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# A contribution to the study of Hookworm disease in infants

by

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As pointed out in a previous publication (9), presented at the Second Central American Congress of Pediatrics, ancylostomiasis in infants shows great resistance to the usual forms of treatment. The fact should also be noted that severe forms of hookworm infestation in infants exhibit peculiar characteristics which make them different, to a certain extent, from the well known clinical pictures of cases in the pre-school age or older children and adults.

Let us briefly recall the acute and early manifestation of anemia, the frequent conservation of subcutaneous tissue, infiltration of the skin, anorexia, in some cases vomiting, and the typical aspect of the feces, normal in color or ranging from a pinkish tint to brick red, terracotta or wine red.

In the Department of Pediatrics of Hospital San Juan de Dios are admitted yearly, to the infants' wards, about 3000 patients aged from 0 to 18 months. LIZANO and DE ABATE (6), investigating incidence of intestinal parasites in children hospitalized in the Departament of Pediatrics of Hospital San Juan de Dios, showed that 2.7 per cent of children 0 to 18 months old give positive results for hookworm in feces, which would mean some 80 cases of ancylostomiasis in infants for each year. The severe character of this disease and the relatively poor results of therapy used in infants prolong the period of hospitalization; to emphasize this, we have included in our case studies the clinical histories of the children (cases Nos. 1 and 2) who remained one year or more in the hospital and were finally released with unsatisfactory blood counts and positive results for hookworm in the stool.

The usual therapeutic measures used in the treatment of infants (transfusions, iron therapy, a well balanced diet, and tetrachlorethylene in doses of 100

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mg. per kilogram not followed by a laxative) were so unsatisfactory that we sought for other anthelmintics which could give better results. It also seemed indispensable to decrease the number of transfusions indicated in each case, which, as we shall show further on, was excessively high.

This study comprises 14 cases of hookworm disease in infants, 2 of them corresponding to previous years.

In all cases with severe anemia there is intense paleness of the skin and mucous membranes. Edema is present in 35% of the cases, in appreciable form; however, the fact that weight curve is always low during the first days in the hospital seems to indicate that superficial edema is frequent although it may be sub-clinical.

In most cases there is tachycardia; a functional murmur was found in only five cases. We should recall here that in older children with a similar clinical picture there is a higher incidence of cardiac murmurs.

In many cases there were gross subcrepitant rales but chest x-rays were always negative. We may add that in two cases there were small tracheobronchial lymphadenitis, and in two other cases, enlargement of the heart was detected.

The abdomen was frequently enlarged, tense and painful. In most cases the liver was somewhat enlarged. The spleen was most often normal, but in one case was found to be greatly hypertrophied. The case was also positive for malaria *(P. falciparum)*.

Vomiting was recorded in 5 cases; but anorexia was present in 10 cases. In 11 cases, feces with microscopically perceptible blood were recorded. Most of these were liquid, but they soon became pasty, remaining fetid and requiring some time for the blood to disappear. All patients showed great mental depression upon admission to the hospital.

The records are presented below for some of the most significant cases regarding laboratory examinations and results of the therapy employed.

CASE Nº 1 (F.S.V.)

Remained in the hospital over a year, receiving 26 transfusions, iron therapy and 16 doses of tetrachlorethylene.

Feces were positive for hookworm before release. Weight remained almost the same during the first 8 months in the hospital.

On departure from the hospital the patient had 8 g of hemoglobin per 100 cc and less than 3.000.000 red cells, returning to the hospital some months later with a count of 1.000.000 red cells, 1.5 g of hemoglobin and heavily positive stool for hookworm.

CASE Nº 2 (J.R.L.D.)

This child remained one year in the infants' ward, receiving 6 transfusions, 8 doses of tetrachlorethylene and ferrous sulfate orally. Blood counts on leaving

were 8 g of hemoglobin and 2.800.000 red cells. Feces were consistently positive for hookworm.

CASE Nº 4 (M.P.B.)

Remained in the hospital 9 months. Received 5 transfusions. Four treatments with piperazine and 3 with tetrachlorethylene. Blood values remaining about equal, with high leucocytosis and eosinophilia. After three treatments with hexylresorcinol, feces were negative for hookworm with increased hemoglobin and decreased leucocytes and eosinophiles. Weight gained rapidly after hexylresorcinol treatment. The lowest leucocyte and eosinophile counts were recorded during measles.

CASE Nº 6 (M.M.C.)

Remained 9 months in the hospital. Twelve transfusions, iron and vitamin B-12 therapy given. Two doses of piperazine and 5 of tetrachlorethylene had no noticeable effects on the blood values or the fecal hookworm egg counts. Four heavy doses of hexylresorcinol resulted in negative stool egg counts and in a rapid favorable effect on red cells counts and hemoglobin content; there was also a rapid gain in weight. Leucocytosis and eosinophilia decreased. Liver function tests on leaving the hospital were normal.

CASE Nº 7 (C.L.A.R.)

Eight months in the hospital. Received 8 transfusions. Four doses of tetrachlorethylene, ferrous sulfate and liver extract. Four hexylresorcinol treatments had the same favorable effects as in foregoing cases with regard to blood picture, weight curve, and elimination of hookworm after the treatments.

CASE Nº 8 (W.G.P.)

Remained in the hospital 7 months. Received 4 transfusions, iron therapy and vitamin B-12; this treatment resulted in improved blood values and decreased egg counts without eliminating the parasites. A heavy trichocephalosis was cured with hexylresorcinol enemas. Gain in weight and negative stool exams for hookworm were the results of treatment with heavy doses of hexylresorcinol.

CASE Nº 9 (G.Z.CH.)

Five months in the hospital. One transfusion and iron therapy; 2 doses of tetrachlorethylene, with no effect on hookworm egg counts. Three treatments with hexylresorcinol in heavy doses caused disappearance of eggs from feces. Rapid improvement in blood values and weight followed.

CASE Nº 11 (Z.V.C.)

Remained 3 months in the hospital. Received three transfusions, and iron therapy, three doses of tetrachlorethylene, with no significant effect on blood values or fecal hookworm egg counts. Five hexylresorcinol treatments in heavy doses resulted in sharp increase of red cells and hemoglobin, in decreased leucocyte counts, and less marked decrease in eosinophile counts; negative stool exams and satisfactory gain in weight.

## SOME REMARKS ON HEMATOLOGY AND PARASITOLOGY

Parasitological and hematological tests were made before, during and after treatments. The first parasitological datum recorded was the presence of hookworm in direct examination of feces with physiologic saline solution added. Egg counts were made following Stoll's method (cited in ANIDO & ANIDO, 1).

Hematological examinations were carried out in blood obtained from a finger, using for hemoglobin figures the Sahli-Adams hemoglobinometer and making the differential leucocyte count on Schilling's classification.

Blood values in infants with hookworm do not differ much from those of older children. In both groups, almost all cases show microcytic and hypochromic anemia. Leucocytosis is present, as well as eosinophilia. The manifestation in these children, over a long period of time, of low hemoglobin values and red cell counts, leucocytosis, and, to some extent, eosinophilia, was due to the lack of an effective anthelminthic for the total elimination of hookworms.

As the graphs show, most of our cases were children who remained with anemia for several months in spite of numerous transfusions (26 in case Nº 1), iron therapy, a well balanced diet and anthelmintic treatment. There are case histories of infants who, after a year of hospitalization, were released slightly less anemic than they arrived, still with abundant hookworm eggs in their feces.

Our records show that it was not until the hookworm were eliminated that a remarkable change occurred toward normalization of hematic values. At the same rate that we approached the total elimination of hookworms we came closer also to normal values in hemoglobin, erythrocytes, leucocytes and differential

NAME : FRANCISCO SEGNINI VENEGAS
AGE : 4 MONTHS
N° 19054

ADMISSION : AUGUST 25 - 1952
DISCHARGE : SEPTEMBER 11 - 1953

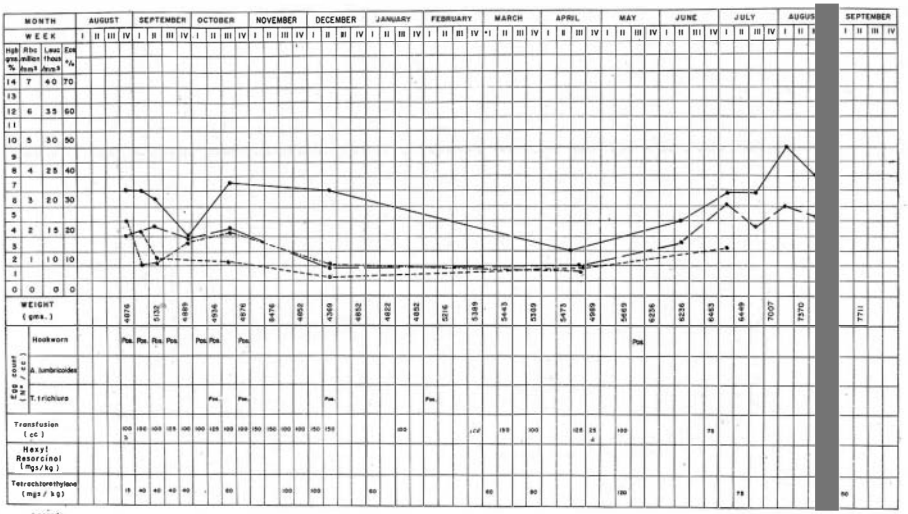



FIGURE No. 1

NAME : JOSE RAMON LOBO DURAN
AGE : 7 MONTHS
N° 24878

ADMISSION : OCTOBER 22 - 1953
DISCHARGE: FEBRUARY 19 - 1955

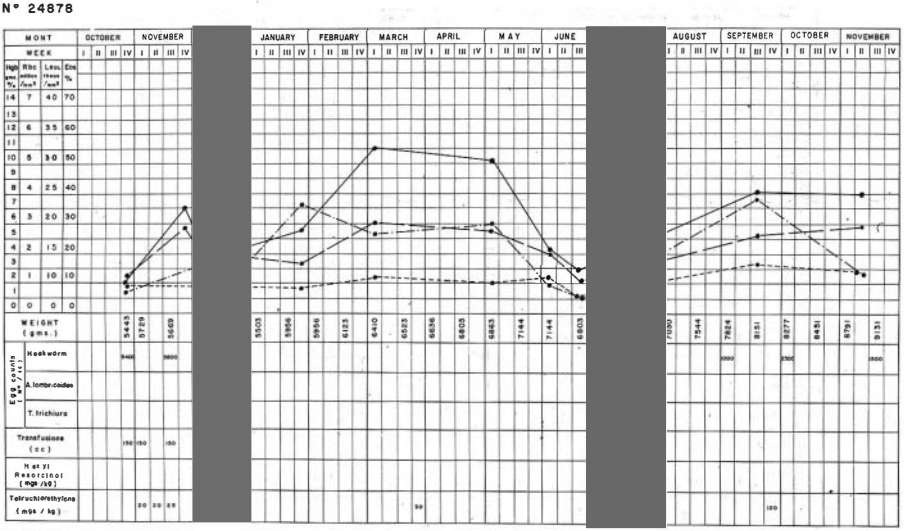



FIGURE No. 2

NAME : MARCIANO PADILLA BADILLA
AGE : 1 YEAR
N° 29133

ADMISSION: DECEMBER 23-1955
DISCHARGE: OCTOBER 16-1956

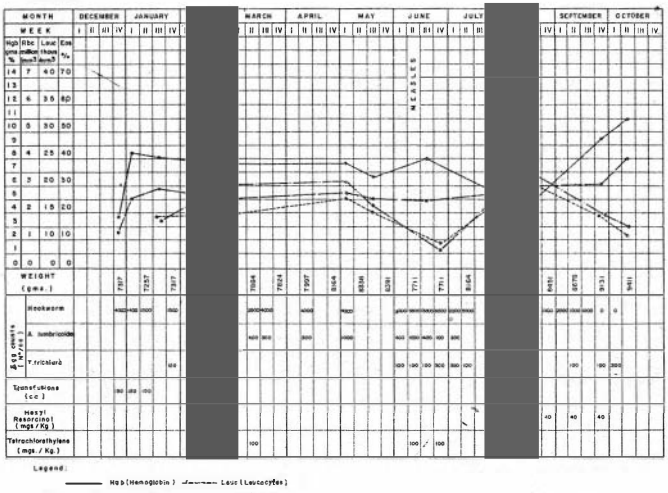



FIGURE NO. 3

NAME: MIRIAM MORA CUBILLO
AGE : 1 YEAR
N° 621

ADMISSION: JANUARY 8 - 1956
DISCHARGE: OCTOBER 15 - 1956

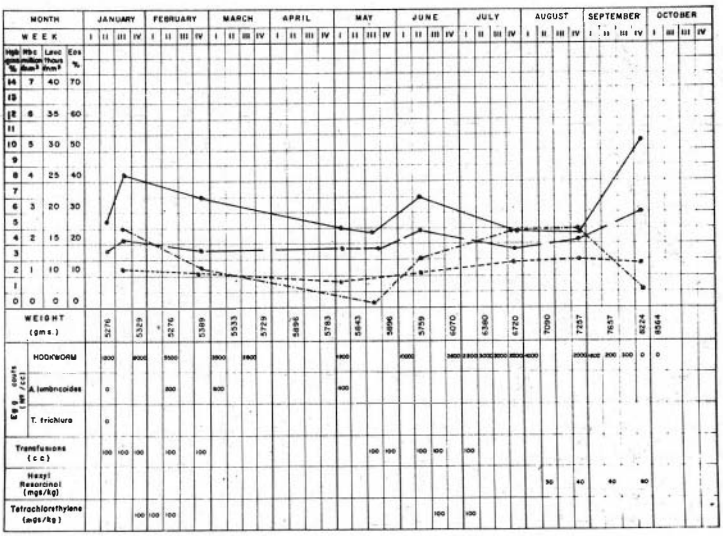



FIGURE N° 4

NAME : CARLOS LUIS ARIAS ROJAS
AGE : 7 MONTHS
N° 1820

ADMISSION : JANUARY 20 - 1956
DISCHARGE : OCTOBER 6 - 1956

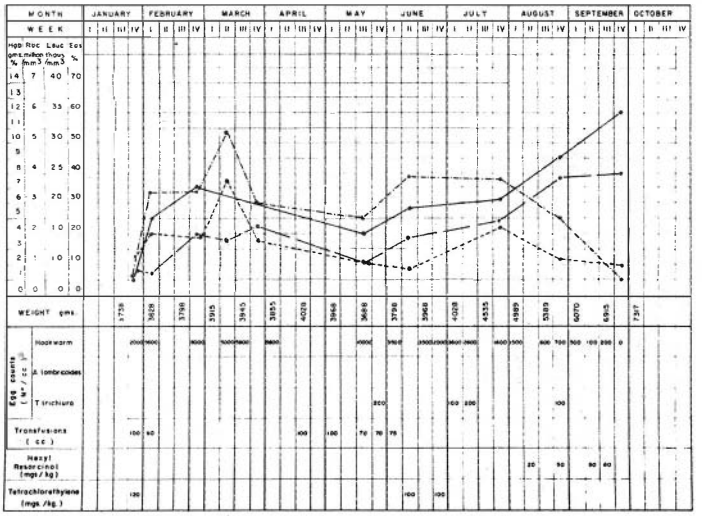



FIGURE N° 5

NAME : WALTER FCO. GUERRERO PRADO
AGE : 13 MONTHS
N° 6106

ADMISSION : MARCH 9 - 1956
DISCHARGE : OCTOBER 4 - 1956

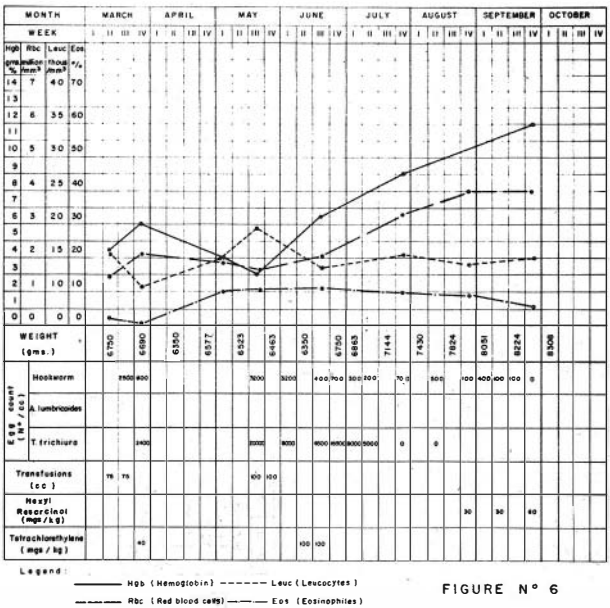
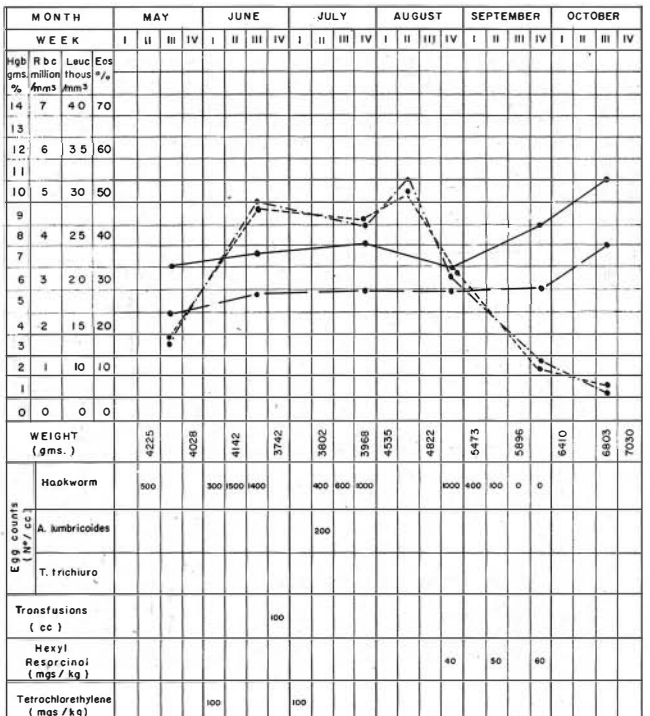



FIGURE N° 6

NAME: GERARDO ZAMORA CHAVES ADMISSION: MAY 9 - 1956

AGE : 4 MONTHS DISCHARGE: OCTOBER 31 - 1956

Nº 11261




Legend:

——— Hgb (Hemoglobin) ------ Leuc (Leucocytes)

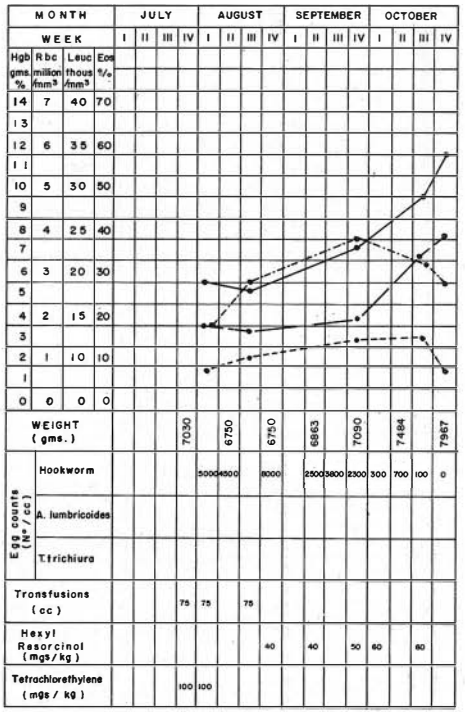
—— —— Rbc (Red blood cells) —·—·— Eos (Eosinophiles)

FIGURE No. 7

NAME: ZENEIDA VARGAS CALDERON

AGE : 9 MONTHS ADMISSION: JULY 28 - 1956

Nº 18224 DISCHARGE: NOVEMBER 11 - 1956




Legend:

——— Hgb (Hemoglobin) ------ Leuc (Leucocytes)

—— —— Rbc (Red blood cells) —·—·— Eos (Eosinophiles)

FIGURE No. 8

count. There is an appreciable divergence in the curves for hemoglobin and red cells on the one hand, and for leucocytes and eosinophiles on the other, all of them tending to normal values after the administration of heavy doses of hexylresorcinol.

Experience has taught us that the effects of parasitism can not be made to disappear without the elimination of parasites, in this case hookworms. None of our findings supported the opinions of authors like GARRAHAN (5) who stated that with a good diet and iron therapy alone, the clinical picture which was due to no other cause than the direct and indirect action of the hookworm could be made to disappear. It is likely that even the complete elimination of the parasite would not restore the infants to normal health immediately.

Success depends on the joint action of elimination of the parasites and administration of iron and a well balanced diet. Logic points to this conclusion and the results support it.

We have not had occasion to observe cases of hookworm disease complicated by anemia tending to aplasia as reported by some authors, including GARRAHAN (5). In studies made by MIRANDA (7), in which infants were included, he showed that there is active regeneration of the erythrocytic series in the bone marrow of hookworm patients. He found no relation of the anemia to the number of nucleated elements or to the proportion of inmature cells of the erythrocytic series in the bone marrow.

In our cases we found initial hemoglobin values as low as 1 g per cent and 800.000 erythrocytes per $mm^3$.

After administration of hexylresorcinol, and even before complete elimination of the hookworms, the increase in hemoglobin and red cell values was clearly noticeable. As complete elimination of the parasites was achieved, values reached normal or nearly normal figures. Release of the children was indicated when they reached 12 g per cent or more hemoglobin, and 4.000.000 or more erythrocytes per $mm^3$.

Leucocyte values were above the maximum accepted as normal, as is always observed in hookworm cases seen in our Departament. No cases of leucopenia were found, such as GARRAHAN (5) reported following an initial leucocytosis. It was not until we were close to complete elimination of the hookworms that leucocyte values tended to return to normal.

Eosinophilia was not always present when the children entered the hospital; the higher values were found some time after admission. In many cases eosinophiles in circulating blood increased after anthelmintic and iron therapy and transfusions had begun. The proportion of eosinophiles decreased in almost parallel fashion to the leucocyte values, that is, when the parasites were nearly eliminated and hemoglobin and erythrocyte values were approaching normal.

## TREATMENT

From the therapeutic viewpoint, the effectiveness of oral hexylresorcinol, given in doses higher than that previously recommended, was evident. As early

as 1934 BROWN (2) pointed out that while tetrachlorethylene is more effective than hexylresorcinol, and is preferred for mass treatment, the latter is preferable in some individual cases, as in the treatment of children, weakened patients, and pregnant women. He also pointed out that except for possible local irritation, there is no contraindication for the oral administration of hexylresorcinol.

In 1941 FAUST (4) also stated that tetrachlorethylene should be the preferred drug, but recommended the use of Caprokol (hexylresorcinol), considering its administration safer in anemic or undernourished children. He pointed out that no good anthelmintic could be used safely, without the necessary medical control, with the possible exception of hexylresorcinol crystoids.

We came to have a similar opinion in our work in 1955 (9) in which we stated our preference for the use of tetrachlorethylene without a laxative in infantile ancylostomiasis, according to the experience of CARR *et al.* (3). However, in those cases, negative results for hookworm in feces were rarely obtained, i. e. only in 5 out of 22 cases treated with tetrachlorethylene in repeated doses of 100 mg per kilogram of weight (9). Besides, at that time we stressed the poor response obtained in heavily parasitized infants to the various anthelmintics prescribed. In the same publication we stressed that the use of tetrachlorethylene orally, and even after the necessary intubation, did not give really satisfactory results.

We decided therefore to increase progressively the doses of hexylresorcinol, usually recommended as 10 mg per kilogram of body weight. In previous experiences even this dosage had given fairly satisfactory results. Much larger doses such as 50 mg, and recently, even 100 mg per kilogram of body weight were given, focusing attention not so much on the physical characteristics of the patient, such as age, weight, or size, but rather on the doses required to attack the parasites effectively. We have thus come to give total doses of approximately 500 to 600 mg hexylresorcinol without having to restrict them according to age or weight. They were given in 0.10 g pills which the nurse causes to be swallowed by placing them at the back of the tongue of the child, giving at the same time a spoonful of water. In no case did we have any difficulty in having the drug swallowed, although admittedly the procedure does not have a sufficient margin of safety for home use.

Tables 1 and 2 are presented to allow comparison of results obtained with tetrachlorethylene and hexylresorcinol.

In the tables a remarkable difference may be seen between the results of treatment with tetrachlorethylene and hexylresorcinol in infants. With the former drug, given in doses of from 20 to 120 mg per kilogram weight, we obtained no favorable results, as the mean number of hookworm eggs per gram of feces changed from 3.768 to 3.240 after treatment. It should be noted here that response of preschool children with hookworm to treatment with tetrachlorethylene in high doses and without a laxative, is quite satisfactory or at least much better than that of infants, as shown by the mean figures of 3.672 eggs per gram feces before, and 1.218 after treatment, values shown in our study presented at the previous Central American Pediatrics Congress (9).

TABLE 1

EGG COUNT BEFORE AND AFTER TREATMENT WITH TETRACHLORETYLENE (ORALLY)

| CASE Nº | NAME | COUNT BEFORE TREATMENT Eggs/g feces | TREATMENT | | | COUNT AFTER TREATMENT Eggs/g feces |
|---|---|---|---|---|---|---|
| | | | Doses mg | Nº | Doses mg/Kg | |
| 2 | J.R.L.D. | 3.400 | 100 | 2 | 20 | 5.800 |
| " | " " " " | 5.800 | 150 | 1 | 25 | 10.800 |
| " | " " " " | 10.800 | 150 | 2 | 30 | 2.800 |
| " | " " " " | 2.800 | 1.000 | 3 | 120 | 1.900 |
| 3 | G.Ch.M. | 900 | 1.000 | 1 | 100 | 600 |
| " | " " " | 600 | 1.000 | 1 | 100 | 100 |
| 4 | M.P.B. | 2.500 | 800 | 1 | 100 | 3.000 |
| " | " " " | 3.000 | 850 | 1 | 100 | 11.100 |
| " | " " " | 11.100 | 850 | 1 | 100 | 4.000 |
| 5 | J.M.G. | 1.300 | 850 | 1 | 120 | 2.800 |
| " | " " " | 4.200 | 1.000 | 1 | 120 | 2.300 |
| " | " " " | 2.300 | 1.000 | 1 | 100 | 700 |
| 6 | M.M.C. | 7.900 | 650 | 1 | 100 | 3.000 |
| " | " " " | 3.000 | 650 | 1 | 100 | 2.500 |
| 7 | C.L.A.R. | 6.100 | 500 | 1 | 100 | 3.500 |
| " | " " " " | 3.500 | 500 | 1 | 100 | 1.600 |
| 8 | W.G.P. | 2.500 | 300 | 1 | 40 | 2.900 |
| " | " " " | 2.900 | 700 | 1 | 100 | 400 |
| " | " " " | 400 | 700 | 1 | 100 | 300 |
| 9 | G.Z.Ch. | 500 | 450 | 1 | 100 | 1.400 |
| " | " " " | 1.400 | 450 | 1 | 100 | 8.600 |
| 10 | A.S.V. | 6.000 | 1.000 | 2 | 120 | 1.200 |
| AVERAGE | | 3.768 | | | | 3.240 |

TABLE 2

EGG COUNT BEFORE AND AFTER TREATMENT WITH HEXYLRESORCINOL CRYSTOID'S (ORALLY)

| N° CASE | NAME | COUNT BEFORE TREATMENT Eggs/g feces | TREATMENT | | COUNT AFTER TREATMENT Eggs/g feces |
|---|---|---|---|---|---|
| | | | Doses mg | Doses mg /Kg | |
| 4 | M.P.B. | 4.000 | 400 | 40 | 1.800 |
| " | " " " | 1.800 | 400 | 40 | 1.100 |
| " | " " " | 1.100 | 600 | 60 | 0 |
| 5 | J.M.G. | 750 | 500 | 40 | 200 |
| " | " " " | 200 | 500 | 40 | 0 |
| 6 | M.M.C. | 250 | 500 | 50 | 0 |
| 7 | C.L.A.R. | 150 | 400 | 60 | 0 |
| 8 | W.G.P. | 100 | 600 | 60 | 0 |
| 9 | G.Z.Ch. | 100 | 400 | 60 | 0 |
| 10 | A.S.V. | 1.200 | 500 | 60 | 100 |
| " | " " " | 100 | 500 | 60 | 50 |
| " | " " " | 50 | 500 | 60 | 0 |
| 11 | Z.V.C. | 3.100 | 400 | 50 | 2.400 |
| " | " " " | 2.400 | 500 | 60 | 700 |
| " | " " " | 700 | 500 | 60 | 0 |
| 12 | C.V.C. | 4.700 | 500 | 100 | 200 |
| 13 | G.Z.O. | 5.800 | 400 | 60 | 400 |
| AVERAGE | | 1.558 | | | 432 |

In the tables it can be seen that some of our cases treated with hexylresorcinol had received previously one or more and up to five doses of tetrachlorethylene without the desired results (Case Nº 6). The data of tabla 2 show that, at least in infants, hexylresorcinol is the drug of choice for treatment of severe forms of hookworm disease; the minimum effective dose must still be investigated, although it appears to be between 500 and 600 mg, whatever the age or the weight of the infant.

These amounts gave us the best results to date in our search for a solution to the problem of infants' hookworm disease. All children treated with such doses showed no hookworm eggs in their feces.

Even though hexylresorcinol, according to many authors, including FAUST (4), is one of the few drugs which may be used without medical supervision, we preferred to begin our experiments with low doses, such as 150, 200 and 300 mg. Most cases showed a decrease in the number of eggs in fecal matter, although not completely satisfactory

Thus, hexylresorcinol in doses below 400 mg, whatever the weight and age of the infant has no advantage over tetrachlorethylene. We obtained no negative counts after several doses of 100 to 300 mg. It was doses of 400 to 600 mg, which, given singly or repeatedly, achieved the complete elimination of the parasite in question. We have therefore included in table 2 the most significant cases, that is, those treated with doses which were successful in eliminating the hookworms. All children under study showed good tolerance for the anthelmintic drug; in only one case there was vomiting several hours after the patient had been given the dose, and there were no other side effects.

The cases which were given transfusions whenever indispensable, ferrous sulfate elixir U.S.P., in doses of approximately 100 mg per kilogram of body weight (which we consider advantageous because of its high citric content favoring assimilation of iron) (8) and during the last weeks, hexylresorcinol, as described above, reacted quickly and favorably. The general condition improved rapidly, as may be noted from an increase in weight of 200 or more grams weekly.

These first results reported lead us to expect a remarkable shortening of the period of hospitalization of infant hookworm cases and of the possibility of rendering their feces negative for hookworm by means of heavy doses of hexylresorcinol and of hemotherapy and iron therapy, combined with a good diet and attention to the patients morale.

## SUMMARY AND CONCLUSIONS

Fourteen cases of serious hookworm disease in infants (0 to 18 months old) are studied, in an effort to analyse the unsatisfactory results obtained with the therapy we had been using. The clinical aspects and laboratory analysis results are discussed. The results given by tethrachlorethylene and hexylresorcinol

crystoids as anthelmintic are compared. Heavy doses of hexylresorcinol given orally have proved to be superior to other drugs as anthelmintics in infants. The good tolerance and apparent non toxicity of the substance are stressed.

Good results are reported with a treatment including hexylresorcinol, transfusions, iron therapy, a well balanced diet and psychotherapy, regarding the general condition of the child and its blood values. With this treatment we obtained an important shortening of the period of hospitalization in serious forms of hookworm disease in infants. For the first time we can report a fully satisfactory condition on release of children hospitalized with this disease.

## RESUMEN

Se estudian catorce casos de anquilostomiasis seria en niños de 0 a 18 meses, con el fin de analizar los resultados poco satisfactorios obtenidos con los métodos terapéuticos empleados hasta ese momento. Se comparan los resultados obtenidos con tetracloretileno y hexilresorcinol. Dosis altas de hexilresorcinol por vía oral dan mejores resultados que otras drogas como antihelmínticos para infantes. Se hace hincapié en la buena tolerancia y ausencia de toxicidad de la droga.

Se obtuvieron buenos resultados en cuanto al estado general del niño y a los valores hematológicos, con un tratamiento que incluía hexilresorcinol, transfusiones sanguíneas, ferroterapia, una dieta bien balanceada y psicoterapia. Con este tratamiento se puede obtener un acortamiento importante del período de hospitalización en formas serias de anquilostomiasis en infantes. Por primera vez podemos informar de condición completamente satisfactoria de niños con tal enfermedad, al salir del hospital.

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