1969).

The 49 positive sera included in this battery had been tested previously and found to have low antibody concentration. Sera of low titre were chosen so that the most rigorous test of sensitivity might be made. Including many sera of high antibody titres, which are readily detected by serological tests, would give a sensitivity rate that might be misleading. As noted in the footnote to Table 6, two of the sera retested gave no reaction at the 1:16 dilution with any of the antigens. This constituted a false negative rate of less than 5%. All other sera were positive at 1:16 with at least one antigen. Some sera reacted only with their homologous antigen. For a diagnostic procedure with the highest sensitivity, homologous antigens of the human species should be employed. For this reason we maintain P. vivax and P. falciparum in Aotus sp. and Ateles sp. monkeys, respectively. If homologous human plasmodial antigens are not available however, a P. vivax antigen may be used. With this antigen, the specificity would be better than 95%; the sensitivity with sera of low titre about 92%.

Reproducibility of titres with the thick smear antigen on a test-to-test basis is excellent (Table 7). Two positive sera were tested with each of four antigen species many times. All titres were replicated within plus or minus one fourfold dilution except for the MOR serum tested with the P. falciparum antigen.

The IFA test can be used to determine the infecting plasmodium species when one cannot make a determination with stained blood slides (Gleason et al., in press). Etiological diagnosis may be difficult because the parasites may have been distorted by the effect of drugs, the parasitaemia too scanty to reveal diagnostic forms, or the species identification in doubt because the slides were improperly prepared. The method may also be used to detect the responsible donors in transfusion malaria.

An evaluation of species identification was made with 206 sera from 93 military personnel who, after returning from South East Asia, relapsed with malaria infections. Both acute and convalescent sera were tested. In each case, the infecting plasmodium species was determined by stained blood slides. Since only P. vivax and P. falciparum infections were involved, antigens of these two species alone were employed in the evaluation.

Comparisons were made on the basis of fourfold titre differences with the two antigens. The species representing the antigen that gave the highest titre was designated as the infecting species. When matched with the slide results, the correct species was identified serologically for 89% of the specimens. Six per cent. gave the same titre for both antigens; one case (0.5%) was misdiagnosed, and 5% were negative. Species determinations have become routine in our laboratory and have proven to be very useful in transfusion malaria and in correcting some misdiagnoses based on improperly stained blood films.

The rise and fall of antibody titre in returning military personnel may be useful diagnostically in that a high antibody titre may indicate recent or current infection, especially if there is no history of recent treatment (Wilson et al. in press). Sera from 69 individuals reporting to a military hospital in the United States of America with clinical cases of malaria were studied. In the first two weeks after onset of symptoms the titres were relatively high, with a geometric mean of 1:184. After six months of treatment the titres fell to a mean of 1:9. In this group only one serum had a titre of 1:256. If there is no history of treatment and if parasitaemia is not detectable, an antibody titre of 1:256 may be regarded as serological evidence of current malaria infection.

In summary, when a washed-cell thick-smear antigen is used, the IFA test for malaria gives good reproducibility, sensitivity, and specificity. The infecting species of malaria can be identified serologically. When malaria is suspected but definitive diagnosis cannot be made by stained blood film, IFA test results may be useful. In our experience, for maximum diagnostic sensitivity, except in the case of P. malariae, homologous plasmodial species antigen should be used. Human plasmodial species from infections in Aotus and Ateles monkeys make excellent antigen. P. brasilianum appears to give serological results identical with those of P. malariae antigen.

TABLE 1. INDIRECT HAEMAGGLUTINATION TESTS ON THE SERA OF INDIVIDUALS HAVING NO KNOWN HISTORY OF MALARIA

Source of sera	Titre						Total
	0	2	4	8	16	32+	
Normal Alaskans	54	3	4				61
Syphilitic patients, primary and secondary	28	2	8	4	1		43
Chronic tuberculosis patients	5	4	2				11
Parasitology diagnostic battery	105	13	19	19	6*	4*	166
Total	192	22	33	23	7	4	281

* Includes three cases of schistosomiasis and four cases of filariasis.

TABLE 4. BRAZIL: COMPARISON OF SEROLOGICAL AND BLOOD SLIDE RESULTS
FOR MALARIA FROM STATES FROM WHICH BOTH DATA WERE AVAILABLE
STATES ARE RANKED FROM HIGHEST TO LOWEST VALUES

Rank	Serology		Slide examination	
	Name of State	Per cent. positive	Name of State	Per cent. positive
1	Roraima	100	Roraima	16.8
2	Amazonas	39.8	Goias	15.7
3	Para	39.3	Maranhão	15.5
4	Acre	37.5	Para	14.1
5	Pernambuco	33.6	Bahia	8.7
6	Maranhão	27.6	Piaui	6.6
7	Goias	25.6	Amazonas	5.5
8	Mato Grosso	25.4	Acre	4.7
9	Alagôas	25.0	Espirito Santo	4.6
10	Piaui	23.3	Mato Grosso	3.5
11	Minas Gerais	18.6	Minas Gerais	3.4
12	Bahia	17.3	Santa Catarina	3.3
13	Rio Grande do Norte	15.8	Ceará	2.3
14	Santa Catarina	12.5	Paraná	2.0
15	Paraiba	8.8	Pernambuco	1.3
16	Rio de Janeiro	8.3	Rio de Janeiro	0.6
17	Ceará	4.6	Paraiba	0.4
18	Paraná	4.3	Guanabara	0.3
19	Sergipe	0.0	Sergipe	0.1
20	Espirito Santo	0.0	Alagôas	0.0
21	Guanabara	0.0	Rio Grande do Norte	0.0

TABLE 5. ETHIOPIA: SEASONAL FLUCTUATION OF MALARIA ANTIBODY LEVELS

Location	June, 1968 (Dry)		October, 1968 (Wet)	
	Per cent. positive	Mean titre	Per cent. positive	Mean titre
Om Hagar School	50.0	18.8	65.5	30.5
Humera Farms	68.4	56.1	78.2	113.0

TABLE 6. NUMBER AND PER CENT. OF REACTORS TO THREE PLASMODIUM ANTIGENS AMONG 184 SERA FROM INDIVIDUALS NOT EXPOSED TO MALARIA AND 49 SERA FROM INDIVIDUALS WITH A POSITIVE SLIDE DIAGNOSIS¹

Sera group	Titres	Washed-cell thick-smear antigens					
		<u>P. falciparum</u>		<u>P. vivax</u>		<u>P. brasilianum</u>	
		No.	%	No.	%	No.	%
Donors not exposed to malaria	Negative	157	85.3	180	97.8	183	99.5
	1:4	26	14.2	4	2.2	1	0.5
	1:16	1	0.5	0	0.0	0	0.0
Donors with positive slide diagnosis ²	Negative	6	12.2	4	8.2	9	18.4
	1:4	10	20.4	4	8.2	3	6.1
	1:16	33	67.4	41	83.6	37	75.5

¹ From Sulzer et al. (1969)

² All sera in this group had previously had titres of at least 1:16 with one of the three antigens. On this second titration, two of these sera had negative reactions with all three antigens.

TABLE 7. DISTRIBUTION OF TITRES FOR TWO ANTISERA WITH FOUR ANTIGENS IN THE INDIRECT FLUORESCENT ANTIBODY (IFA) TEST FOR MALARIA¹

Reciprocal titre	Plasmodium antigens							
	<u>P. vivax</u>		<u>P. falciparum</u>		<u>P. brasilianum</u> ⁴		<u>P. fieldi</u>	
	E.T. ²	MOR. ³	E.T.	MOR.	E.T.	MOR.	E.T.	MOR.
Negative				6		4		2
4				14		9	2	3
16	16	9	22	27		25	10	8
64	29	30	28	2				
256		1			6			
1 024					34			
4 096					2			
Total replicates	45	40	50	49	42	38	12	13

¹ From Sulzer et al. (1969)

² Plasmodium malariae demonstrated in circulating blood. Mother of an infant with congenital malaria.

³ District medical officer, Sepik, Territory of Papua and New Guinea. Reported Plasmodium vivax infection with treatment one year prior to sampling.

⁴ P. brasilianum antigen was used as an equivalent to P. malariae.

SUMMARY

Studies in progress on the application of the indirect haemagglutination test for epidemiological purposes in malaria are outlined. The test is both sensitive and specific and the antibody can be titrated from plasma eluted from filter paper. The technique may be used to determine positive serological rates in a population, to determine the extent of malaria transmission, and to characterize the endemicity of malaria.

The indirect fluorescent antibody test is also under evaluation for diagnostic purposes. Evaluation of sensitivity and specificity using a washed-cell thick-smear antigen indicates a procedure of high sensitivity and specificity. Species identification by using homologous malarial antigen is possible. The significance and duration of antibody in individuals who have undergone radical cure by chemotherapy shows a fall in titre to levels below 1:256 in six months. Human plasmodial species in monkeys may be used as antigen.

RESUME

Au cours de la dernière décennie, de nouvelles techniques sérologiques, notamment la méthode indirecte d'immunofluorescence et l'épreuve d'hémagglutination, ont été envisagées du point de vue de leur application à l'épidémiologie, au diagnostic d'espèce et au diagnostic du paludisme. Le présent document indique les études en cours sur l'utilisation de l'épreuve indirecte d'hémagglutination à des fins épidémiologiques. Elle s'est révélée à la fois sensible et spécifique et permet le titrage des anticorps dans un éluat de plasma obtenu à partir de papier-filtre. Une collection de plusieurs milliers de sérums peut être titrée en quelques jours par une micro-méthode. On peut utiliser ce procédé pour établir la proportion de sujets séro-positifs dans une population, pour déterminer l'étendue de la transmission du paludisme ou caractériser son endémicité. Toutefois, du fait de la persistance de l'anticorps antipaludique chez un sujet précédemment infecté, les poussées épidémiologiques récentes ne peuvent être dépistées qu'en appliquant l'épreuve à de jeunes enfants ou en constatant l'augmentation du titre moyen (moyenne géométrique) sur une période donnée.

La méthode indirecte d'immunofluorescence fait, quant à elle, l'objet d'une évaluation à des fins diagnostiques. On a observé que l'emploi comme antigène d'un frottis épais de cellules lavées donnait une sensibilité et une spécificité élevées. L'utilisation des antigènes paludiques homologues permet le diagnostic d'espèces. Chez les sujets à qui la chimiothérapie a apporté une guérison radicale, l'étude du taux et de la persistance des anticorps met en évidence une chute du titre à moins de 1:256 en six mois. On peut utiliser comme antigènes les espèces plasmodiales humaines isolées chez le singe. Ainsi les sérologies obtenues avec P. brasilianum paraissent identiques à celles obtenues avec l'antigène à P. malariae.

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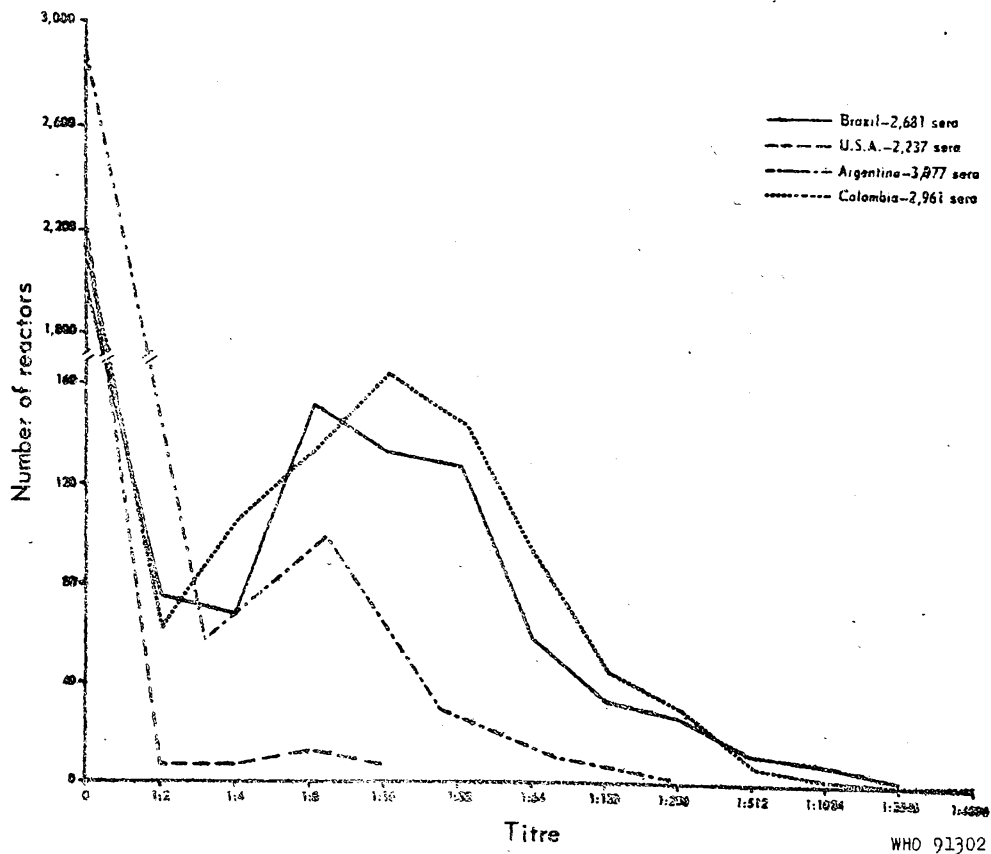
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FIG. 1

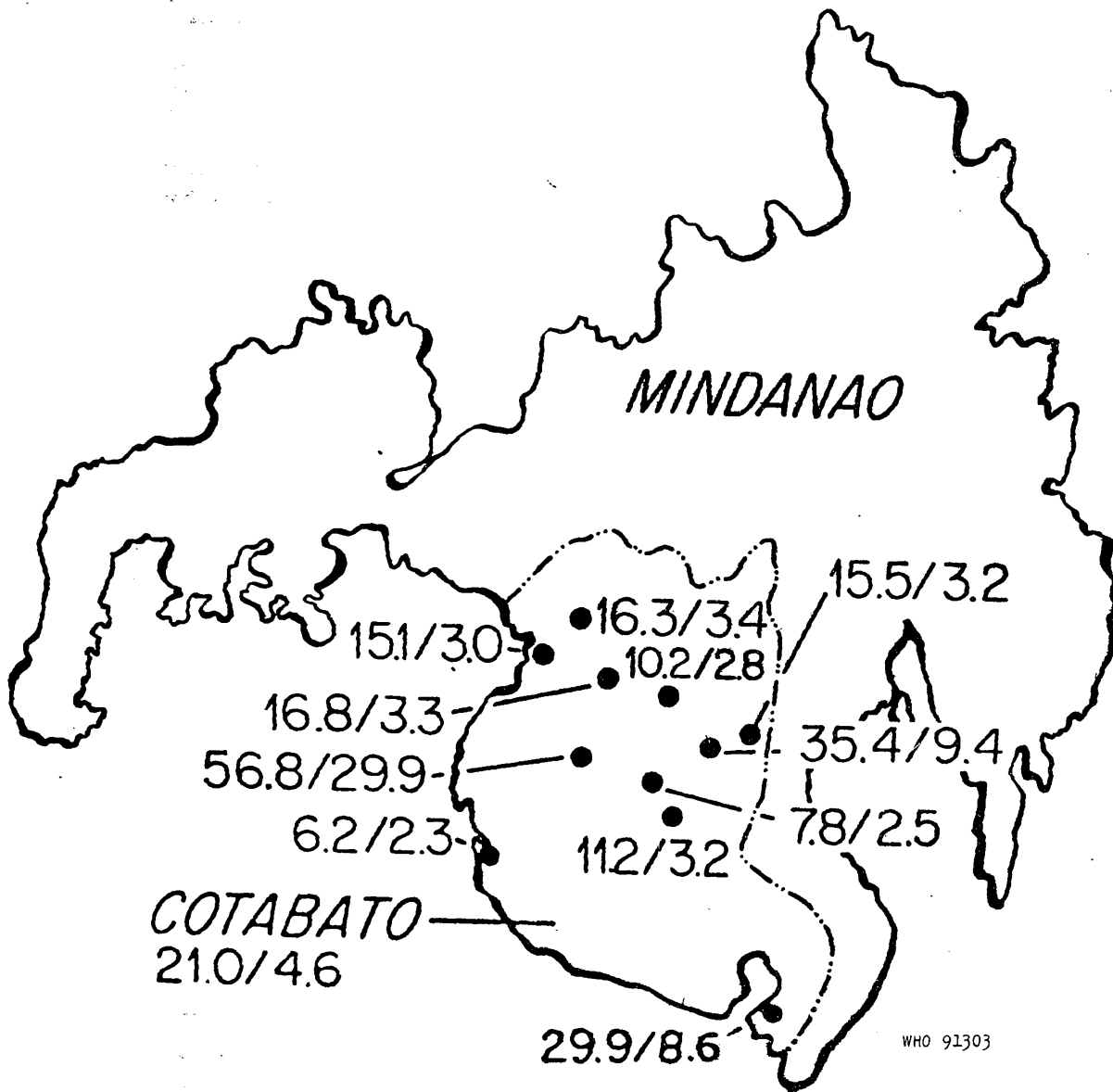
THE FREQUENCY DISTRIBUTION OF INDIRECT HAEMAGGLUTINATION TITRES FOR MALARIA OBTAINED WITH SERA OF MILITARY RECRUITS



WHO 91302

FIG. 2

DISTRIBUTION OF MALARIA ANTIBODIES AND GEOMETRIC MEAN RECIPROCAL
TITRES FOR A NUMBER OF VILLAGES IN THE PROVINCE OF CATABATO ON
THE ISLAND OF MINDANAO, PHILIPPINE REPUBLIC

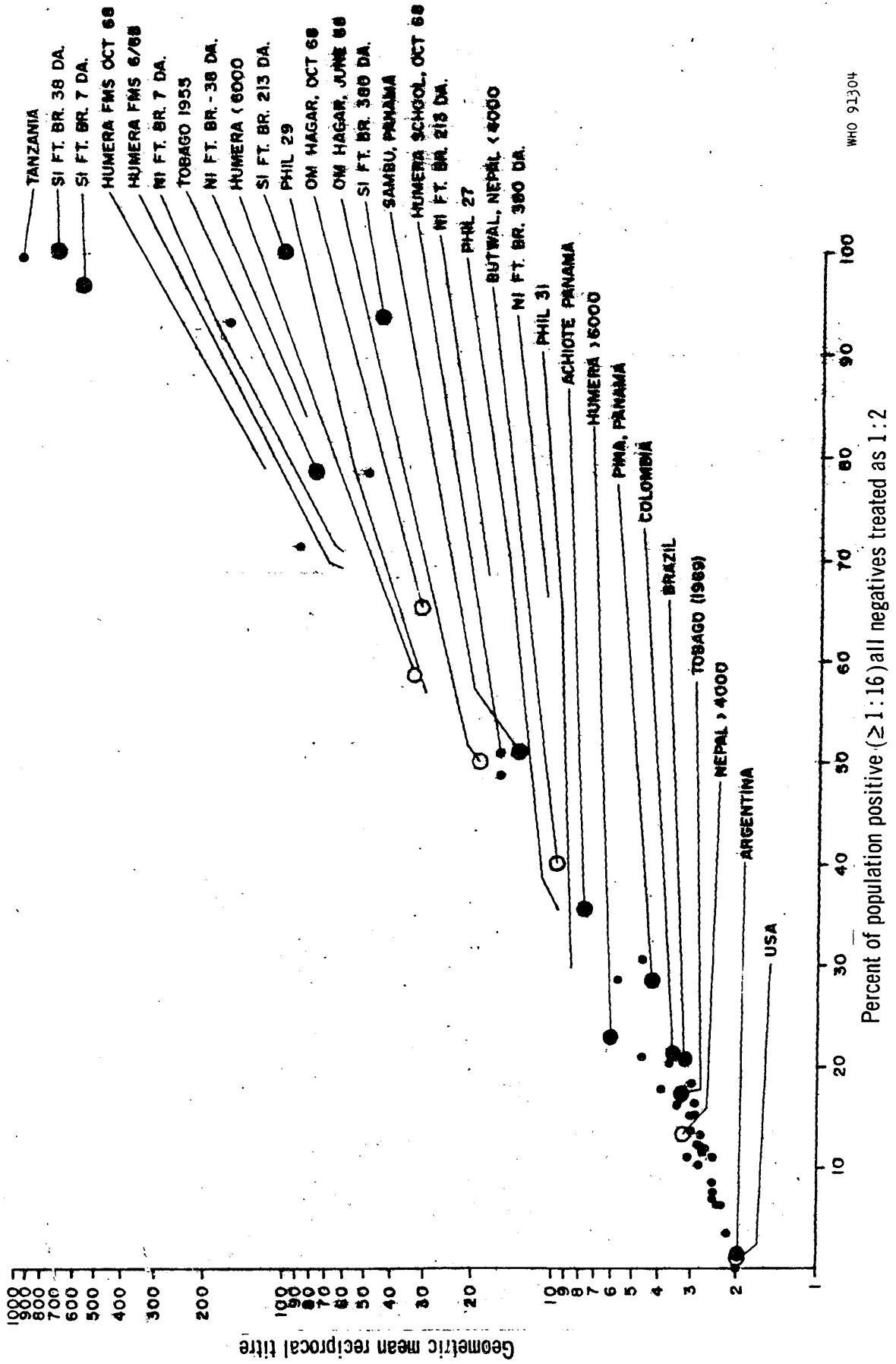


WHO 91303

Numbers refer to percent positive/mean titre

FIG. 3

RELATIONSHIP BETWEEN THE PERCENT OF THE POPULATION SAMPLED AND THE GEOMETRIC MEAN RECIPROCAL TITRE FOR MALARIA HAEMAGGLUTINATION ANTIBODY IN A NUMBER OF SURVEYS



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- (a) to acquaint WHO staff, national institutes and individual research or public health workers with the changing trends of malaria research and the progress of malaria eradication by means of summaries of some relevant problems;
- (b) to distribute to the groups mentioned above those field reports and other communications which are of particular interest but which would not normally be printed in any WHO publications;
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It should be noted that the summaries of unpublished work often represent preliminary reports of investigations and therefore such findings are subject to possible revision at a later date.

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