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REMOVAL OF S. MANSONI IN PATIENTS WITH HEPATOSPLENIC SCHISTOSOMIASIS: AN ESTIMATE OF THE PARASITOLOGICAL LOAD BY MEANS OF QUANTITATIVE COPROSCOPY (*)

Luiz DOMINGUES (1), Marcello SILVEIRA, J. F. Corrêa LIMA F.º (2), J. C. Porto CARREIRO JR. (2) and Salomão KELNER (3)

SUMMARY

32 Patients with an average age of 18.9 years suffering from schistosomiasis mansoni in its compensated hepatosplenic from who never taken schistosomicidal drugs were studied. All the patients were submitted to splenectomy and filtration of the portal blood for the removal of **S. mansoni.** A study was made of the relationship between the average number of eggs per gram of faeces obtained from the analysis of 10 successive samples of each patient's faeces by the Kato-Katz method and the number of worms removed from the portal blood. The statistical procedure used revealed a significant relationship between the parameters studied, permitting the establishment of the respective regression equations designed to estimate the numbers of female worms, pairs of worms and total worms. From the results and the application of a technique for the constitution of extreme subgroups, the authors propose a classification of the intensity of infection; a) light parasitic load: average number of eggs per gram of faeces less than 808, corresponding to an estimated parasitic load of less than 226 female worms; b) moderate parasitic load: average number of eggs per gram of faeces between 808 and 3968, corresponding to an estimated parasitic load of between 226 and 528 female worms; c) intense parasitic load: average number of eggs per gram of faeces greater than 3968, corresponding to an estimated parasitic load greater than 528 female worms. On the basis of the proposed classification the Authors discuss the indication of specific treatment for schistosomiasis mansoni in patients with the hepatosplenic form of the disease.

INTRODUCTION

Schistosomiasis mansoni is one of the great endemic diseases found in Brazil, with a tendency to spread throughout the country, particularly in the Northeast, as a result of the precarious medical and sanitary facilities.

This disease, on account of its high morbidity and potential progression to serious clinical forms, hinders the development of the populations exposed to infection by parasites (PRATA & BINA [31]).

Efforts have been made with the aim of controlling and even eradicating this parasitosis. The various methods and drugs used however, have not yet produced effective results. In isolated areas, where pilot studies have been carried out, a small temporary fall

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(1) Assistant Professor
(2) Associate Professor
(3) Full Professor of Abdominal Surgery

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in the prevalence of the disease has been noted (BINA [7]; COURA [18] & KLOETZEL [29]). Clinical treatment has led only to a reduced incidence in its serious clinical forms (BINA [7]), for the progressive increase in the number of schistosomotic individuals continues, the number of sufferers being currently estimated at about 10 million.

This fact confirms that, in addition to chemotherapy, preventive measures for the control and eradication of the parasitosis are of prime importance.

In advanced forms of the disease the removal of worms from the portal system has been carried out since 1967, following the pioneering reports undertaken by (CARVALHO LUZ et al. [10]) in Bahia.

An analysis of the number of worms removed from the portal in the filtrations carried out in the Division of Abdominal Surgery of the University Hospital of the Federal University of Pernambuco showed that there was a great variation in the parasitic load of the patients studied, though all of them presented the hepatosplenic form of the disease and came from the area where schistosomiasis mansoni is highly endemic (ARAUJO [2]; BARBOSA [3] and BARBOSA [4]).

Whilst admitting that there is a significant quantity of patients that harbour a large number of worms, it would be in order to question the employment of chemotherapeutical drugs in these cases, since the death of the worms could worsen the preexisting lesion of the liver. In this situation the removal of the worms from the portal system may be a better choice of treatment.

It would thus be of fundamental importance to have previous knowledge of the parasitic load in order to select the method of treatment of the parasitosis.

In this connection (CHEEVER [12]) in 1968, working on cadavers, demonstrated the relationship between the number of eggs gram of faeces and tissues and the number of worms removed from the portal system.

Several studies based on clinical, laboratory and experimental data (BARBOSA [3]; BARBOSA [4]; BARBOSA [5]; BARBOSA [6]; CAMUS et al. [8]; CHEEVER [11]; CHEEVER [12]; CHEEVER [13]; CHEEVER [14]; KATZ & ZICKER [27]; KLOETZEL [29]; PRATA & BINA [31]; SADUN et al. [32]; SCOTT [33]; SIONGOK et al. [36]; SMITH et al. [37]; VON LICHTENBERG [38]; VON LICHTENBERG [39]; VON LICHTENBERG [40]; WARREN [41]) have also been attempting over the years to establish this relationship.

The importance of the question encouraged the Authors to study **in vivo** the estimated parasitic load of patients suffering from schistosomiasis mansoni in its hepatosplenic form from a knowledge of the number of eggs per gram of faeces.

MATERIAL AND METHODS

A study was made of 32 patients suffering from schistosomiasis mansoni in its hepatosplenic form, all of whom came from the coastal plain of Pernambuco, where the parasitosis is endemic, and had no previous treatment with schistosomicidal drugs.

Patients presenting clinical manifestations of liver failure, pulmonary arterial hypertension and renalor cardiovascular diseases were excluded from the present study. The average age was 18.9 years, the oldest patient being 29 and the youngest 10; there was a predominance of white, male patients.

The patients were submitted to a preoperative clinical and laboratory evaluation — haematological, biochemical and coproscopic tests by the Kato-Katz and Hoffman, Pons and Janer methods. For the coproscopy performed by the Kato-Katz method a daily sample of faeces was collected for 10 days from each patient, all patients being on a standardized diet (DOMINGUES et al. [23]).

Splenectomy was performed by the standard technique utilized in the Division of Abdominal Surgery (KELNER [28]) of the University Hospital of the Federal University of Pernambuco.

Heparine was injected in a dose of 300 U/kg of body weight, diluted in 50 ml of a 0.9% sodium chloride solution, intravenously and a silastic or polivinil cannula was inserted through the splenic vein as far as the middle third of the portal vein.

The system of extracorporal circulation, described previous (SILVEIRA [34]) was assembl-

ed, filled with Dextran 40 and connected to the cannulas of the splenic and internal saphenous veins.

Filtration was begun immediately after the intravenous injection of the dislodging drug, sodium and antimonium gluconate in a dose of 6 mg/kg of body weight, using the six filters in sequence, one for every 15 minutes.

After 90 minutes filtration was stopped and the splenic and jejunal veins were ligatured following the withdrawal of the catheters.

For each 1500 U of heparine 1 ml of 1% protamine sulphate was used as a neutralizer, diluted in 50 ml of a 0.9% sodium chloride solution, in continuous infusion for approximately 10 minutes.

In nine patients with a history of digestive haemorrhage the intraesophageal ligature of the varices was performed at the end of the filtration. A biopsy on the lower edge of the left lobe of the liver was performed in all 32 cases.

STATISTICAL ANALYSIS

The present study analysed the relationship between the average number of eggs eliminated per gram of faeces in ten samples collected preoperatively and the number of worms removed during filtration of the blood of each patient, leading to the establishment of three sets of two variables — Table I. The association relationships were investigated at a 0.05 level of significance.

TABLE I
Distribution of the sets of two variables

No. of set of variables	Independent X	Dependent Y
1	Average number of eggs per gram of faeces	Number of female worms removed from the portal blood
2	Average number of eggs per gram of faeces	Number of pairs of worms removed from the portal blood
3	Number of female worms removed from the portal blood	Total number of worms removed from the portal blood

PROCEDURE FOR THE STATISTICAL TREATMENT

1. For each set of two variables independent X and dependent Y

1.1. a table was compiled showing the results obtained from the respective measurements, together with the corresponding averages and standard deviations, and the following were calculated:

1.1.1. — the degree of variation between variables (r_{XY})

1.1.2. — the equation of linear regression ($\overline{Y} = a + bX$)

1.1.3. — the estimated value of the dependent variable ($\overline{Y}$)

1.1.4. — the standard linear results of the estimated values of the dependent variable ($z\overline{Y}$)

2. To each distribution of the standard linear results of the estimated values for the dependent variable ($z\overline{Y}$) a technique was applied for the constitution of two extreme subgroups, a technique that assumes that each of these is formed by 27% of the total group.

RESULTS

The result of the number of eggs per gram of faeces obtained from ten samples collected preoperatively is represented in Table II. The distribution of the number of worms removed from the portal blood during filtration is shown in Table III.

The results of the statistical analysis applied to each set of variables — Table I — showed a significant degree of relationship for $p \leq 0.05$. The r_{XY} degree of relationship, the $\overline{Y} = a + bX$ regression equation and the R^2_{YX} regression

TABLE II

Number of eggs per gran of faeces
In preoperative

PATIENT NUMBER	DAY										MEAN	STANDARD DEVIATION
	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th		
1	8712	8736	8712	8736	8688	8760	8760	8832	8760	8784	8748,0	41,18
2	4392	4464	4512	4464	4464	4584	4488	4584	4560	4488	4500,0	61,19
3	3000	2976	3000	2976	3024	3000	3048	3024	3000	3120	3016,8	42,41
4	1632	1680	1704	1752	1728	1680	1728	1752	1752	1800	1720,8	48,07
5	216	264	312	264	288	288	312	288	288	312	283,2	29,50
6	1080	1104	1080	1104	1104	1104	1080	1104	1128	1104	1099,2	15,18
7	696	672	672	696	672	696	648	672	696	720	684,0	20,40
8	9792	9456	9432	9408	9648	9600	9552	9600	9696	9648	9583,2	122,92
9	168	168	120	144	144	168	192	168	192	168	163,2	22,05
10	2760	2688	2784	2760	2808	2808	2760	2808	2808	2832	2781,6	41,49
11	5712	5952	5640	5832	5688	5688	5640	5736	5664	5712	5726,4	96,80
12	744	696	744	720	720	696	744	720	696	720	720,0	19,60
13	792	1008	936	984	816	792	888	912	888	864	888,0	75,05
14	936	960	984	960	1008	960	960	936	960	960	962,4	21,01
15	3696	3768	3720	3744	3720	3672	3744	3696	3792	3648	3720,0	43,82
16	3000	3024	3024	2976	3000	3000	2976	2976	2952	2952	2983,2	22,77
17	792	744	744	912	960	744	840	888	864	912	808,8	150,96
18	336	528	528	576	504	456	504	456	456	456	470,4	64,20
19	456	456	456	456	408	408	408	456	480	432	436,8	27,25
20	2256	2520	2520	2448	2568	2544	2472	2400	2472	2520	2455,2	96,03
21	408	384	384	384	456	480	408	456	432	432	432,0	35,78
22	576	480	480	528	624	480	552	456	528	600	540,0	55,71
23	600	552	552	648	600	528	600	504	648	576	595,2	58,57
24	5184	4920	4920	5280	5136	4896	5280	4992	5088	5040	5078,4	139,58
25	576	576	576	576	600	576	576	576	576	600	583,2	11,59
26	840	864	864	768	816	816	744	816	792	816	799,2	43,89
27	4488	4536	4536	4704	4632	4800	4680	4608	4704	4800	4651,2	106,01
28	864	960	984	912	888	960	912	864	984	864	919,2	49,38
29	8160	8112	8088	8400	8304	8040	8160	8112	8064	8160	8160,0	111,43
30	480	456	528	480	432	504	552	552	504	480	496,8	39,27
31	1008	1032	1080	1056	1032	960	1104	1056	1008	960	1029,6	47,26
32	768	960	864	960	1032	936	960	1008	936	984	940,8	75,73

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TABLE III

Distribution of **Schistosoma mansoni** removed from portal blood during the filtration

PATIENT NUMBER	NUMBER OF S.mansoni REMOVED FROM PORTAL BLOOD			
	MALE WORMS	FEMALE WORMS	PAIRS OF WORMS	TOTAL WORMS
1	803	762	762	1565
2	710	679	679	1389
3	388	398	388	786
4	651	540	540	1191
5	82	72	72	154
6	154	175	154	329
7	294	321	294	615
8	1009	982	982	1991
9	267	264	264	531
10	754	792	754	1546
11	355	377	355	732
12	264	259	259	523
13	523	414	414	937
14	256	238	238	494
15	537	500	500	1037
16	263	223	223	486
17	137	135	135	272
18	184	192	184	376
19	34	40	34	74
20	902	958	902	1860
21	81	44	44	125
22	200	163	163	363
23	109	125	109	234
24	726	747	726	1473
25	306	243	243	549
26	151	68	68	219
27	528	444	444	972
28	124	128	124	252
29	1355	1248	1248	2603
30	116	93	93	209
31	167	155	155	322
32	314	242	242	556

coefficient that were calculated, are shown in Tables IV, V and VI and Figs. 1, 2 and 3 respectively for each set studied.

A great dispersion was noted both in the average values of the number of eggs per gram of faeces and in the total number of worms.

The values of the upper and lower extreme subgroups are to be found in Table VII.

COMMENTS

The oviposition mechanism has been the subject of considerable controversy, although

T A B L E IV

Set of variables — mean of number of eggs per gram of faeces (independent (X) and number of female worms (dependent (Y) — estimated value of dependent variable ($\overline{Y}$); results of standard linear of estimated values of dependent variable (z (Y))

PATIENT NUMBER	X	Y	$\overline{Y}$	z ($\overline{Y}$)
08	9583,2	982	1065	2,5502
01	8748,0	762	985	2,4689
29	8160,0	1248	929	2,2415
11	5756,4	377	696	1,2955
24	5078,4	747	634	1,0437
27	4651,2	444	595	0,8772
02	4500,0	679	579	0,8204
*	3968,3	-	528	0,6127
15	3720,0	500	504	0,5159
03	3016,8	398	437	0,2439
16	2983,2	223	434	0,2317
10	2781,6	792	415	0,1545
20	2455,2	958	383	0,0246
04	1720,8	540	313	0,2596
06	1099,2	175	254	0,4992
31	1029,6	155	247	0,5276
14	962,4	238	241	0,5519
32	940,8	242	239	0,5600
28	919,2	128	237	0,5682
13	888,0	414	234	0,5803
**	808,8	-	226	0,6127
17	808,8	135	226	0,6129
26	799,2	68	225	0,6169
12	720,0	259	218	0,6453
07	684,0	321	214	0,6616
23	595,2	125	206	0,6941
25	583,2	243	204	0,7022
22	540,0	163	200	0,7184
30	496,8	93	196	0,7346
18	470,4	192	194	0,7428
19	436,8	40	190	0,7591
21	432,0	44	190	0,7591
05	283,2	72	176	0,8159
09	163,2	264	164	0,8646
$\overline{X}$	2374,28	375,656	376,94	-
SD	2583,13	306,979	246,28	-

* The fictitious case in which the parasite amount represents the limitrofe value of the superior subgroup.

** The fictitious case in which parasite amount represents the limitrofe value of inferior subgroup.

Degree of regression $r_{x.y} = 0,804204026^{o}$

Coeficiency of regression $R^2_{y.X} = 0,646744116$

Equation of regression $\hat{Y} = 148,7430094+0,095571592\ X$

Significant $P < 0,05$

TABLE V

Set of variables — mean of number of eggs per gram of faeces (independent (X) and number of pairs of worms (dependent (Y) — estimated value of dependent variable (Y); results of standard lineares of estimated values of dependent variable (z ($\bar{Y}$))

PATIENT NUMBER	X	Y	$\bar{Y}$	z ($\bar{Y}$)
08	9583,2	982	1057	2,7473
01	8748,0	762	977	2,4280
29	8160,0	1248	921	2,2046
11	5726,4	355	689	1,2787
24	5078,4	726	627	1,0313
27	4651,2	444	586	0,8676
02	4500,0	679	571	0,8078
*	3982,2	-	522	0,6127
15	3720,0	500	497	0,5124
03	3016,8	388	430	0,2451
16	2983,2	223	427	0,2331
10	2781,6	754	407	0,1533
20	2455,2	902	376	0,0296
04	1720,8	540	306	0,2498
06	1099,2	154	247	0,4853
31	1029,6	155	240	0,5132
14	962,4	238	234	0,5371
32	940,8	242	232	0,5451
28	919,2	124	230	0,5531
13	888,0	414	227	0,5651
17	808,8	135	219	0,5970
26	799,2	68	218	0,6010
**	766,3	-	215	0,6127
12	720,0	259	211	0,6289
07	684,0	294	207	0,6449
23	595,2	109	299	0,6768
25	583,2	243	298	0,6808
22	540,0	163	293	0,7008
30	496,8	93	289	0,7167
18	470,4	184	287	0,7247
19	436,8	34	284	0,7367
21	432,0	44	283	0,7407
05	283,2	72	169	0,7965
09	163,2	264	157	0,8444
$\bar{X}$	2374,28	368,50	368,59	-
SD	2583,13	302,93	250,57	-

* The fictitious case in which the parasite amount represents the limitrofe value of the superior subgroup.

** The fictitious case in which parasite amount represents the limitrofe value of inferior subgroup.

Degree of correlation $r_{X.Y} = 0,8140^{o}$

Coeficiency of regression $R^2y.x = 0,66264492$

Equation of regression $\bar{Y} = 141.8471062 + 0,09546194\ X$

Significant $p < 0,05$

T A B L E VI

Set of variables — number of females worms (independent (X)) and total number of worms (dependent (Y)) — estimated value estimated values of dependent variable (z ($\bar{Y}$))

PATIENT NUMBER	X	Y	$\bar{Y}$	($\bar{Y}$)
29	1248	2603	2530	2,8418
08	982	1991	1994	1,9744
20	958	1860	1946	1,8968
10	792	1546	1612	1,3562
01	762	1565	1552	1,2592
24	747	1473	1521	1,2090
02	679	1389	1385	0,9889
*	564	-	1153	0,6127
04	540	1191	1105	0,5358
15	500	1037	1024	0,4047
27	444	972	911	0,2218
13	414	937	851	0,1247
03	398	786	819	0,0729
11	377	732	777	0,0050
07	321	615	664	0,1779
09	264	531	549	0,3639
12	259	523	539	0,3801
25	243	549	507	0,4319
32	242	556	505	0,4352
14	238	494	497	0,4481
16	223	486	467	0,4966
18	192	376	404	0,5986
**	188	-	395	0,6127
06	175	329	370	0,6537
22	163	363	346	0,6924
31	155	322	330	0,7183
17	135	272	289	0,7847
28	128	252	275	0,8073
23	125	234	269	0,8171
30	93	209	205	0,9206
05	72	154	163	0,9886
26	68	219	155	1,0016
21	44	125	106	1,0501
19	40	74	98	1,1327
$\bar{X}$	375,656	773,91	773,91	-
SD	306,979	619,48	617,93	-

* The fictitious case in which the parasite amount represents the limitrofe value of the superior subgroup.

** The fictitious case in which parasite amount represents the limitrofe value of inferior subgroup.

Degree of correlation $r_{x.y} = 0,997584529^{o}$

Coeficiency of regression $R^2y.x = 0,995174894$

Equation of regression $\bar{y} = 17,66260906 + 2,013126737\ X$

Significant $p < 0,05$

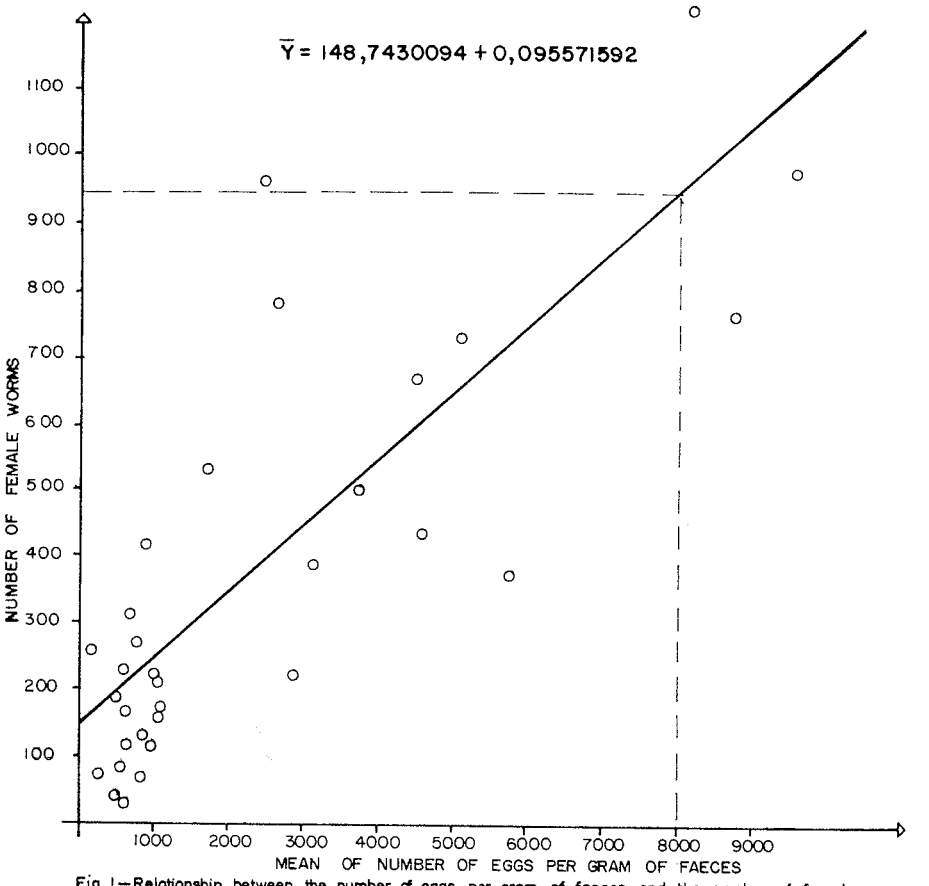

Fig. 1 — Relationship between the number of eggs per gram of faeces and the number of female worms removed from portal blood.

T A B L E VII
Values of the extreme subgroups

Borderline values	Mean of eggs	No. female worms	No. couple worms	No. total worms
Upper	3 982	528	522	1 153
Lower	766	226	215	395

some observations reported in the literature have shown some light on the problem. Observations made on hamsters showed that a female would be able to eliminate an average of 300 eggs per day. Bearing in mind that these eggs are not entirely eliminated in the faeces a proportion of them would be retained in the intestinal tissue or transported by the blood stream to other structures, such as the liver (SILVEIRA et al.[35]).

There is reason to believe that in man the eggs eliminated should not be transported to the liver by the bloodstream. Thus, the females would insinuate themselves into the mesenteric venulae, occlude their lumens and deposit the heaped up eggs on the submucosa of the intestine, and these eggs would then be fixed to the endothelium by the lateral spicula and a subsequent inflammatory reaction. This would help to prevent their migration to the liver, leading to the retention of a large number of eggs in the intestinal tissue as well as their elimination by the faeces. Notwithstanding the evidence in support of these arguments the presence of eggs in liver tissue has been noted on histological sections.

It is agreed that the peculiar characteristics of the different evolutive phases of the disease may contribute to the variation in the number of eggs eliminated in the faeces (CHIEFFI & MARQUES[15]).

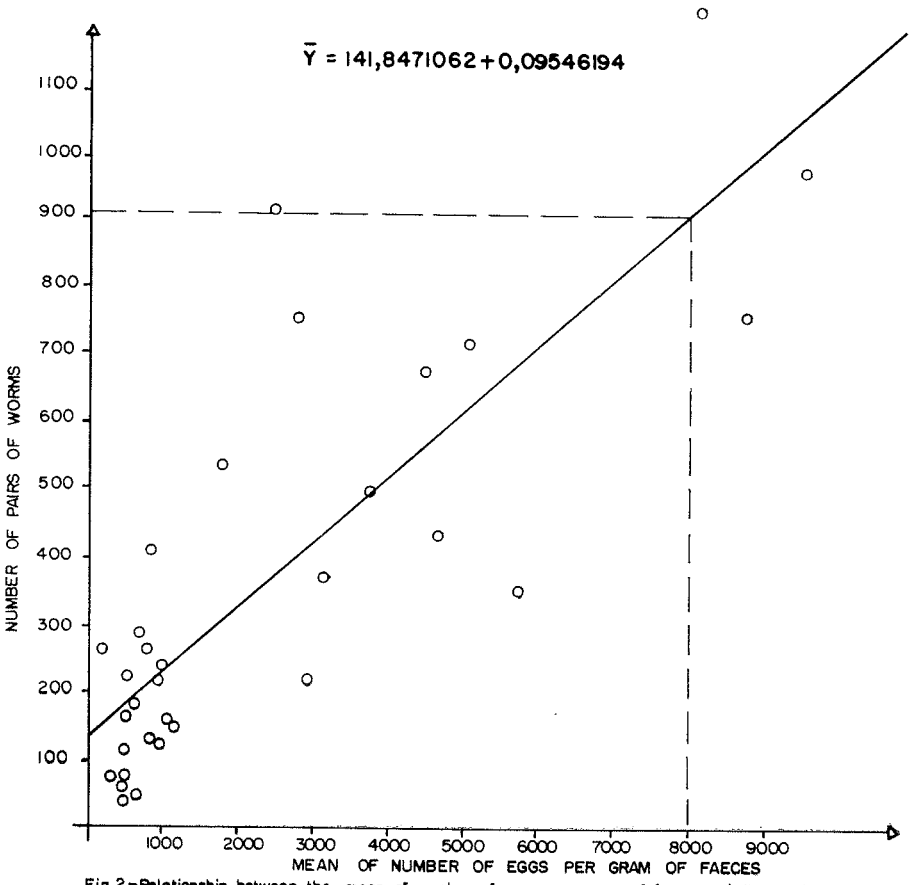

Fig.2 – Relationship between the mean of number of eggs per gram of faces and the number of pairs of worms removed from portal blood

In view of this, in the hepatosplenic form of schistosomiasis the number of eggs eliminated should be related to the number of worms present in the portal system, since in this evolutive phase of the disease the rates of production and destruction of the eggs should be in equilibrium. (CHEEVER[12]) showed on cadavers that this relationship also exists in different evolutive phases of the disease.

The similarity between the distribution of the average values of the number of eggs per gram faeces and the number of worms removed from the portal blood of the patients studied suggests that there is a relationship between these two parameters. This hipothesis, confirmed statistically and the regression equations — Figs. 1, 2 and 3 — defined, made it possible to estimate the number of worms from a knowledge of the number of eggs per gram of faeces.

In spite of the possibility of error in the estimate, this relationship offers the prospect, through quantitative coproscopy techniques for estimating the number of **S. mansoni** eggs, of classifying the schistosomotic population according to its parasitic load.

In this way the determination of the borderline values of the extreme subgroups, Table VII, made it possible to classify these patients as follows in accordance with with their parasitic load: a) patients carrying a parasitic load considered light: female worms not exceeding 226, couples of worms not exceeding 215, and a total of adult worms not exceeding 215, and a total of adult worms not exceeding 395; b) patients carrying a parasitic load considered moderate: from 226 to 528 female worms, from 215 to 522 couples of worms and a total of from 395 to 1153 worms; c) patients carrying

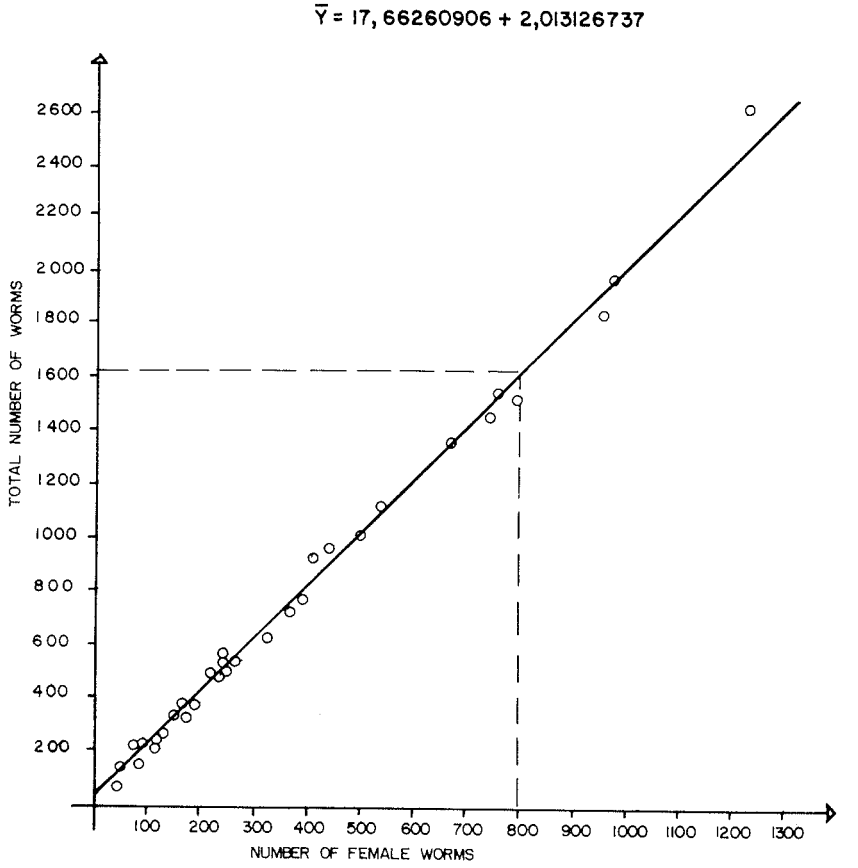

Fig. 3 — Relationship between the number of female worms and the total number of worms removed from portal blood.

a parasitic load considered intense: more than 518 female worms, more than 522 couples of worms and a total of worms greater than 1153.

This proposed classification may be of practical importance in the indication of specific treatment for the parasitosis if it is recognized that the embolization of the intrahepatic portal rami by worms destroyed by schistosomicidal drugs would have a significant repercussion on the liver (COUTINHO [22]).

There are references to fatal cases (COUTINHO & DOMINGUES [21]) following specific treatment, but without conclusive evidence as to whether death was brought about by the hepatotoxic action of the drug or by the massive embolization of worms.

In the light of present knowledge there are no figures for establish the number of worms capable of aggravating the pre-existing hepatic lesion to the point of clinically decompensating the patient.

Provided that the basic requisites are observed in the indication of the clinical treatment of the parasitosis it can be assumed that patients carrying a light parasitic load would have a greater likelihood of success than those carrying a larger number of worms.

Consequently, the removal of **S. mansoni** from the portal system can be recommended in those patients indicated for surgery who are carriers of an intense parasitic load, clinical treatment being reserved for the carriers of a light or moderate parasitic load.

RESUMO

Remoção de S. mansoni em pacientes com Esquistossomose hépato-esplênica: estimativa da carga parasitária a coproscopia quantitativa

DOMINGUES, L.; SILVEIRA, M.; LIMA FILHO, J. F. C.; CARREIRO JR., J. C. P. & KELNER, S. — Removal of S. **mansoni** in patients with hepatosplenic schistosomiasis: an estimate of the parasitological load by means of quantitative coproscopy. **Rev. Inst. Med. trop. São Paulo** 25:2-15, 1983.

Foram estudados 32 pacientes portadores de esquistossomose mansônica, forma hépato-esplênica compensada, com idade média de 18,9 anos, virgem de drogas esquistossomicidas, submetidos a esplenectomia e filtração do sangue portal para remoção de **S. mansoni.**

Foi estudada a relação entre a média do número de ovos por grama de fezes, obtidos da análise de 10 amostras sucessivas das fezes de cada paciente, pelo método Kato-Katz e o número de vermes removidos do sangue portal.

O procedimento estatístico utilizado mostrou relação significativa entre os parâmetros estudados, permitindo a elaboração das respectivas equações de regressão, com o objetivo de estimar o número de vermes fêmeas, de pares de vermes e o total de vermes.

A partir dos resultados e aplicando técnica para constituição de subgrupos extremos os Autores propõem uma classificação de intensidade da infecção: a — carga parasitária leve: número médio de ovos por grama de fezes inferior a 808, o que corresponde a uma carga parasitária estimada inferior a 226 vermes fêmeas; b — carga parasitária moderada: número médio de ovos por grama de fezes entre 808 e 3968, o que corresponde a uma carga parasitária estimada entre 226 e 528 vermes fêmeas; c) — carga parasitária intensa: número médio de ovos por grama de fezes superior a 3968, o que corresponde a uma carga parasitária estimada superior a 528 vermes fêmeas.

A classificação proposta pode servir para a indicação do tratamento específico da esquistossomose mansônica em pacientes portadores da forma hépato-esplênica da doença.

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