Rev. Inst. Med. trop. São Paulo
18(5):322-348, *setembro-outubro*, 1976

UDC 616.936
616.993.161

THE ASSOCIATION BETWEEN SPLENOMEGALY AND MALARIA IN INDIANS FROM THE ALTO XINGU, CENTRAL BRASIL

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SUMMARY

A high prevalence of big spleen or gross splenomegaly was found in Brazilian Indians from the Alto Xingu region, reaching 33.4% in a population of 730 with equal distribution between sexes. In a sample of the population, antibodies for plasmodia were detected by fluorescence test in 98.7% of the people and malaria parasites in the peripheral blood in 14.3%. In association with gross splenomegaly and high titres of antibodies for plasmodia there are increased values of IgM and hepatic sinusoidal lymphocytosis. These findings have been considered as characteristics of the Tropical Splenomegaly Syndrome first noticed in various areas of tropical Africa and New Guinea, where malaria is endemic. In the Alto Xingu region some episodes of hematemesis and melena were observed among the Indians having the Tropical Splenomegaly Syndrome and the X-ray examination made in a few cases revealed enlargement of portal vein system and the presence of esophagical varices.

INTRODUCTION

The presence of enlarged spleen is a common clinical finding in the tropical areas where malaria is endemic. Despite the fact that splenomegaly can be present in the clinical picture of many diseases, parasitic or not, an association with malarial infection has been suggested in a large proportion of cases. This supposition is reinforced by the absence of other etiologic agents involved in the spleen enlargement and supported by epidemiological data [29, 34].

An additional evidence for the hypothesis of association between malaria and enlarged spleen is given by the regression of splenomegaly observed in those receiving prolonged antimalarial therapy [3, 16, 21, 38].

On the other hand, the development and use of serological surveys in Malaria Epidemiology has allowed a better knowledge of the distribution of malarial antibodies in different populations to be obtained [5, 40]. It was possible with the new serological techniques to detect the presence of malarial antibodies in many people with persistent gross splenomegaly, in whom the search for plasmodia was negative in the peripheral blood, using the habitual slide techniques [24].

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BARUZZI, R. G.; FRANCO, L. J.; JARDIM, J. R.; MASUDA, A.; NASPITZ, C.; PAIVA, E. R. & FERREIRA-NOVO, N. — The association between splenomegaly and malaria in Indians from the Alto Xingu, Central Brasil. *Rev. Inst. Med. trop. São Paulo* 18:322-348, 1976.

A field study was made amongst the Indians from Alto Xingu, Central Brazil, and the first results, already presented [4], showed the presence of gross splenomegaly in 33.4% of the total population of 730 Indians. At the same time, the immunofluorescence reaction using *P. vivax* and *P. falciparum* as antigens was positive in 98.7% of 77 Indians representing a sample of the population.

In Alto Xingu where there is a high percentage of the population with enlarged spleens and high titres of malarial antibodies the opportunity to make a longitudinal study of the clinical pictures and laboratory data is presented. Another question to be considered is the hypothesis of the identification between the gross splenomegaly observed in Alto Xingu and the Tropical Splenomegaly Syndrome described in Algeria [7], Saudi Arabia [17], India [8], Uganda [23], Sudan [27] and New Guinea [31].

MATERIALS AND METHODS

The region called Alto Xingu encompasses the headwaters of the Xingu River and its first tributaries, in the northern part of the State of Mato Grosso, within the area of the Xingu National Park. It is situated between 12.° and 13.° south of the equatorial line and between 50.° and 54.° west of the Greenwich line. The Alto Xingu has an average altitude of 250 metres and a maximum daily temperature varying between 26.° and 36.°, there is a significant drop at night. It is possible to distinguish two seasons: the "Winter" or the "rainy" season, from October to March, and the "Summer" or the dry season, from April to September.

The population of Alto Xingu is composed of Indian (both in the biological and cultural sense) [35], who are living in a state of relative isolation. The total population of 730 Indians is divided into 10 tribes, each one having its own village:

Tribe	Linguistic group
Aueti	Tupy
Kamayura	Tupy
Yawalapiti	Aruak
Meinaco	Aruak
Uaura	Aruak
Kalapalo	Carib
Cuicuro	Carib
Matipu-Nafuqua	Carib
Txikão	Carib
Trumai	Isolated language

The Escola Paulista de Medicina (São Paulo Medical School), has been developing a medical programme in Alto Xingu since 1966, which is primarily orientated to assist the native population.

To determine the Indians' health conditions, an individual medical card was adopted and some laboratory investigation were made.

Data of Physical Examination

For a better evaluation of the physical examination data some features were observed by the medical groups participating in the field work. The approximate ages of the Indians were calculated from their physical appearance and family correlation. In children and adolescents an examination of the teeth was also brought into consideration.

In order to determine the blood pressure the Tycos anaroid sphygmomonometer was used, the person being examined was sitting in a comfortable position or was lying down. The measurement of the radial pulse rate was made with the instruction that it should be taken for a minimum time of 30 seconds. The abdomen was examined while the patient was in a supine position, and the usual techniques for liver and spleen palpation were observed. An adult was considered to have hepatomegaly when the liver was discovered to be at least 5 cm below the right costal border at the intersection of the right hemi-clavicular line. In making the evaluation of spleen volume the classification proposed by HACKETT [41] in 1944 was used.

At the same time as the physical examination was made, 5 or 10 ml of venous blood

were taken for serological testing. Once the serum was separated, it was conserved at 4°C for two or three days. Then this serum was transfered in styrofoam ice boxes to São Paulo, where it was stored in a deepfreeze at −20°C.

LABORATORY EXAMS

Population samples

The laboratory investigation was made on a sample of the population. This sample consisted of Indians belonging to the different tribes of Alto Xingu that came to the place where the physical examination was being held and the blood specimen was taken at this time. At the end of this period 77 Indians of both sexes, adults and children, had been examined. Although a true random sample could not be obtained due to the difficulties posed by the local conditions, it is reasonable to assume that a representative sample was taken from those who attended the physical examination.

Serological reactions and Plasmodium *research*

Serological investigation for antibodies against *Plasmodium vivax, Plasmodium falciparum, Leishmania braziliensis* and *Schistosoma mansoni* was made on the 77 Indians that constituted the population sample. The search for *Plasmodium* was made on glass slides using thick peripheral blood smears.

Total serum Protein measurement and Electrophoresis of Proteins

The measurement was made on 73 out of the 77 sera (four of the serum specimen were lost during transportation). The method used for total serum measurement was the method of Gornall-Bardawill-David (Biuret reaction) with spectrophotometer reading. The fractionation of proteins was made by cellulose acetate electrophoresis.

Immunoglobulin measurements

It was possible to perform measurements of Immunoglobulins IgG, IgM, IgA and IgE in 40 serum samples, children under 10 years of age were excluded from this examination because the volumes of blood samples taken are generally insufficient in this group also as already has been mentioned, some specimens of serum were lost during transportation. The method of radial immunodiffusion of MANCINI [22] was employed to measure IgG, IgM and IgA levels, and the Rowe's method of radioimmunodiffusion for IgE.

The Standard immunoglobulins IgG, IgM and IgA that were used came from Hyland Laboratories (Uppsala, Swenden). Specific antisera anti-IgG, anti-IgM and anti-IgA were obtained by the immunization of sheep with immunoglobulins purified by columm-cromatography and anti-IgE was obtained by the immunization of sheep with Fc fragments of IgE (Pharmacia, Uppsala, Sweden).

Liver Biopsy

In the 9 Indians of Alto Xingu that were admitted as inpatients to the Hospital São Paulo (in São Paulo) for clinical or surgical treatment, a liver biopsy was made either surgically or by using Silvermann's biopsy needle.

Statistical Analysis

The definition of the alternative hypothesis as one-sided was accepted only when there were theoretical and logical reasons for the indication of the direction of the difference. In such cases the nature of the hypothesis is indicated in the text.

Null hypothesis was rejected when the risk of error of the first species was equal to or smaller than 0.05.

The following methods was used: Chi-square tests for the analysis of association or contingency tables, employing the additive decomposition, when indicated, in tables $2 \times k$ [9] and in one case the hierarchical classification [2]; The exact test of Fisher for the analysis of a 2×2 table when the Cochran's conditions for the use of the chi-square test were not present; The Kolmogorov-Smirnov test for comparison of the

distribution of titers of reaction in two independent samples [37]; The Mann-Whitney test for comparison, regarding the positions, of the distribution of quantitative variable values in two independent samples [37].

RESULTS

Data of Physical Examination

Spleen

Table I shows the distribution of splenomegaly in the population of Alto Xingu according to age groups using the classification of Hackett (W.H.O., 1963) [41].

In order to analyse this data further the splenomegaly degrees 3, 4 and 5 were included under the title of "gross splenomegaly" or "big spleen" allowing a comparison to be made with the group having the spleen sizes 0, 1 and 2, according to Hackett's classification system. The distribution of the frequency of gross splenomegaly when considering specific age groups is presented in Table II.

The percentage of gross splenomegaly cases increases significantly until the fourth age groups i.e. 20 —| 30 years of age. This group is not significantly different from the next which includes individuals older than 30 years of age (Table II).

The distribution of individuals with gross splenomegaly according to sex and age group is presented in Table III.

Therefore, there is no significant differences between the sexes in the percentage of those with gross splenomegaly in each of the age groups.

In Table IV the percentages of Indians with gross splenomegaly in each age group is correlated with each tribal linguistic group. This data refers to 715 Indians from the population studied.

The percentages of Indians with gross splenomegaly in the linguistic groups considered did not differ significantly in any of the age groups.

Skin and mucosae

The oral and ocular aspects of conjunctival mucosae were important to evaluate the presence of anaemia. The examination of the skin was complicated because of the frequent use of colouring substances adopted by the Indians, who are normally exposed to the sun without the protection of clothing. The distribution of the 730 Indians examined, according to the colour of their mucosae and the presence or absence of gross splenomegaly is presented in Table V, in which a classification ranging from + to ++++

TABLE I

Indians of Alto Xingu, according to the degree of splenomegaly (Hackett's classification) and age group, 1970

Age (years)	Degree of splenomegaly					Total
	0	1	2	3	4 e 5	
≤ 2	46	5	35	9	2	97
2 —| 10	44	40	73	34	7	198
10 —| 20	20	24	69	42	12	167
20 —| 30	12	10	45	44	30	141
> 30	19	15	29	44	20	127
Total	141	94	251	173	71	730

TABLE II

The Indians of Alto Xingu (Central Brasil) having gross splenomegaly, distributed according to age group, 1970

Age (years)	Individuals studied	Gross Splenomegaly	
		No.	(%)
A — ≤ 2	97	11	11.3
B — 2 —| 10	198	41	20.7
C — 10 —| 20	167	54	32.3
D — 20 —| 30	141	74	52.5
E — > 30	127	64	50.4
Total	730	244	33.4

$X^2 = 75.187$ $(P < 0.001)$ d.f. = 4

Additive decomposition of Chi-square (X^2):

(A+B+C) × (D+E):	$X^2 = 62.122$	$(P < 0.001)$	d.f. = 1
(A+B+C):	$X^2 = 12.933$	$(0.001 < P < 0.005)$	d.f. = 2
(A) × (B+C):	$X^2 = 7.429$	$(0.005 < P < 0.01)$	d.f. = 1
(B) × (C):	$X^2 = 5.505$	$(0.01 < P < 0.02)$	d.f. = 1
(D) × (E):	$X^2 = 0.131$	$(0.70 < P < 0.80)$	d.f. = 1

TABLE III

The Indians of Alto Xingu (Central Brasil), with gross splenomegaly, classified according to sex and age group, 1970

Age group (years)	Male			Female		
	Individuals studied	Gross splenomegaly		Individuals studied	Gross splenomegaly	
		No.	(%)		No.	(%)
≤ 2	48	6	12.5	49	5	10.2
2 —| 10	101	20	19.8	97	21	21.6
10 —| 20	94	26	27.6	73	28	38.4
20 —| 30	72	34	47.2	69	40	58.0
> 30	77	41	53.2	50	23	46.0
Total	392	127	32.4	338	117	34.6

Differences between groups, according to age:

≤ 2:	$X^2 = 0.127$	$(0.70 < P < 0.80)$	d.f. = 1
2 —| 10:	$X^2 = 0.103$	$(0.70 < P < 0.80)$	d.f. = 1
10 —| 20:	$X^2 = 2.149$	$(0.10 < P < 0.20)$	d.f. = 1
20 —| 30:	$X^2 = 1.632$	$(0.10 < P < 0.30)$	d.f. = 1
> 30:	$X^2 = 0.637$	$(0.30 < P < 0.50)$	d.f. = 1

TABLE IV

The Indians of Alto Xingu (Central Brasil) having gross splenomegaly, according to linguistic group and age groups, 1970

Age group (years)	Linguistic group									Total
	Aruak			Carib			Tupy			
	Individuals studied	Gross splenomegaly		Individuals studied	Gross splenomegaly		Individuals studied	Gross splenomegaly		
	No.	No.	%	No.	No.	%	No.	No.	%	No.
≤ 2	28	2	7.1	28	6	21.4	41	3	7.3	97
2 —| 10	43	5	11.6	69	13	18.8	80	22	27.5	192
10 —| 20	26	9	34.6	53	16	30.2	81	29	35.8	160
20 —| 30	34	15	44.1	42	22	52.4	64	36	56.2	140
> 30	30	15	50.0	42	19	45.2	54	30	55.5	126
Total	161	46	28.6	234	76	35.2	320	120	37.5	715

Differences among linguistic groups according to age groups:

≤ 2:	$X^2 = 3.985$	$(0.10 < P < 0.20)$	d.f. = 2
2 —| 10:	$X^2 = 4.531$	$(0.10 < P < 0.20)$	d.f. = 2
10 —| 20:	$X^2 = 0.462$	$(0.70 < P < 0.80)$	d.f. = 2
20 —| 30:	$X^2 = 1.311$	$(0.50 < P < 0.70)$	d.f. = 2
> 30:	$X^2 = 1.016$	$(0.50 < P < 0.70)$	d.f. = 2

is employed to indicate the progressive degree of mucosae pallor.

Therefore the percentage of gross splenomegaly was significantly lower among Indians with normally coloured mucosas. There were no significant differences between the other groups, although the small number of individuals in the last group with more serious pallor of the mucosas (+++ and ++++) must be noted.

Jaundice

Table VI shows the number of Indians with jaundice according to the degree of splenomegaly among the 730 Indians examined.

The proportion of Indians with jaundice was significantly higher in the group with gross splenomegaly once the exact text of Fisher gave the value of $P = 0.033$.

The Circulatory System

The radial pulse rate in both sexes above 20 years of age, according to the degree of splenomegaly is shown in Table VII.

In analyzing these results two groups were considered, one with rates below and another with rates above 80 b.p.m. The results then showed $X^2 = 5.961$ $(0.01 < P < 0.02)$, demonstrating that individuals high pulse rate are significantly more frequent in the gross splenomegaly group than in the group with degrees of splenomegaly classified as 0-1 and 2.

TABLE V

Indians of Alto Xingu, Central Brasil, according to the colour of mucous membranes and the presence or absence of gross splenomegaly

Mucous Membranes	Degree of splenomegaly				Total	
	0-1-2		3-4-5			
	No.	(%)	No.	(%)	No.	(%)
A — normal	327	70.0	140	30.0	467	100.0
B — pallor +	100	61.3	63	38.6	163	100.0
C — pallor ++	52	61.9	32	38.1	84	100.0
D — pallor +++ and ++++	7	43.8	9	56.2	16	100.0
Total	486	66.6	244	33.4	730	100.0

Additive decomposition of Chi-square (X^2):

	$X^2 = 9.062$	$(0.02 < P < 0.05)$	d.f. = 3
(A) + (B+C+D):	$X^2 = 6.917$	$(0.001 < P < 0.01)$	d.f. = 1
(B+C+D):	$X^2 = 2.144$	$(0.30 < P < 0.050)$	d.f. = 2

TABLE VI

Indians of Alto Xingu, Central Brasil, according to the presence or absence of gross splenomegaly and jaundice, 1970

Jaundice	Degree of splenomegaly				Total
	0-1-2		3-4-5		
	No.	(%)	No.	(%)	
Present	2	0.4	8	3.3	10
Absence	484	99.6	236	96.7	720
Total	486	100.0	244	100.0	730

Arterial Blood Pressure

A comparative study was made of the blood pressure levels envolving 268 Indians of both sexes over 20 years of age. No significant difference was observed in the measurements taken when a comparison was made between those with gross splenomegaly and the remainder. Thus, in males with gross splenomegaly, the systolic blood pressure varied between 90 and 140 mmHg, whereas in the group with spleen size classified as 0, 1 and 2, it varied between

TABLE VII

Indians of Alto Xingu, Central Brasil, over 20 years of age, according to the rate of radial pulse and the presence or absence of gross splenomegaly, 1970

Radial pulse rate (Beats per minute)	Degree of splenomegaly				Total	
	0-1-2		3-4-5			
	No.	(%)	No.	(%)	No.	(%)
40 |— 60	5	3.7	1	0.8	6	2.3
60 |— 80	81	60.0	63	48.1	144	54.1
Sub-total	**86**	**63.7**	**64**	**48.9**	**150**	**56.4**
80 |— 100	46	34.1	62	47.3	108	40.6
100 |— 200	3	2.2	5	3.8	8	3.0
Sub-total	**49**	**36.3**	**67**	**51.1**	**116**	**43.6**
Total	135	100.0	131	100.0	266	100.0

80 and 145 mmHg; the median value being 110 mmHg for each group. The diastolic blood pressure, in males with gross splenomegaly varied between 40 and 90 mmHg and in the group with spleen size 0, 1 and 2, it varied between 50 and 90 mmHg; the median value being 170 mmHg in each group.

Among females systolic blood pressure varied between 70 and 120 mmHg in individuals with gross splenomegaly and between 80 and 130 mmHg in the group with spleen size 0, 1 and 2; the median value was the same in each group i.e. 100 mmHg. The diastolic blood pressure varied between 40 and 85 mmHg in females with gross splenomegaly and between 40 and 80 mmHg in those with degrees 0, 1 and 2; the median value for both groups was 60 mmHg.

Heart

There were no physical sign suggesting cardiomegaly in any of the 730 Indians examined. Both the cardiac auscultation and the radial pulse measurement did not reveal the presence of arythmia. The cardiac auscultation showed murmurs present in 47 Indians. These cardiac murmurs were classified as systolic murmurs of mitral focus in 33 cases and as systolic murmurs of pulmonary focus in 14 cases.

The distribution of the cardiac murmurs when related to the presence or absence of gross splenomegaly was the following: a) Among the 33 systolic murmurs of mitral focus, 11 occurred among the 244 individuals with gross splenomegaly and 22 among the 486 individuals with spleen size classified as 0, 1 and 2. The percentage was 4.5% in both groups; b) Among the 14 systolic murmurs of pulmonary focus, 7 occurred among the 244 individuals with gross splenomegaly (2.9%) and 7 among the 486 individuals with spleen size 0, 1 and 2 (1.4%). This difference in percentages is not significant: $X^2 = 1.762$ ($0.10 < P < 0.20$).

Liver

During the physical examination of the group over 20 years of age, it was possible to recognize the presence of hepatomegaly in 57 Indians. Table VIII shows the distribution of hepatomegaly amongst males and

TABLE VIII

Indians of Alto Xingu, Central Brasil, over 20 years of age, according to the presence or absence of gross splenomegaly and hepatomegaly, in both sexes, 1970

Hepatomegaly	Males						Females						Total
	Degree of splenomegaly				Total		Degree of splenomegaly				Total		
	0-1-2		3-4-5				0-1-2		3-4-5				
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
Presence	3	4.0	21	28.4	24	16.1	12	21.8	21	32.8	33	27.7	57
Absence	72	96.0	53	71.6	125	83.9	43	78.2	43	67.2	86	72.2	211
Total	75	100.0	74	100.0	149	100.0	55	100.0	64	100.0	119	100.0	268

Decomposition of Chi-square (X^2):

$X^2_{Total} = 20.694$ d.f. = 3 $P < 0.001$

Between sexes:

$X^2_{Sexes} = 5.339$ d.f. = 1 $(0.2 < P < 0.05)$

Between spleen sizes:

$X^2_{Spleen} = 15.355$ d.f. = 2 $P < 0.001$

females according to the presence or absence of gross splenomegaly.

The presence of hepatomegaly was significantly higher in females. On the other hand, when considering each sex separately, the presence of hepatomegaly was significantly higher in the group having gross splenomegaly.

Ascites

No case of ascites was found in the 730 Indians examined in the medical survey of the Alto Xingu population.

LABORATORY EXAMS

Antibodies to P. vivax *and* P. falciparum

The indirect immunofluorescence reaction was used for the titration of antibodies directed to *P. vivax* and *P. falciparum* utilizing specific antigens. A reaction with titers equal to or greater than 1/33 was considered positive and the subsequent titers were 1/100, 1/300, 1/900 and 1/2700 (this was the highest dilution used).

Table IX displays the titers of the serological reactions in individuals with gross splenomegaly and also in individuals with spleen sizes was 0, 1 and 2.

The Kolmogorov-Smirnov test for two independent samples was used. The alternative hypothesis considered was that the titers of the reaction for the gross splenomegaly group would be higher than in the other group. The value of T given by the test was 0.281 and that led to the rejection of the null hypothesis because the critical value of this statistical method was 0.279 for the one-tail test, at the level of significance of 5%.

Detection of Plasmodium in the peripheral blood

Examination for parasites in peripheral blood smears was made on 97 Indians, giving positive results in 11 cases. Data referring to these positive cases is shown on Table X.

Total serum protein measurement and electrophoresis of protein

The measurement of total serum protein and its fractions was made in 73 out of 77 Indians of the population sample; the indi-

TABLE IX

Indians of Alto Xingu, Central Brasil, according to the titers of the serological reactions for Malaria, by the indirect immunofluorescence method, and the degree of splenomegaly, 1970

Titers of reaction	Degree of splenomegaly					
	0-1-2	3-4-5	Accumulated frequencies 0-1-2	Accumulated frequencies 3-4-5	Accumulated percentages 0-1-2	Accumulated percentages 3-4-5
< 1/33	1	0	1	0	2.4	0
1/33	0	0	1	0	2.4	0
1/100	3	0	4	0	9.5	0
1/300	9	1	13	1	31.0	2.9
1/900	14	18	27	19	64.3	54.3
1/2700	15	16	42	35	100.0	100.0

TABLE X

Age, sex, spleen size, species of Plasmodia found and titers of serological specific reactions by the indirect immunofluorescence method. Indians with positive peripheral blood examination, Alto Xingu, Central Brasil, 1970

Age (years)	Sex	Spleen size degree	Blood smear positive for	Titers of serological reaction	
				P. vivax	*P. falciparum*
5	F	3	*P. vivax*	1/900	1/300
10	M	2	*P. vivax*	negative	1/100
11	F	1	*P. falciparum*	1/300	1/100
11	M	2	*P. falciparum*	1/900	1/300
17	F	3	*P. vivax*	1/300	1/300
28	F	2	*P. falciparum*	1/900	1/900
30	M	2	*P. vivax*	1/2700	1/2700
35	M	3	*P. vivax*	1/900	1/2700
35	M	4	*P. falciparum*	1/900	1/900
40	M	2	*P. falciparum*	1/900	1/900
40	M	1	*P. vivax*	1/900	1/2700

Note: Highest dilution tested was 1/2700

vidual results are shown in Table A in the Appendix.

In Table XI the averages corresponding to the total serum protein levels and their different fractions are shown in the two groups of Indians classified according to sex and degree of splenomegaly.

Using the Mann-Whitney test for differences between average values of each serum component measured and comparing the group having spleen size grades 0.1 and 2 with grades 3, 4 and 5, for each sex, the values of Z that were obtained are shown in Table XII.

Therefore, the null hypothesis could be rejected only in the case of fractions alpha-2-globulin and gamma-globulin in males and gamma-globulin in females.

In males, the average value for alpha-2-globulin was lower in the group with gross splenomegaly, while the average for gamma-globulin was higher in this group. In females, the average value of gamma-globulin was also higher in the group with gross splenomegaly.

Immunoglobulins

The measurement of immunoglobulin classes was made on 40 Indians over 10 years of age. In Table B, added in the Appendix, these measurements are shown.

The averages corresponding to the values of each immunoglobulin class, classified according to sex and degree of splenomegaly are presented in Table XIII. Also in this table are the values considered normal for the techniques employed for measurement.

Using the Mann-Whitney test for differences between averages of values of each immunoglobulin measured and comparing the group with spleen size grades 0, 1 and 2 and with grades 3, 4 and 5, for each sex, the values of that were obtained are shown in Table XIV.

Therefore, it was possible to reject the null hypothesis only in the case of IgG and IgM in females; the average values of IgG and IgM in females were significantly higher in the group with gross splenomegaly in relation to the group with spleen sizes graded 0, 1 and 2.

TABLE XI

Average values of total serum protein and fractions, for male and female, according to the degree of splenomegaly, in 73 Indians of Alto Xingu, Central Brasil, 1970. Normal values for the techniques used

Total serum protein and fractions (g/100 ml)	Males		Females		Normal values for techniques employed (g/100 ml)
	Degree of splenomegaly				
	0-1-2 (n = 24)	3-4-5 (n = 20)	0-1-2 (n = 15)	3-4-5 (n = 14)	
Total protein	7.4	7.6	7.2	7.7	6.0 to 8.0
Albumin	3.84	4.10	4.13	3.76	4.0 to 5.0
Alpha-globulin	0.30	0.26	0.20	0.28	0.2 to 0.4
Alpha-2-globulin	0.64	0.43	0.55	0.62	0.4 to 0.7
Beta globulin	0.87	0.84	0.83	0.87	0.7 to 0.9
Gamma globulin	1.71	1.95	1.55	2.22	1.2 to 1.8

n = number of people

TABLE XII

Values of Z or U (Mann-Whitney test) and the corresponding probability (P), for the differences between averages in individuals with different degrees of splenomegaly, according to the serum component measured and sex

Total serum protein and fractions	Males		Females	
	Z	P	U	P
Total protein	0.79	0.43	66	$0.05 < P < 0.10$
Albumin	1.50	0.13	71.5	$0.10 < P < 0.20$
Alpha-1-globulin	0.99	0.16	73.5	$0.10 < P < 0.20$
Alpha-2-globulin	3.61 *	0.01	86	> 0.20
Beta-globulin	0.48	0.31	87	> 0.20
Gamma-globulin	1.78 *	0.04 (one-tail)	35.5 *	< 0.001 (one-tail)

For a comparative study the immunoglobulin measurement was performed on 25 accultured Indians, living on a farm in the State of São Paulo, where malaria has been erradicated for many years. The average values for IgG, IgM and IgA were 2.746 mg/100 ml, 84 mg/100 ml and 169 mg/100 ml respectively. The highest values for IgE did not exceed 300 ng/ml and in 10 of the sera results were below 175 ng/ml. Therefore, the average values for IgM in this group of Indians from São Paulo were considered to be within the normal limits for the technique employed, while in Alto Xingu the IgM average values are quite high in the various groups, classified according to age, sex and spleen size. The average values for IgE observed in Alto Xingu are

TABLE XIII

Average values for immunoglobulin classes (IgG, IgM, IgA and IgE) for males and females, according to the degree of splenomegaly, in 40 Indians of Alto Xingu, Central Brasil, 1970. Values considered normal for the techniques employed

Immunoglobulins	Males		Females		Normal values for the techniques employed
	Degree of splenomegaly				
	0-1-2 (n = 12)	3-4-5 (n = 13)	0-1-2 (n = 7)	3-4-5 (n = 8)	
IgG	2042	2382	2225	2856	1217 to 1529 mg/100 ml, average 1373
IgM	254	301	173	242	58 to 158 mg/100 ml, average 108
IgA	196	192	194	217	94 to 206 mg/100 ml, average 150
IgE	1594	1535	1507	1953	≤ 175 ng/ml (1)

n = number of people (1) nanogram per ml

TABLE XIV

Values of U (Mann-Whitney test) and of corresponding probability (P), for the differences between averages in individuals with different degrees of splenomegaly, according to the immunoglobulin class measured and sexes

Immunoglobulins	Males		Females	
	U	P	U	P
IgG (mg/100 ml)	50.5	0.10 < P < 0.20 (one-sided)	13.5 *	0.025 < P < 0.05 (one-sided)
IgM (mg/100 ml)	58.5	> 0.20 (one-sided)	13.0 *	0.025 < P < 0.05 (one-sided)
IgA (mg/100 ml)	73.0	> 0.10	18.0	> 0.10
IgE (ng/ml)	71.0	> 0.10	22.0	> 0.10

very high when compared with the values obtained from the accultured Indians already mentioned.

Liver biopsy

Surgical or needle liver biopsy was performed on 8 Indians of Alto Xingu admitted to Hospital São Paulo (São Paulo) from 1968 to 1973. The Table XV includes the findings of the liver histological examination (*).

The histological picture of the liver was classified according to the concentration of lymphocytes in the sinusoids in degrees 0, I, II and III as used by MARSDEN et al.[24] in the study of the TSS.

(*) Slides with histological specimens of the liver of cases 1, 2, 3, 4, 5 and 6 were kindly reviewed by Prof. Hutt, Department of Pathology of St. Thomas's Medical School of London

Hematemesis and Melena

Episodes of hematemesis and melena were observed in 11 Indians from Alto Xingu between 1969 and 1973. In 4 of them hospital admission made the liver biopsies possible. Table XVI shows some data referring to the 11 cases mentioned including the deaths following the hematemesis and melena episodes.

DEATH CAUSES

An attempt was made to identify the causes of death in the age group over 20

TABLE XV

Age, sex, spleen volume, degree of jaundice and ascites, presence of esophagical varices, search for Plasmodium and histological findings of 8 Indians submitted to liver biopsy. Alto Xingu, Central Brasil, 1968 to 1973

Number of order	Age (years)	Sex	Spleen volume (degrees)	Jaundice	Ascites	Esophagical varices	Search for Plasmodium	Liver biopsy (+)
1	13	F	5	–	–	–	positive	TSS-III
2	22	M	3	–	–	–	–	TSS-I
3	25	F	4	–	–	–	–	TSS-I
4	26	M	3	–	–	–	–	TSS-II
5	30	M	4	–	+++	present	positive	Initial cirrhosis
6	35	M	3	++	–	–	–	TSS-III
7	38	M	5	+++	+	–	positive	TSS-II
8	37	M	5	++	–	present	–	TSS-I

(+) TSS — Tropical Splenomegaly Syndrome

TABLE XVI

Age, sex, spleen size, liver biopsy and death occurrences of 11 Indians with hematemesis and melena. Alto Xingu, Central Brasil, 1968 to 1973

No.	Age (years)	Sex	Spleen size	Liver biopsy	Follow-up
1	13	F	5	TSS-III	survived
2	26	M	2	—	died
3	25	F	4	TSS-I	survived
4	26	M	0	—	survived
5	30	M	4	initial cirrhosis	survived
6	32	M	3	—	died
7	27	M	3	—	died
8	37	M	5	TSS	died
9	31	M	2	—	died
10	42	M	4	—	died
11	52	M	3	—	died

Note: Cases 1, 3, 5 and 8 were also included under the same numbers in the previous table

years of age during the period from 1968 to 1973. A total of 32 deaths occurred in this age group in the period mentioned. In several cases it was difficult to obtain information about the clinical manifestation that preceded death specially when it occurred in the more distant villages. The main clinical manifestations present or the probable causes of death were the following:

Hematemesis and melena	7
Fever (malaria)	3
Respiratory infection, non-specific	3
Hepatic coma	1
Cachexia	2
Obstetrical causes	4
Gynecological cancer with metastasis	1
Sudden deaths (accidents, etc.)	3
No information available	8
Total	32

DISCUSSION

The presence of a large spleen without a well defined etiology has been described in many countries in Africa and Asia where malaria occurs as an endemic disease. This situation has been called by several names: criptogenic splenomegaly, gross splenomegaly, idiopathic splenomegaly, tropical splenomegaly, big spleen disease, *Splenomegalie algeriene, Bengal splenomegalie.* Most recently the term Tropical Splenomegaly Syndrome has been applied [6].

The Tropical Splenomegaly Syndrome (TSS) is characterized by the presence of a persistent and large spleen, hepatic sinusoidal lymphocytosis, and disproportionate elevation of serum IgM levels and antimalarial antibody titres [25]. The occurrence of Tropical Splenomegaly Syndrome in malarious areas only, the exclusion of the other causes of splenomegaly and the amelioration of the clinical picture and laboratory tests under the prolonged antimalarial therapy indicate that the infection by plasmodia must be considered to be one of the etiologic factors involved in this syndrome. The TSS could be considered as an aberrant response to recurrent malarial infection but the whole process involved remains to be established.

In the Alto Xingu region, malaria has a high endemic prevalence, the transmission being more intense from November to April. The search for plasmodium in the peripheral blood performed during the years of 1966-1967 and 1969 [13, 14] was positive in 52.5% and 46.5% of the individuals examined, respectively. The first survey showed a predominance of *P. vivax* (52.1%), followed by *P. falciparum* (35.0%) and *P. malariae* (10.3%), but in the second survey there was a predominance of *P. falciparum* (61.7%), followed by *P. vivax* (28.3%) and *P. malariae* (2.8%).

In the Indian population from the Alto Xingu we found gross splenomegaly, high titres of antibodies against plasmodium antigens by the indirect immunofluorescence technique and elevation of serum IgM levels. Hepatic biopsy performed in 8 Indians showed the presence of sinusoidal lymphocytosis in 7 of them. Therefore, all the features needed to characterize the Tropical Splenomegaly Syndrome were observed. The percentage of adults with gross splenomegaly (51.5%) is similar to that of 60% described in New Guinea by CRANE & PRIOR [10].

To investigate in more detail the prevalence of marked splenomegaly in the different tribes of the Alto Xingu region they were divided in groups according their linguistic origins: Aruak, Carib and Tupy. This grouping is justified by the fact that the total Indian population of the area is only 730, and intertribal marriage is still more frequent in the same linguistic group. The linguistic group gives some indications about the geographical provenance of the tribes who in the past emigrated to the Alto Xingu region. No significant differences were found between the linguistic groups already mentioned, in relation to the prevalence of gross splenomegaly in the various age groups. It was impossible to study the familial distribution of TSS, but the data presented by us do not confirm the existence of a genetic predisposition factor as suggested by some Authors [29, 44]. The glucose-6-phosphate dehidrogenase deficiency was not found among the Indians [20], in contrast to the description of some Authors in malarious areas

of Africa where the infection by *P. falciparum* is predominant [1, 26]. A survey for abnormal hemoglobin in the Alto Xingu Indians was negative also [28].

According to CHAUDHURI et al. [8] malnutrition facilitates the installation of TSS, however experimental studies in mice did not support this hypothesis [39]. In the Alto Xingu region the nutritional status of the population was generally satisfactory and no remarkable difference in the nutritional conditions was observed between the groups of individuals separated according to the presence or absence of gross splenomegaly.

When considering the proportion of Indians with gross splenomegaly in each age group, the data from Alto Xingu showed no difference in relation to sex. The percentage of individuals with discoloured mucous membranes was significantly higher in the group with spleen sizes graded 3, 4 and 5 than in the group with grades 0, 1 and 2. Similarly in the presence of jaundice, which was observed in 10 of the 730 Indians examined, most of these cases were included in the group with gross splenomegaly.

A study of the radial pulse rate was made on individuals over 20 years of age. Table VII shows that the percentage of individuals with a frequency above 80 per minute was significantly higher in the group with gross splenomegaly. Arterial blood pressure was measured in 268 adults. Individuals with gross splenomegaly had systolic and diastolic preassures very similar to those included in the group without gross splenomegaly, in either sex. The median values were identical.

Cardiac auscultation revealed the presence of murmurs in 47 Indians among the 730 adults and children that were examined. Systolic murmurs in the mitral focus were detected with the same percentage (4.5%) in the two groups separated according to the degree of splenomegaly. Systolic murmurs in the pulmonary focus did not show a significant difference either.

Hepatomegaly has been described as a frequent finding in the individuals with gross splenomegaly [29]. In Alto Xingu, only adults being considered, hepatomegaly was detected in 57 of 268 examined. Both in women and in men there was a significantly higher proportion of cases of hepatomegaly in the group with gross splenomegaly. Women had a significantly higher proportion of hepatomegaly than men (Table VIII).

Table IX shows the results observed in a population sample of 77 Indians. It is possible from these results to infer that plasmodium antibodies, detected by the indirect immunofluorescence technique, are present in most Indians living in Alto Xingu. Individuals with gross splenomegaly had a predominance of reactions with higher titres as compared to the group with spleen sizes graded 0, 1 and 2. Plasmodium parasites were found in peripheral blood in 11 Indians of the 77 included in the population sample. No relation was observed between the presence of malaria parasites and the titres of the serological reactions (Table X). From the 11 individuals with malaria parasites found on blood smears, 4 had gross splenomegaly and 7 spleen size graded 0, 1 and 2. According to CRANE & PRYOR [10], in New Guinea, parasitemia was less common in patients with gross splenomegaly than in the control population.

In TSS a reduction in the levels of serum albumin and an elevation of gammaglobulin have been referred [36]. In Alto Xingu no significant difference was found into the levels of serum albumin when patients with gross splenomegaly were compared to individuals with spleen sizes 0, 1 and 2, in either sex. The gammaglobulin levels however were significantly higher in the gross splenomegaly group, both in men and women.

A study of immunoglobulins was made among the Indians, measuring IgM, IgG, IgA and IgE in 40 individuals over 10 years of age. The values for IgM, IgG and IgE were all above the normal range for the technique employed (Table XIII). A comparison was made with measurements obtained in 25 accultured Indians living on the State of São Paulo, in a developed region where malaria was erradicated many

years ago. In the Alto Xingu the average values of IgM and IgG were 235 mg/100 ml and 2346 mg/100 ml respectively as compared to 84 mg/100 ml and 2746 mg/100 ml in the Indians of São Paulo. The average IgE value in Alto Xingu was 1644 ng/ml while in the Indian group from São Paulo the highest values did not exceed 300 mg/ml.

In New Guinea, WELLS [42] found a definite correlation between high titres of IgM and the presence of splenomegaly. Also in New Guinea, CRANE et al. [11] comparing the values of IgM and IgG in individuals over 11 years of age with spleen sizes graded 0 and 1 and individuals with degrees 2, 3, 4 and 5 observed that this latter group had higher IgM levels but the levels of IgG were approximately the same for both groups. In the Alto Xingu a comparison of the average immunoglobulin values among patients with gross splenomegaly and individuals with spleen sizes graded 0, 1 and 2 showed significant differences only for IgM and IgG, and then, only in females. The more elevated values being found in women with gross splenomegaly.

Due to the technical difficulties found in field work the liver biopsy was made only on 8 patients admitted to the Hospital for surgical or clinical treatment. All these patients had gross splenomegaly and the histological exams showed in 7 cases the presence of lymphocyte infiltration in the sinusoid capillaries, a picture similar to that described in the Tropical Splenomegaly Syndrome, in the other case the histological diagnosis was of an initial stage of cirrhosis. As noted in Table XV, four out of the seven cases with histological diagnosis of Tropical Splenomegaly Syndrome had jaundice or ascites, the presence of plasmodium in the peripheral blood was observed in three patients and the diagnosis of portal hypertension with esophagical and gastric varices by radiological examination was made in two cases [32].

As a rule individuals with gross splenomegaly in Alto Xingu do not demonstrate limitation of their physical capacity, but sometimes after acute episodes of hemolyses the patients start showing physical prostation, intense anemia, increase in the reticulocyte counts and bilirrubin levels. Usually these patients have a prolonged period of convalescence. Similar features have been described by various Authors who studied the TSS [25].

During the period of 1968 to 1973 the occurrence of hematemesis and melena was observed in 11 Indians, seven of which died in first or subsequent hemorrhagic episodes. Liver histological examinations made in 4 of these 11 cases revealed the presence of sinusoidal capillary infiltration in 3 cases and initial cirrhosis in the other (Table XVI). Sometimes the episodes of hematemesis and melena occurred suddenly, when the individuals were in apparently good health, at their usual occupations. Portal hypertension has been described in the Tropical Splenomegaly Syndrome [19, 43] but, according to these Authors, the presence of esophagical varices and the occurrence of hematemesis and melena was a rare finding, as opposed to the high incidence found in Alto Xingu population.

In the areas where the control of malaria resulted in a great decrease in the transmission of the disease, an important reduction has been observed in the prevalence of the TSS. Furthermore, in areas where an intense transmission of malaria persists prolonged use of antimalarial drugs has been recommended to improve the clinical and laboratory manifestations of the Tropical Splenomegaly Syndrome, without the risks of splenectomy and with better results [18]. However, if the rate of transmission of malaria remains at a high level, when the prophylactic use of antimalarial drugs is suspended the individual is liable to have severe plasmodium infections due to the decrease immunity to the parasite. Probably, he will show the same clinical picture of TSS as he presented before the prophylactic treatment [15]. In Alto Xingu splenectomy was employed in three patients with TSS, two of which died a few months after the surgery due to new episodes of hematemesis and melena. The third patient, female, 13 years of age, presented intense anemia and a spleen size graded 5 (Fig. 1); the spleen weighed 4.600 g, measuring about 40 cm in its great diameter (Fig. 2). Now, 6 years after the surgery, the patient is in satisfactory health.

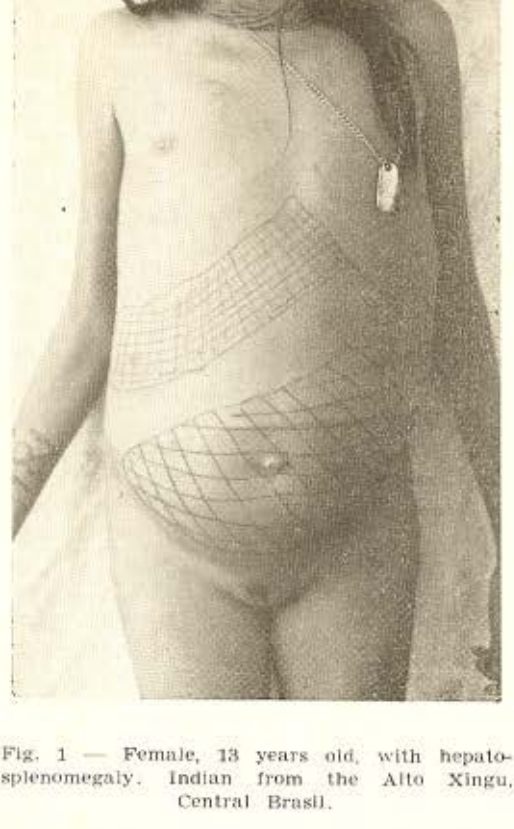

Fig. 1 — Female, 13 years old, with hepato-splenomegaly. Indian from the Alto Xingu, Central Brasil.

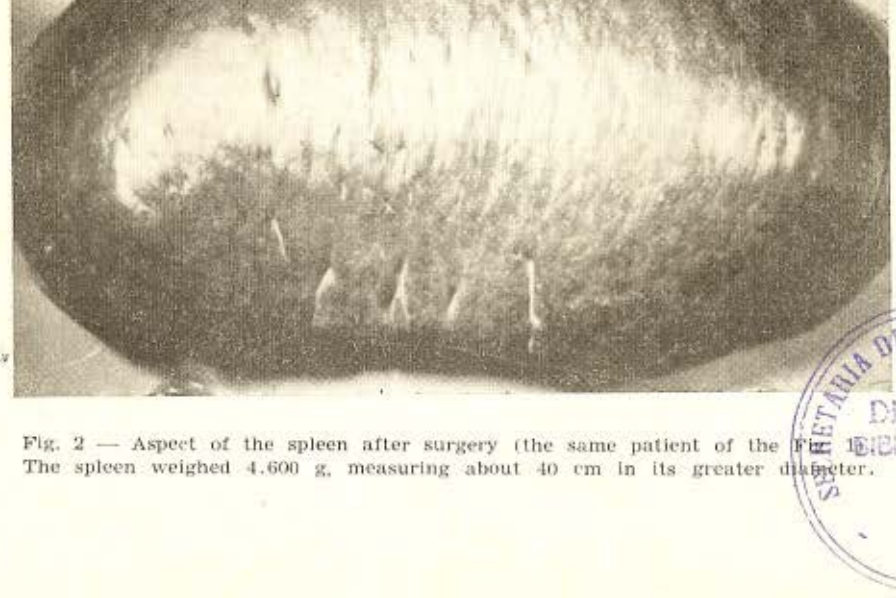

Fig. 2 — Aspect of the spleen after surgery (the same patient of the Fig. 1). The spleen weighed 4.600 g, measuring about 40 cm in its greater diameter.

CRANE et al. [12], in New Guinea, studied 75 adult natives with TSS in a clinical follow-up of six and half years. At the end of this period 27 deaths had been noted. An indication of the probable cause of death was given only in 10 cases: two by septicemia and eight resulting from acute febril diseases. The Authors accentuated the high mortality rate observed in the group of natives with TSS and suggested that this must be because of a reduction in the individual resistence against infectious diseases in general.

In Alto Xingu from 1968 to 1973 there were 32 deaths in adults. Seven of these were due to episodies of hematemesis and melena. The second cause of death was occupied by febrile diseases including malaria infection and nonspecific pulmonary infections. Our data, until now, does not allow us to establish an association between the presence of TSS and in increasing the risk of death from infectious diseases.

The occurrence of gross splenomegaly in non-Indian population was observed by us in the Tapirapes and Araguaia Rivers area in the Amazonic Basin. These cases were detected in small villages where malarial transmission was very intensive, and it was possible to exclude other causes of spleen enlargement as Kalazar and Schistosomiasis. PRATA et al. [30] described the presence of gross splenomegaly in patients from the Amazonic Region.

Malaria remains one of the most serious health problems in the Alto Xingu region, being the principal cause of death among the children exposed to acute attacks of the disease. After long exposure to malaria infections some people develop in the adult age the Tropical Splenomegaly Syndrome. In this paper one attempt was made to evaluate the importance of this Syndrome in terms of morbility and mortality.

CONCLUSIONS

The presented data suggests that gross splenomegaly which was observed in 33.4% of the Alto Xingu population is associated with frequent plasmodium infections. The presence of persistent gross splenomegaly, hepatic sinusoidal lymphocytosis, and disproportionate elevation of serum IgM levels and antimalarial antibody titres confirm that the Tropical Splenomegaly Syndrome is present in the Indians from the Alto Xingu.

In each of the age groups considered no significant difference was found in respect to gross splenomegaly prevalence when subjects were separated according to sex or linguistic groups. Physical examination demonstrated a significant increase in the number of patients with pallor of mucous membranes in the group with gross splenomegaly as compared to the group with spleen size 0, 1 and 2. The same conclusion was achieved in regard to jaundice which was present in 10 of 730 examined Indians. Blood pressure readings in the gross splenomegaly group and in the other were similar. There was a higher proportion of patients with radial pulse above 80 per minute in the gross splenomegaly group. There was no difference in the incidence of cardiac murmurs in the two groups. In both sexes there was a higher proportion of individuals with hepatomegaly in the gross splenomegaly group. When only the sex was considered, hepatomegaly was more frequent in women.

Antimalarial antibodies detected by immunofluorescence technique was positive in 98.7% of the population sample. Elevated titres were more commonly detected in the individuals with gross splenomegaly. There was no relation between elevated titres of immunofluorescence and the detection of plasmodium in the peripheral blood. The average value of gamma-globulin was higher in the group with gross splenomegaly, in both sexes, than in the group with degrees 0, 1 and 2 of spleen size. The average of alpha-2-globulin was smaller in the group with gross splenomegaly only in men. The average values of IgG, IgM and IgE in the population of Alto Xingu were higher than the values considered as normal for the techniques employed. The average values of IgM and IgE in Alto Xingu were also much higher than those observed in a group of 25 accultured Indians living in an area where malaria was erradicated many

years ago. When groups separated according to the degree of splenomegaly were studied, significant differences were detected only for IgM and IgG and only in women, with higher values in the group with gross splenomegaly.

Liver biopsy was performed in 8 Indians of Alto Xingu with gross splenomegaly. In 7 of which, histological findings were similar to the picture described for the Tropical Splenomegaly Syndrome. Hematemesis and melena, were recorded in 11 Indians during a period of five years. Liver biopsy was performed only in 4 of these cases, and the histological picture of TSS was found in 3 of them. This data indicates that hematemesis and melena, probably due to rupture of esophagical varices is an important cause of death in Alto Xingu, when compared with other causes.

RESUMO

Associação entre esplenomegalia e malária em índios do Alto Xingu, Brasil Central

A presença de baços volumosos, palpáveis próximos da cicatriz umbelical, foi evidenciada em 33,4% da população indígena do Alto Xingu, Brasil Central, com igual distribuição nos dois sexos. Inquérito sorológico e parasitário, realizado na área, acusou a presença de anticorpos contra o plasmódio, pela imunofluorescência, em 98,7% dos indivíduos incluídos na amostra populacional, e a presença de plasmódios no sangue periférico em 14,3%. Estes resultados indicam que é intensa a transmissão da malária na área do Alto Xingu. Ao lado da esplenomegalia acentuada e títulos elevados de anticorpos contra o plasmódio, estão presentes valores aumentados de IgM e infiltrado linfocitário dos sinusóides hepáticos. Estes achados caracterizam a Síndrome de Esplenomegalia Tropical, que tem sido descrita em áreas malarígenas de vários países da África e da Ásia. Episódios de hematêmese e melena tem sido referidos no Alto Xingu, e o estudo radiológico, realizado em alguns casos, acusou a presença de grande dilatação do sistema porta e, por vezes, de varizes esofagianas.

ACKNOWLEDGEMENTS

The Authors acknowledge with gratitude the co-operation of all the people who have taken part in the medical field work among the Indians from the Xingu National Park. We are grateful to Dr. Walter Leser, former Professor of Epidemiology in this Medical School for his invaluable orientation, to Dr. Mario E. Camargo and his collaborators and tc the Laboratory Fleury for the serological tests. We equally express our thanks to the Fundação Nacional do Índio and the Força Aérea Brasileira without whose collaboration would not have been possible this work.

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Recebido para publicação em 24/3/1975.

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APPENDIX

TABLE A

Values of total proteins and fractions, Indians of Alto Xingu, Central Brasil, 1970

Males — Spleen sizes 0-1-2 — (n = 24)

No.	Age (years)	Total protein	Albumin	Alpha-1-glob.	Alpha-2-glob.	Beta-glob.	Gamma-glob.
1	7	6.8	3.46	0.37	0.75	0.74	1.48
2	8	7.3	4.82	0.19	0.52	0.64	1.13
3	9	7.5	4.41	0.18	0.57	0.68	1.66
4	10	6.4	2.24	1.49	0.82	0.76	1.09
5	11	7.2	4.03	0.30	0.64	0.74	1.49
6	11	7.3	4.25	0.19	0.69	0.89	1.28
7	17	7.7	4.49	0.15	0.56	1.09	1.41
8	17	7.9	2.74	0.25	0.91	1.47	2.53
9	18	7.5	3.72	0.22	0.40	1.11	2.05
10	19	7.9	4.65	0.12	0.52	0.87	1.74
11	20	7.3	3.70	0.15	0.61	0.95	1.89
12	20	6.5	4.13	0.11	0.33	0.72	1.21
13	23	8.3	4.55	0.14	1.27	0.94	1.40
14	25	7.9	3.75	0.12	0.51	0.79	2.73
15	30	8.4	4.74	0.23	0.54	0.90	1.99
16	30	7.9	3.47	0.18	0.54	1.07	2.64
17	30	6.9	2.45	1.31	0.77	0.71	1.66
18	30	6.6	3.63	0.30	0.61	0.72	1.34
19	35	7.9	4.06	0.15	0.95	0.87	1.87
20	40	7.2	3.76	0.18	0.55	1.10	1.61
21	40	6.8	3.71	0.13	0.41	0.90	1.65
22	55	7.1	3.74	0.27	0.62	0.86	1.61
23	60	8.0	3.66	0.26	0.86	0.96	2.26
24	60	7.4	3.96	0.24	0.38	0.38	1.24
$\bar{X}$		7.4	3.84	0.30	0.64	0.87	1.71

TABLE A

Values of total proteins and fractions, Indians of Alto Xingu, Central Brasil, 1970

Males — Spleen sizes 3-4-5 — (n = 20)

No.	Age (years)	Total protein	Albumin	Alpha-1-glob.	Alpha-2-glob.	Beta-glob.	Gamma-glob.
25	12	6.9	4.27	0.14	0.39	0.66	1.44
26	15	7.5	4.07	0.17	0.44	1.06	1.76
27	20	7.4	4.85	0.24	0.44	0.73	1.14
28	22	6.4	3.93	0.13	0.37	0.58	1.39
29	24	8.1	4.28	0.15	0.27	1.13	2.27
30	25	8.6	5.00	0.22	0.39	0.99	2.00
31	25	6.9	4.34	0.11	0.28	0.64	1.53
32	25	7.1	2.68	0.18	0.59	1.09	2.56
33	26	7.2	2.93	0.22	0.63	0.84	2.58
34	30	7.4	3.67	0.19	0.61	0.97	1.96
35	32	7.5	4.55	0.15	0.36	0.76	1.68
36	33	7.0	3.95	0.17	0.50	0.75	1.63
37	34	7.7	4.00	0.16	0.54	1.11	1.89
38	35	7.3	3.34	1.72	0.39	0.72	1.13
39	35	8.7	4.74	0.18	0.42	0.86	2.50
40	38	8.6	4.33	0.18	0.42	0.86	2.81
41	39	8.1	4.37	0.20	0.44	0.81	2.28
42	39	7.8	4.55	0.17	0.23	0.71	2.14
43	40	7.9	3.82	0.24	0.52	0.97	2.35
44	50	7.3	4.25	0.18	0.34	0.63	1.90
$\bar{X}$		7.6	4.10	0.26	0.43	0.84	1.95

TABLE A

Values of total proteins and fractions, Indians of Alto Xingu, Central Brasil, 1970

Females — Spleen sizes 0-1-2 — (n = 15)

No.	Age (years)	Total protein	Albumin	Alpha-1-glob.	Alpha-2-glob.	Beta-glob.	Gamma-glob.
45	3	5.9	4.06	0.15	0.55	0.38	0.76
46	6	7.5	4.29	0.17	0.92	0.99	1.13
47	11	7.2	4.40	0.37	0.34	0.63	1.46
48	12	6.9	4.03	0.12	0.46	0.57	1.72
49	12	7.7	3.87	0.34	0.71	1.02	1.76
50	18	7.2	4.22	0.11	0.43	0.72	1.72
51	22	7.0	3.50	0.17	0.60	1.12	1.61
52	22	7.4	4.34	0.16	0.50	0.67	1.73
53	25	7.5	4.20	0.17	0.57	0.93	1.63
54	26	7.1	4.60	0.18	0.33	0.61	1.38
55	35	7.5	3.93	0.29	0.96	0.77	1.55
56	40	7.1	4.19	0.07	0.33	0.80	1.71
57	40	7.8	3.43	0.25	0.66	1.04	2.42
58	40	6.8	4.38	0.22	0.40	0.75	1.05
59	42	8.1	4.51	0.19	0.43	1.39	1.58
$\bar{X}$		7.2	4.13	0.20	0.55	0.83	1.55

TABLE A

Values of total proteins and fractions, Indians of Alto Xingu, Central Brasil, 1970

Females — Spleen sizes 3-4-5 — (n = 14)

No.	Age (years)	Protein total	Albumin	Alpha-1-glob.	Alpha-2-glob.	Beta-glob.	Gamma-glob.
60	5	6.9	4.39	0.27	0.78	0.66	0.80
61	17	7.2	3.16	0.24	0.58	0.94	2.28
62	20	7.5	3.42	0.20	0.68	0.97	2.23
63	22	7.7	4.28	0.10	0.29	0.89	2.14
64	22	6.9	2.85	0.33	0.61	0.99	2.12
65	25	8.4	4.05	0.22	0.69	1.02	2.42
66	26	8.3	4.06	0.15	0.48	0.95	2.66
67	26	9.2	4.62	0.18	0.60	0.79	3.01
68	27	8.3	3.81	0.33	0.41	0.94	2.81
69	28	7.7	4.95	0.28	0.61	0.89	0.97
70	30	6.6	2.80	0.22	0.67	0.68	2.23
71	40	7.4	3.60	0.17	0.45	0.78	2.40
72	41	7.7	4.07	0.21	0.40	0.81	2.21
73	45	8.1	2.55	1.06	0.77	0.87	2.85
$\bar{X}$		7.7	3.76	0.28	0.62	0.87	2.22

TABLE B

Values of IgG, IgM, IgA and IgE, Indians of Alto Xingu, Central Brasil, 1970

Males — Spleen sizes 0-1-2 — (n = 12)

No.	Age (years)	IgG	IgM	IgA	IgE
1	11	1333	81	163	175
2	17	2046	226	374	2450
3	17	1815	81	202	2450
4	18	3000	151	202	2000
5	20	1815	133	163	825
6	30	2046	100	240	2350
7	30	2370	298	163	900
8	35	2370	400	107	1300
9	40	1815	544	107	2450
10	43	2520	196	304	3150
11	55	1333	133	163	900
12	60	2046	710	163	175
	$\overline{X}$ =	2042	254	196	1594

Males — Spleen sizes 3-4-5 — (n = 13)

No.	Age (years)	IgG	IgM	IgA	IgE
13	12	2670	94	107	500
14	24	2670	232	107	175
15	25	2670	544	374	2000
16	25	1333	202	163	3150
17	30	1120	151	281	175
18	32	2370	298	133	2000
19	33	2370	163	81	175
20	34	2370	263	240	2450
21	35	2046	133	133	175
22	38	2046	335	227	2000
23	39	4080	900	163	2000
24	40	2224	335	281	3150
25	50	3000	263	202	2000
	$\overline{X}$ =	2382	301	192	1535

TABLE B

Values of IgG, IgM, IgA and IgE, Indians of Alto Xingu, Central Brasil, 1970

Females — Spleen sizes 0-1-2 — (n = 7)

No.	Age (years)	IgG	IgM	IgA	IgE
26	11	2370	133	60	900
27	12	1333	101	440	500
28	22	2046	196	240	500
29	22	2670	232	202	2450
30	25	2670	202	163	2450
31	26	2670	81	151	1300
32	35	1815	263	94	2450
	$\overline{X}$ =	2225	173	194	1507

Females — Spleen sizes 3-4-5 — (n = 8)

No.	Age (years)	IgG	IgM	IgA	IgE
33	17	2670	133	202	3150
34	20	2046	263	240	500
35	22	2670	232	163	2450
36	22	3520	202	281	2000
37	25	2670	335	281	1175
38	26	4080	202	240	2450
39	40	2670	232	163	2450
40	41	2520	335	163	2450
	$\overline{X}$ =	2856	242	217	1953