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1918–1920

SECOND PAPER

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BY WILSON G. SMILLIE, M.D.

(From the Instituto de Hygiene, São Paulo, Brazil.)

(Received for publication, November 16, 1920.)

CONTENTS.

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INTRODUCTION.

Certain special problems connected with the technique of diagnosis and method of treatment of hookworm disease have been studied by the Institute of Hygiene of São Paulo during the past 2 years. Exact data concerning all patients treated in the course of these studies have been kept, and on analysis are seen to present forcibly certain fundamental principles in regard to the nature of hookworm disease. The facts so revealed agree perfectly with our theoretical knowledge of the life history of the parasite but are somewhat at variance with the popular conceptions of the disease. We can state with certainty that these principles apply to hookworm disease in rural Brazil only, for our studies have been limited almost exclusively to the rural districts of that country. As the habits and customs of rural Brazilians, however, have many things in common with the customs of other nations and other races, certain fundamental facts concerning the disease that apply to Brazilians should apply to other rural populations.

Customs of the Rural Brazilian.

It may be worth while at this point to describe briefly the customs of the typical rural Brazilian in so far as they pertain to his infection with hookworm disease and to his reaction to this infection.

The rural Brazilian lives in a small house with mud walls and a thatched or tiled roof. The floor is of dried packed earth. The native prefers to place his house several hundred yards from his neighbors, but on the large plantations in São Paulo and Rio de Janeiro the owners have grouped their laborers in collections of from 5 to 200 houses with two to four families in each house. The house is usually situated near a running stream, where the native's wife washes the clothes and from which she brings all the water necessary for household use, including the drinking water. This stream is always polluted. The chief articles of diet of the rural Brazilian are beans, greens, mandioca, and coffee. When occasion offers, he eats rice, sugar, and meat, and he nearly always sprinkles dried corn or mandioca meal over all food. He also eats bananas and oranges when he can get them,

as well as some wild fruits of the woods. His clothes are very scanty, usually two cotton garments; only the aged members of the family or the well-to-do wear shoes. The men, boys, and girls work long hours in the fields, the children beginning field work when about 8 years old, the girls a little later than the boys. Almost the only agricultural tool is the long-handled heavy hoe, though the men use a curved axe for cutting wood and brush. The girls work side by side with the boys in the fields until they marry, usually at 17 to 19 years of age. From this time on, their work in the field is sporadic; they may help, for example, during the busy harvest season. As the field labor is very heavy and the diet limited in quantity and of poor quality, the productive period of life is short; a man is old and broken at 50 and can do very little more heavy work. Abuse of alcohol is common among the men and among black women but not among white women. Cigarette smoking among the men and boys is universal. There are no latrines. The little children evacuate near the house, the adults usually some distance — 50 to 100 yards — away, though there is seldom a definitely understood place set aside for this purpose. The men and boys usually evacuate in the field, wherever they are working. Conditions of life vary somewhat in different localities, but this brief sketch gives a general summary of the customs and mode of life that are common to all, even to the immigrants who have so largely replaced the natives on the large plantations.

Our Methods of Study.

A description of the methods of study used by the Malaya Board in Java has been given previously. Briefly, they are as follows: A typical community is chosen; the inhabitants are registered; their stools are examined microscopically; and their hemoglobins are tested by the Dare method. From among those registered there is chosen a typical group of from twenty-five to thirty persons, of different ages, different sexes, various families, various occupations, etc. To this group of about thirty persons sufficient chenopodium is given to remove 98 to 99 per cent of the hookworms harbored. All stools are saved, and the worms are counted and classified. For each person the following data are carefully recorded: name, race, age, sex, occupation, and length of residence on the plantation, hemoglobin, spleen

index by palpation, and previous worm treatment; also, the results of our preliminary microscopic examination of stools, the mode of treatment, the symptoms produced by the treatment, the number of resulting evacuations, and the number of worms expelled classified in detail as *Ancylostoma duodenale*, *Necator americanus*, or other intestinal parasites. The record of each case in itself is a complete study of hookworm disease. Only cases upon which we have the complete data in every detail are included in the series studied in the compilation of this report.

Problems to Be Considered.

Almost 600 completely recorded cases, chosen from twenty-one different localities, enable us to arrive at some interesting conclusions in regard to the nature of hookworm disease. From such a mass of data various problems can be studied. Let us consider these problems in the following order:

1. Distribution of hookworm disease in relation to age and sex.
2. Hookworm disease in children.
3. Hookworm disease a soil disease.
4. The influence of the use of shoes in preventing hookworm disease.
5. The hookworm a parasite that is slowly acquired and slowly lost.
6. The hemoglobin index in relation to the number of hookworms harbored.
7. The influence of nutrition on hookworm disease.
8. Distribution of *Ancylostoma duodenale* in Brazil.
9. The value of the routine microscopic examination of stools in field treatment.
10. The efficiency of the undivided dose of chenopodium in field treatment.

After a consideration of these various problems, I will take up the general results of the findings and make some recommendations in regard to effective and practical methods for a campaign treatment of hookworm disease.

DISTRIBUTION OF HOOKWORM DISEASE IN RELATION TO AGE AND SEX.

The popular belief in regard to hookworm disease is that it is principally a disease of children, particularly of young children. This is not the case. Hookworm disease is primarily a disease of young adults, chiefly of young men, whom it attacks most severely during the productive period of life. In Table I and Chart 1 (page 7), this fact is strikingly apparent.

Rise and Fall of the Infection Rate in Both Sexes.

Chart 1, representing a summary of 562 cases (all that were completed), illustrates the hookworm infection in both sexes divided into 10 year age-groups. Children under 4 years of age were not studied. The chart shows that children under 10 years of age harbored very few hookworms, girls a few less than boys. During the next decade there is seen to be a tremendous increase in the average number of worms harbored by girls and boys both. Between the ages of 25 and 45 years the average number of worms harbored by the men remains very constant and very high. The average number of worms harbored by women falls slowly after the 18th to the 19th year. There is a rapid decrease in the average number of worms harbored in both sexes after the 45th year. The reason for this striking phenomenon is clear, for we have definitely proved that the degree of hookworm infection in Brazil varies directly with the amount of time that the individual spends in labor in the field in direct contact with the soil. This will be demonstrated under the heading "Hookworm disease due to direct contact with humid earth" (page 23).

Children under 9 years of age harbor very few hookworms. At about the age of 8 to 9 years, however, it is customary for boys to begin field work; girls usually take up the hoe a year later than boys. The girls work by the side of the boys in the fields until they reach the age of 18 to 19, when they marry and assume household duties. From this point, instead of their hookworm infection continuing parallel with that of the boys, a diminution in the infection

TABLE I.

Hookworm Infection in Relation to Age and Sex.

Age-group.	No. of cases.		Average No. of hookworms per case.	
	Males.	Females.	Males.	Females.
yrs.				
0– 9	27	29	39	20
10–19	181	94	169	114
20–29	61	49	227	89
30–39	34	16	229	70
40–49	22	18	219	79
50+	20	11	87	24

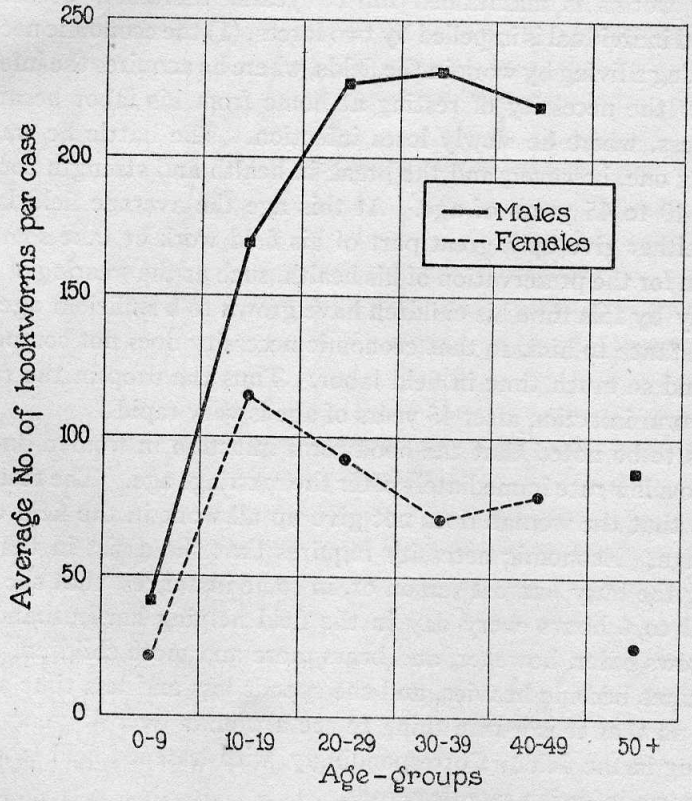

CHART 1. Hookworm infection in relation to age and sex.

rate occurs, which is clearly shown in the chart. On the other hand, the infection rate in men increases up to the 25th year, after which it remains surprisingly constant and very high for 20 years. The question at once arises as to why the infection rate, *i.e.* the average number of worms harbored per case, does not continue to increase throughout the laborer's life. The answer is that hookworm disease is a self-limited disease. When an adult field laborer becomes infected with many more than the average number of worms of his age-period (250 to 300 worms), he is unable to work as many hours in the field as his less heavily infected fellow workmen. Thus he is less exposed to new infection, and as some of the worms harbored die off from natural causes, his infection becomes lighter. The average infection of 230 worms is maintained for 20 years, therefore, because the infected individual is impelled by two forces, (1) the economic necessity of earning a living by work in the fields, where he acquires the infection, and (2) the necessity of resting at home from his labor because of weakness, where he slowly loses infection. The battle he wages is a losing one, however, and the break in health and strength comes at about 40 to 45 years of age. At this age the average field laborer must either give up a great part of his field work or take some precaution for the preservation of his health, such as the wearing of shoes. Usually by this time his children have grown to a sufficient age to be of assistance to him, so that economic necessity does not compel him to spend so much time in field labor. Thus the drop in the rate of hookworm infection after 45 years of age is very rapid.

It is to be noted that the hookworm infection in women does not drop to a low rate immediately after the marriage age. The reason for this is that the woman does not give up all work in the field on her marriage. Economic necessity requires that she assist in the fields during the busy harvest season or, in some instances, that she spend from 2 to 4 hours every day in the field helping her husband. As she grows older, however, and bears more and more children, household cares become heavier, and she spends less and less time at field labor, so that it is a rare thing to see a woman over 45 years of age working in the field. Correspondingly, with lessened field labor, her hookworm infection rate decreases.

Rise and Fall of the Infection Rate in Males.

The very rapid rise in the infection rate in males after the 10th year and the rapid fall after the 40th year are well shown in Chart 2, which is based on a study of 381 cases of males only. The cases were divided into 5 year age-groups, and the curve is somewhat irregular owing to the necessarily small number of cases in each age-

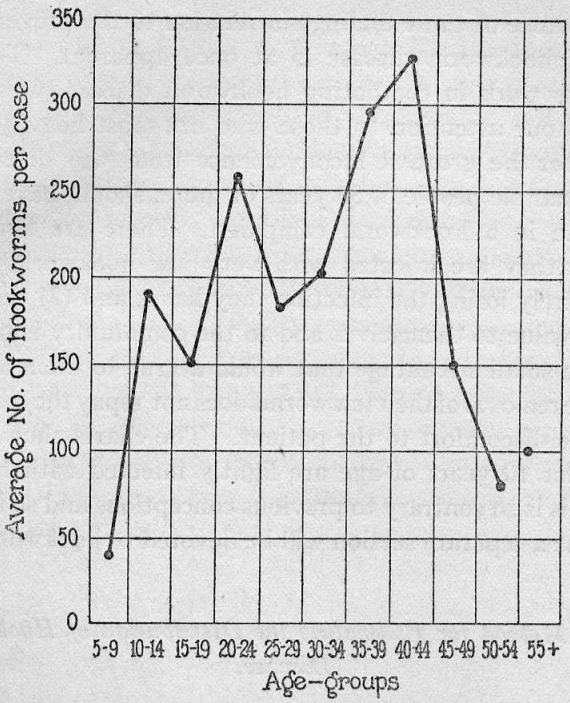

CHART 2. Hookworm infection in relation to age—males.

group. The general tendency of the curve is clearly a rapid increase up to about the 15th year, then a gradual, slow, and steady increase through the active period of the laborer's existence. Then, between the 40th and the 45th years comes the break, followed by a strikingly abrupt fall in the infection rate.

We do not wish to give the impression that these are absolute rules from which there are no exceptions. One encounters many young individuals who harbor 400 or even 600 worms and still are able to

continue work in the fields. Occasionally a child under 10 years has more than 100 worms, and sometimes an old man is found to be heavily infected. In general, however, for a large group of cases and under conditions as they exist in Brazil, the findings remain remarkably constant and clear-cut.

Significance of These Findings.

The importance of these findings in relation to the prevention and treatment of hookworm disease is at once apparent. To do the most effective work in combating hookworm disease, we must devote most of our attention to those who are most heavily infected and who suffer the greatest inconvenience from the disease. Old people, for example people of 50 years or more, should never concern the sanitarian in a hookworm campaign. There are two reasons for this: (1) they are infected with very few hookworms and are slowly but surely losing the infection they have; and (2) their period of economic value to themselves and to the community is practically over, and the small advantage that would accrue to them and to the state from the removal of their few worms does not repay the cost of treatment and the discomfort to the patient. The charts show also that children under 10 years of age are lightly infected with hookworm disease. This is so contrary to previous conceptions and so important a subject that a separate section will be devoted to hookworm disease in children.

Another Method for Estimating the Distribution of Hookworm Disease.

There is another important method by which one is able to estimate the distribution of hookworm disease in a community or in a nation; namely, by calculating the percentages of cases infected with small numbers of worms and large numbers of worms. To make this calculation we divided the cases into groups as follows: Group 1, those who harbored 0 to 10 worms; Group 2, 11 to 50 worms; Group 3, 51 to 100 worms; and so on, using a 50 worm increase as a division up to those cases that harbored more than 300 worms. All cases that harbored 300 or more worms were grouped together. Individuals were also divided into three age-groups; 5 to 14, 15 to 39, and 40 or

TABLE II.

Hookworm Infection by Age-Groups.

No. of hookworms harbored.	Age-groups.		
	5–14 yrs.	15–40 yrs.	41 + yrs.
	Percentage of cases.	Percentage of cases.	Percentage of cases.
0– 10	36	17	30
11– 50	28	26	33
51–100	10	16	18
101–150	7	10	1
151–200	7	8	2.5
201–250	3	6	1
251–300	1	2	2.5
301+	8	14	12

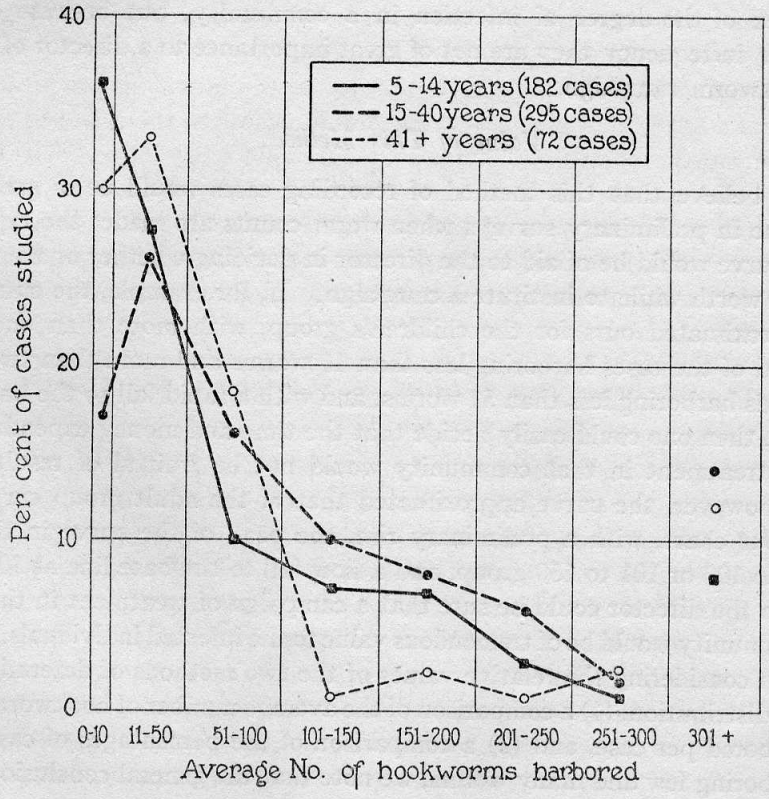

CHART 3. Hookworm infection by age-groups.

more years. The results of our calculations are given in Table II and Chart 3 (page 11). These results show clearly that of the children under 14 years more than one-third had less than 11 worms each (an insignificant infection) and two-thirds less than 51 worms each, and that the tendency of their curve is to fall rapidly to the base line. The curve for adults is quite different, for a smaller percentage, 17 per cent, harbored 0 to 10 worms, 26 per cent harbored 11 to 50 worms, and the tendency of the curve is to fall slowly to the base line. The curve of the age-group 40 years and over resembles more the curve for the adult group than that for children in having a preliminary rise, but the fall to the base line is much more rapid in this group than in either of the others. Only occasional cases harbored more than 300 worms in any of the three groups. These highly infected cases are of great clinical interest and give us some index of the degree of infection in a community, but because of their infrequency they are not of great importance to a director of a hookworm campaign.

Value of This Method.

I believe that this method of recording cases would be of great value in preliminary surveys when worm counts are made; the type of curve would be of aid to the director in deciding whether or not it was worth while to institute a campaign. If, for example, the curve approximated ours for the children's group, with more than one-third of the cases harboring less than 11 worms and more than two-thirds harboring less than 51 worms, and with a rapid fall to the base line, then one could easily decide that the time and money expended for treatment in that community would not be fruitful of results. If, however, the curve approximated that of the adult group curve of our chart, with a preliminary rise, the peak of the curve in the 51 to 100 or 101 to 150 group, and a slow fall to the base line at 300, then the director could be sure that a campaign of treatment in that community would be of tremendous value to the infected individuals.

In considering the relative values of the two methods of determining distribution, (1) a comparison of the average number of hookworms harbored per case, and (2) a comparison of the percentages of cases harboring few and many worms, we note that the general conclusions

arrived at are the same. It is probable that the second method is of greater value to the public health director who has data on a large number of cases in that it gives him accurate information as to the distribution and the degree of infection; in other words, it shows him the percentage of cases that harbor few worms and the percentage that harbor many worms.

Conclusions.

By either method one arrives at the following conclusions in regard to hookworm infection in Brazil: The great proportion of hookworms are harbored by young adults between 15 and 45 years old. Children and elderly people are much less heavily infected. Women are infected to a lesser degree than men, and their infection rate diminishes after the marriageable age.

HOOKWORM DISEASE IN CHILDREN.

Our experiments have shown that hookworm disease is essentially a disease not of children but of adults. Nevertheless, the problem of hookworm disease in children is of great importance, and our findings in regard to it are so striking that we have given the subject separate consideration. In our series there are 178 children under 15 years of age for whom we have complete records. No children under 4 years were studied and very few under 6 years, for the reason that it was difficult to supervise little children so that no stools would be lost. Many cases of young children were treated, but in few cases were we able to secure complete records. The fact does not, however, seriously affect the conclusions drawn from the studies, for reasons that will become apparent. We have also in our series a group of 136 youths between 15 and 19 years of age, and it is interesting to compare their findings with the findings for children.

Distribution of the Infection by Age and Sex.

Table III and Chart 4 illustrate the average hookworm infection found in children of the various age-groups. The cases were divided into 2 year age-periods, and boys and girls were considered separately. These children did not represent local conditions only, for they included representatives from all classes of society in Brazil and from almost every state in the Union. The greater proportion of them were children of field laborers, who had never been to school, never worn shoes, and never been 5 miles from the spot where they were born. They were thus fairly representative of rural Brazilian children.

The striking points about the hookworm infection curve are the very low rate of infection in small children and the rapid rise in every age-period. Though girls have slightly fewer worms than boys, the two curves rise more or less parallel until after the age-period 18 to 19, when there occurs a sudden drop in the hookworm incidence in young women. The reason for this, as we have already explained, is that the girls marry at this age and leave the fields for

TABLE III.

Hookworm Infection in Children by Age and Sex.

Boys.			Girls.		
Age.	No. of cases.	Average No. of hookworms.	Age.	No. of cases.	Average No. of hookworms.
yrs.			*yrs.*		
4– 5	3	1	4– 5	3	0
6– 7	8	20	6– 7	11	12
8– 9	18	52	8– 9	14	31
10–11	19	113	10–11	17	54
12–13	28	185	12–13	21	101
14–15	59	184	14–15	20	87
16–17	53	106	16–17	23	158
18–19	22	167	18–19	12	197
20–24	36	260	20–24	26	108

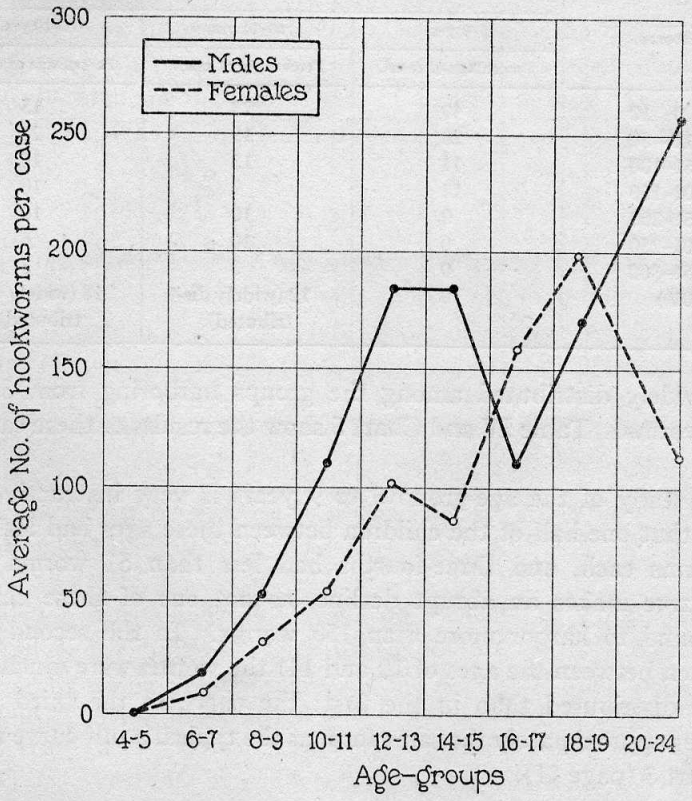

CHART 4. Hookworm infection in children in relation to age and sex.

domestic duties. The average age at which a child begins work in the fields is from 8 to 9 years. This change in the child's habits is accompanied by a rise in infection rate after this age-period for both boys and girls.

The second method of determining the distribution of hookworm infection described in the preceding section was also applied to this group of children; that is, we classified them in 5 year age-periods and divided them into groups harboring 0 to 10 worms, 11 to 50 worms, and so on, increasing the number by 50 up to a total of 300. There were very few cases harboring more than 300 worms, and these

TABLE IV.

Hookworm Infection in Children, by Age-Groups and Number of Hookworms.

No. of hookworms harbored.	Age-groups.		
	5–9 yrs.	10–14 yrs.	15–19 yrs.
	Percentage of cases.	Percentage of cases.	Percentage of cases.
0– 10	49	23	15
11– 50	28	18	24
51–100	11	15	16
101–150	11	9	10
151–200	0	10	10
201–250	0	10	6
251–300	0	3	3
301+	0	12 (widely distributed).	18 (widely distributed).

were widely distributed among the groups harboring from 300 to 1,200 worms. Table IV and Chart 5 show the results of these calculations.

The study of the age-group 5 to 9 years is very instructive. It shows that one-half of the children between these ages had less than 11 worms each, and three-fourths had less than 51 worms each. The curve makes an abrupt decline, as not one of these children was found to harbor more than 150 worms. In the second group (children between the ages of 10 and 14) the worms were much more widely distributed than in the first; the curve of the third group assumes approximately the same form as the typical adult curve shown in Chart 3 (page 11).

Chart 4 shows that hookworm infection gradually and progressively increases as a child increases in age; Chart 5, that hookworm disease is much more widely distributed among children in the older age-

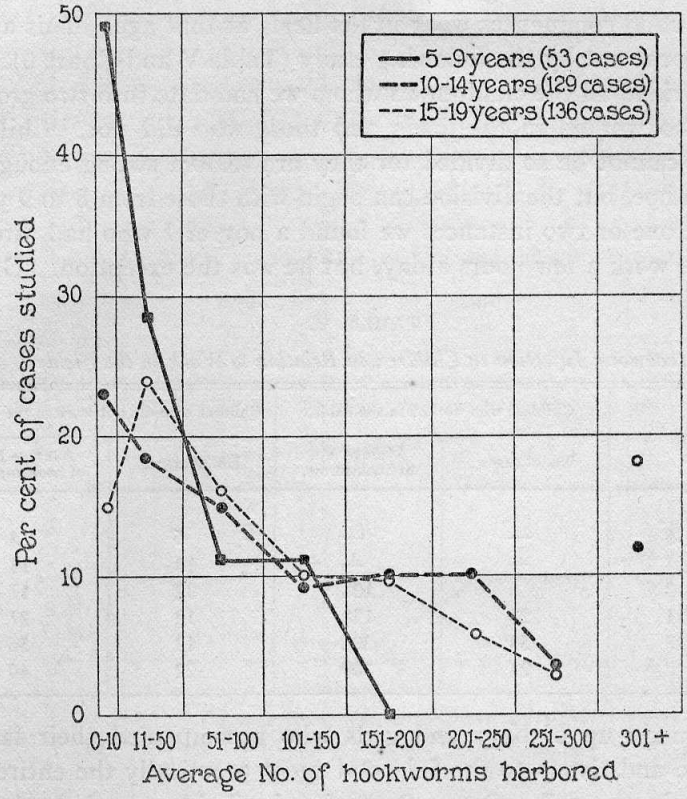

CHART 5. Hookworm infection in children, by age-groups and number of hookworms harbored.

groups than in the younger. From both charts, it is apparent that there enters the children's lives when they are about 9 years of age some factor which greatly increases the degree of infection and the distribution of the disease.

Cause of the Marked Increase of Infection between the Ages of 8 and 9 Years.

The cause of the marked increase of hookworm infection in Brazilian children between the ages of 8 and 9 is the fact that the average country child commences work in the fields at that age. This assertion is borne out by the following study (Table V and Chart 6).

We divided all the children on whom we had data into two groups, those who worked in the fields and those who did not. Children under 8 cannot be so divided for they are seldom strong enough to handle a hoe, but the division can begin with those from 8 to 9 years old. In one or two instances we found a boy of 7 who had already begun to work a few hours a day, but he was the exception. Group

TABLE V.

Hookworm Infection in Children in Relation to Work in the Fields.

Age.	Children who worked in the fields.		Children who did not work in the fields.	
	No. of cases.	Average No. of hookworms.	No. of cases.	Average No. of hookworms.
yrs.				
4– 5	—	—	6	3
6– 7	—	—	18	14
8– 9	8	104	22	17
10–11	23	128	12	27
12–13	34	200	12	36
14	21	309	22	49

1 was made up of boys and girls who accompanied their father, brothers, and sisters to the field and spent practically the entire day working in the soil. Group 2 consisted of girls who helped their mothers about the house, school boys, boys who worked in the engine-house and about the stables, blacksmiths, children of the administrators and overseers, etc. The two groups were comparable in that the children of both went barefoot, ate similar food, were living on the same plantations, and in many cases were of the same house and family.

As shown by Chart 6, the increase in the average number of hookworms harbored by the second group is slow, gradual, and constant—about 5 to 6 hookworms per year. The increase in the number of

hookworms harbored by the first group is very rapid—an average of more than 50 worms a year; so that by the 14th year the first group harbors an average of more than six times as many worms as the second. Thus Chart 6 is a striking substantiation of our contention

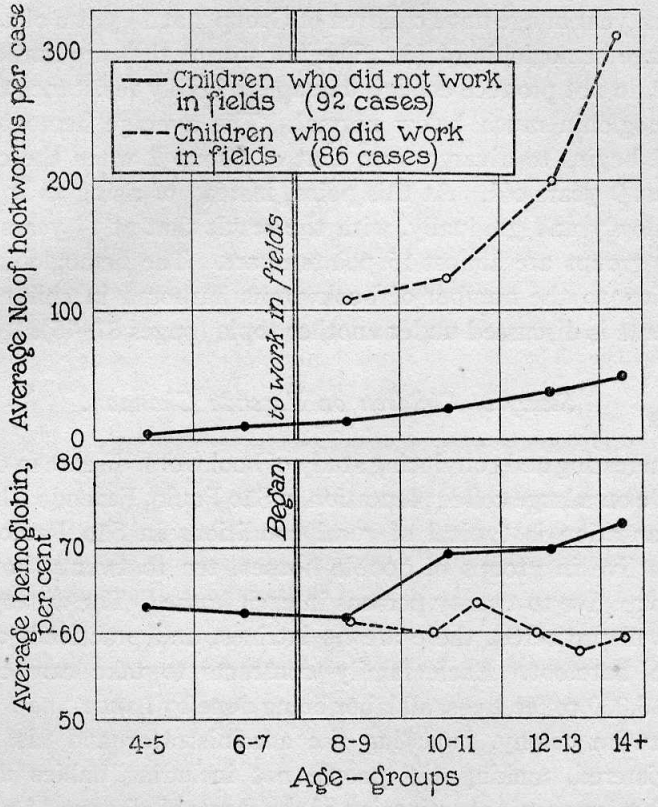

CHART 6. Hookworm infection and hemoglobin index in children in relation to work in the fields.

that hookworm disease is an occupational disease. The slow increase of infection in children who do not work in the fields is incidental infection and does them little harm. They have hookworm infection only. The children who work in the fields are invariably heavily infected. They have hookworm disease.

Effect on the Hemoglobin.

The average hemoglobin of the two groups of children is given on the same chart. The average hemoglobin for a rural Brazilian child of from 5 to 8 years of age is about 62. There is then a gradual rise with each year of age until children of Group 2 at 14 years of age have an average hemoglobin of 73. The few worms that are harbored by Group 2 do not produce enough damage to bodily resistance to lower the hemoglobin much below normal. The average hemoglobin of Group 1 begins to diverge from that of Group 2 when the children are about 9 years old. At this point, instead of rising as it should, it falls slowly and gradually, with the result that at 14 years of age the two groups are almost 15 points apart. The hemoglobin index in relation to the number of hookworms harbored in children and adolescents is discussed under another topic (pages 37–45).

Study of Children on Fazenda Chanaan.

An interesting and convincing study of hookworm disease in children was made on a large coffee plantation in São Paulo, Fazenda Chanaan. This plantation is typical of rural conditions in São Paulo. The colonists live in groups of double houses, ten to twenty houses in each group, five to twenty persons in each house. The water supply is not well protected, there are no latrines, and practically all colonists go barefoot. Each family contracts to take care of from 2,000 to 5,000 coffee trees, all labor being done by hand.

The entire colony, including the administrator and his family, was registered, making 175 people not including babies under 1 year. A microscopic examination of the stools of all gave 44 negative results, or an infection of 74 per cent. We then proceeded to treat the colonists and count their worms. For the purposes of our study we divided the children into the following age-groups:

From 1 to 4 years. Children of this age are so young that one cannot save their stools and count their worms.

From 5 to 8 years. Children who had not yet begun field work.

From 9 to 14 years. Children working in the fields.

A summary of the results obtained is given in Table VI. These children were members of the same families, and all lived under very similar conditions except that those more than 8 or 9 years of age worked in the fields. The table substantiates our previous statements that small children, under 4 years, have almost no infection with hookworms, that children between 5 and 8 years, inclusive, have very few hookworms, and that children over 8 years who work in the fields are heavily infected.

TABLE VI.

Hookworm Infection in Children, Fazenda Chanaan.

Age-group.	No. of cases.	Negative to microscope.	Positive to microscope.	Cases treated.	No hookworms.	Less than 10 hookworms.	Average No. of hookworms per case.
yrs.							
1- 4	21	17	4	0	—	—	—
5- 8	21	12	9	12*	1	6	15.4
9–14	20	0	20	20	0	0	202

* The 12 cases treated in the second age-group were all negative to the microscope; so the average degree of infection for this age-group was probably slightly higher than our figures indicate. As our previous work has shown, the microscope does not diagnose accurately those cases which harbor 15 worms or less, but as a rule a case in this group that is positive to the microscope has a few more hookworms than one that is negative.

Should Young Children Be Treated for Hookworms?

The establishment of these facts brings up an important problem in regard to treatment. Is it necessary to treat children under 5 years at all, even though they give a positive microscopic examination for hookworm ova? In Brazil, at least, we can answer very positively in the negative. The difficulty of treatment and the danger to the child outweigh any advantage to be gained by the removal of their few worms.

Is it worth while to treat children between 5 and 8 years of age even though the microscope reports them as positive? If the post is customarily treating cases of *Ascaris* and other intestinal parasites, I believe that a small dose of chenopodium may be given to the children

between 5 and 8; this will remove their *Ascaris* and most of their hookworms. One should *not* treat them with the full dose of chenopodium in order to remove their hookworms. Children of 8 years or less are particularly susceptible to the toxic effects of chenopodium or other anthelmintics, and almost all the fatalities with chenopodium in the treatment of hookworm disease of which I am aware have occurred in children below the age of 9 years.

HOOKWORM DISEASE DUE TO DIRECT CONTACT WITH HUMID EARTH.

The title of this division of our studies is a fact so well recognized and so generally accepted that at first glance it does not seem necessary to give it further consideration. The work of Looss and his successors thoroughly proved that the chief mode of hookworm infection is through contact of the skin with moist earth (1). Old conceptions die a lingering death, however, and the belief that hookworm disease is spread by food, water, and other agencies is firmly rooted in both the popular and the medical mind. It is true that experimental evidence has shown that hookworm infection can be contracted through the mouth, and it is possible that in heavily infected districts, where the water supply is continually polluted with feces, the mouth is a portal of entry of an occasional larva. We believe, however, that our work shows this to be an incidental and entirely unimportant source of hookworm infection.

The use of the microscope in examination of the stools for ova has been a valuable aid in the diagnosis of hookworm disease but has led to a curious fallacy, for it has been very generally assumed that all cases that are positive to the microscope are affected equally by the disease. I do not mean to infer that the fallacy has been stated as a fact, but in all hookworm campaign work it has been assumed that any case that is positive to the microscope is a case of hookworm disease and should receive intensive treatment.

If we note carefully the classical studies of Looss, we discover that, theoretically at least, hookworm disease is an occupational disease, that it must be limited to those who work in contact with moist soil which has been contaminated with hookworm larvæ, and that though others may be infected with hookworms, they should be so only slightly and quite incidentally. This theoretical reasoning is based upon three premises: (1) the normal and usual portal of entry of hookworm larvæ is through the unbroken skin; (2) the larva requires moist soil for its existence; (3) the skin must come in contact with infected material, and this material must remain for

some time in contact with the skin, so that the larvæ may have time to penetrate. If the reasoning is correct, hookworm disease should be chiefly a disease of infested soil workers, and any hookworm campaign should be conducted on this assumption.

Hookworm Infection in the Better Classes.

We have divided our studies into various groups according to the locality in which they were made and the occupation and mode of life of the patients. In the beginning of our work we treated some individuals who lived in cities with paved streets, latrines, etc., but we soon abandoned this unfruitful field because in no single instance did we find city dwellers infected with more than a few hookworms unless they gave the definite history of having been field laborers or soil workers within recent years. We then limited our studies to rural conditions—small farms, large plantations, and villages in which there was little or no sanitation. To our great surprise the average infection of the people grouped together in the insanitary villages was not so heavy as that of persons living in scattered farm houses, though it would seem inevitable that the soil about these villages should become saturated with hookworm larvæ. The reason the average infection was lighter in the villages was the fact that the shopkeepers, barbers, and non-agricultural workers living in the villages had very light infection. The lightest infection of all was found in individuals in better circumstances. We picked out and grouped together the records of those cases that might be said to belong to the better classes—that is, persons living in houses with board floors, occupied in non-laborious work, eating plenty of food, wearing good clothing, and in adult life wearing shoes. They consisted of storekeepers, school teachers, plantation overseers, etc. These persons represented the best rural conditions, though they lived in very insanitary surroundings, with no latrines, a heavily polluted water supply, etc. A comparison between this group and the average for all rural Brazil is of interest.

Table VII, in which this comparison is presented, shows that individuals of the better class have a negligible infection with hookworms which probably represents occasional incidental infection through food, water, and accidental contact with soil; they are infected with

hookworms but do not have hookworm disease, though living and associating with heavily infected individuals. The reason that they do not have hookworm disease is easily explained. Their skin does not come in contact with infected soil.

TABLE VII.

Comparison of Findings for Better Classes with Those for All Rural Brazil.

	No. of cases.	Average age.	Average hemoglobin.	Average No. of hookworms.
Age-group 5–14 yrs.				
		yrs.	*per cent*	
Better classes	19	10	72	7
Whole of rural Brazil	196	11	64	107
Age-group 15–39 yrs.				
Better classes	15	22	76	28
Whole of rural Brazil	305	22	66	163
Age-group 40+ yrs.				
Better classes	8	52	77	1
Whole of rural Brazil	75	49	66	115

Let us now consider the most important class—those individuals whose work and life are limited to the farm and plantation.

Infection on Fazendas Santa Maria and Magnolia.

The first group studied was made up of the families of field laborers on two large coffee plantations at Brodowski, São Paulo. They all lived in the same row of houses, ate the same food, drank water from the same spring, and had the same customs and mode of life. Each head of a family had contracted to treat from 2,000 to 5,000 coffee trees a year, a laborious task that required all able-bodied members of the family to spend as many hours in the field each day as possible. The work was done by hand, every one went barefoot, and there were no latrines. There was one particular in which the lives of the various members of the families differed—namely, the number of hours per day spent in the field. On the basis of this difference the individuals studied were divided into groups as follows:

Group 1. Adult field laborers. This group included all men and all boys and unmarried girls over 14 years of age. From early morning until late at night these laborers were in the field, barefooted, cutting weeds and working the moist soil into shape. The average day was 14 hours. There were no latrines in the fields, and the individuals evacuated wherever necessity required.

Group 2. Wives and mothers of Group 1. These women did the housework. They lived under exactly the same conditions as Group 1, except that they spent fewer hours in the field. During the very busy seasons they went to the fields for from 2 to 5 hours a day, and were also in contact with moist soil when they washed clothes at the river bank, but they spent more than three-fourths of the day within the house or within the 100 foot circle of hard-packed clay that made the yard.

Group 3. Boys and girls of from 8 to 14 years of age who worked in the fields with their fathers.

Group 4. Children between the ages of 6 and 14 who had not yet begun to work in the fields because they were too young or were needed to help their mothers in the household. None of the children of either group had ever been to school.

The summary of the hookworm infection found in the different groups is given in Table VIII and Chart 7 (page 27). It will be seen that individuals who worked in the fields were heavily infected while those who lived about the house were lightly infected.

Fazenda Chanaan, Jatahy, São Paulo.

A second study was made at another large coffee plantation where all the cases lived in the same row of houses under exactly similar conditions. The type of work and mode of life were similar to those described in the preceding study. The cases were divided as at Fazendas Santa Maria and Magnolia into:

Group 1. Adult field workers, men and women 14 years old and over.
Group 2. Adults who worked about the house.
Group 3. Children of from 8 to 14 years who worked in the fields.
Group 4. Children who had not commenced field work.

Their infection is shown in Table IX.

The results of both these studies are strikingly alike. In both, the degree of infection in adult field workers was severe. The children who worked in the fields were also severely infected. The mothers, who lived under the same conditions as other members of the family except that they spent fewer hours in the field, were very lightly infected, and the children who accompanied their mothers about the house also had light infection.

TABLE VIII.

Fazendas Santa Maria and Magnolia.

	No. of cases.	Average age.	Average hemoglobin.	Average No. of hookworms.
		yrs.	*per cent*	
Adult field workers	50	25	63.6	313
Women doing housework	9	30	69	71
Children, 8–14, field workers	28	11	58	284
Children who did not work in fields	12	8	58	44

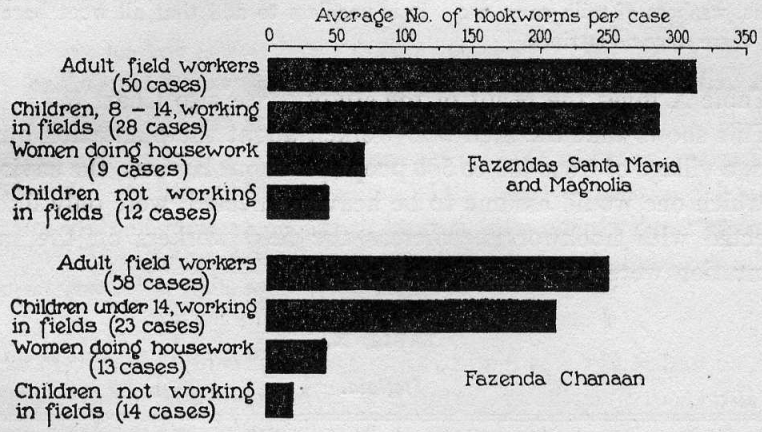

CHART 7. Relative severity of hookworm infection among agricultural workers and persons engaged in other occupations. Fazendas Santa Maria, Magnolia, and Chanaan.

TABLE IX.

Fazenda Chanaan.

	No. of cases.	Average age.	Average hemoglobin.	Average No. of hookworms.
		yrs.	*per cent*	
Adult field workers	58	23	56	250
Houseworkers	13	37	56	42
Children working in fields	23	13	46	213
Children who had not begun work in fields	14	$8\frac{1}{2}$	58	23

Itatiaia.

At Itatiaia, a plantation devoted to the production of milk, the group was divided a little differently. All the laborers lived together in the same group of houses, ate the same food, and drank heavily polluted water, but had different occupations. They were, therefore, classified as:

Group 1. Field laborers who spent the entire day in the fields tilling the soil.
Group 2. Wives of Group 1, who went to the fields only during the busy season.
Group 3. Laborers whose duties did not include field work. In this group were drivers of milk wagons, blacksmiths, stable boys, workers in the sterilizing plant, washers of milk cans, etc. It is needless to add that all went barefoot and there were no latrines.

Table X gives the result of the study. See also Chart 8.

This shows that the men who worked about the plantation buildings, a village of from 400 to 500 people, without latrines, the environs of which one would assume to be heavily infected, were only lightly infected with hookworms, whereas the field workers on the same plantation were very heavily infected.

TABLE X.

Itatiaia.

	No. of cases.	Average age.	Average hemoglobin.	Average No. of hookworms.
		yrs.	*per cent*	
Field laborers, men and women	23	33	57	392
Houseworkers	21	25	68	40
Men only—other occupations than tilling the soil	14	36	70	30

Atibaia.

The Atibaia group consisted of individuals from small villages and small farms, all living under identical conditions. We divided them in the same way as the other groups and included twelve adult males who did not do field work. Table XI gives the results.

TABLE XI.

Atibaia.

	No. of cases.	Average age.	Average hemoglobin.	Average No. of hookworms.
		yrs.	*per cent*	
Adult field workers, men and women.....	40	26	75	190
Women housekeepers.....	41	30	73	11
Men who performed other than field work...	12	42	75	35
Children working in fields.....	9	12	73	132
Children who had not commenced to work in fields.....	40	9	69	12

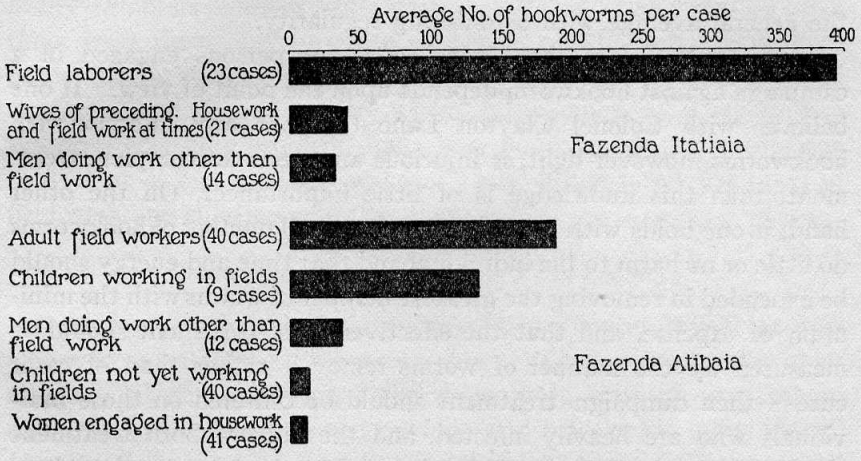

CHART 8. Relative severity of hookworm infection among agricultural workers and persons engaged in other occupations. Fazendas Itatiaia and Atibaia.

Conclusions.

These four studies are described separately because they were based on different groups of people living under somewhat different conditions in widely scattered localities and in different states. They prove conclusively that under Brazilian conditions hookworm disease is an occupational disease, a disease of those who work in the polluted soil. They prove that the infection produced through drinking water and food is negligible. And they prove that it is perfectly possible to live in a heavily infected community and yet remain free from the serious effects of the disease. We can say with certainty that Bra-

zilians who live in cities or villages, or even on farms, if their work does not include field work, are lightly infected with the disease. Individuals—adults or children—who spend long hours working in the fields with their bare feet in contact with moist soil are heavily infected. Women who spend most of their time about the house and work only a few hours in the fields are lightly infected. Children who have not yet begun field work have the lightest infection of all. In general, we may state that the degree of hookworm infection of an individual in Brazil varies directly with the number of hours that he spends barefoot in the fields. Like all other rules this formula has exceptions, but they are rare, and the individual conforms to the general average with astonishing regularity.

The importance of these conclusions for persons engaged in a campaign against hookworm depends upon the point of view. If one believes with Colonel Clayton Lane (2) that any infection with hookworms, however light, is injurious and deserves complete treatment, then this knowledge is of little importance. On the other hand, if one holds with Darling (3) that a small number of hookworms do little or no harm to the individual and that time and energy should be expended in removing the greatest number of worms with the minimum of expense, and that the effectiveness of treatment should be measured by the number of worms removed rather than of cases cured—then campaign treatment should be centered on those individuals who are heavily infected, and the bulk of both treatment and prophylactic work should be devoted to the interest of workers in the soil.

The findings are encouraging in that they show that hookworm disease is not difficult to prevent; for all practical purposes there is but one mode of infection, and very simple means, often unconsciously applied, reduce the degree of infection to a minimum. As a result of our studies we must qualify the general statement that hookworm disease abounds in all people in tropical and subtropical climes. Hookworm infection does exist in all tropical and subtropical countries, but hookworm disease is an occupational disease and is largely limited to soil workers.

INFLUENCE OF THE USE OF SHOES ON INFECTION WITH HOOKWORMS.

In the preceding discussions we have proved that the bulk of hookworm infection in rural Brazil is contracted through the long, constant, and continuous contact of bare feet with moist soil. Any factor that prevents such contact should lower the degree of hookworm infection.

The custom of going barefoot is almost universal in rural Brazil. Many adults have never had a pair of shoes, and those who do have them wear them only on state occasions. In the wet season shoes gather up the sticky mud in the field until each foot weighs from 5 to 6 pounds, and prove therefore a great inconvenience. They are also a serious economic problem, for a very poorly made pair costs the equivalent of 2 or 3 weeks' wages. Thus, adults rarely use shoes in field work and children never use them.

Comparison of Two Groups of Field Laborers.

During our work in the interior we studied a few adult field laborers who were accustomed to wearing shoes. They were usually older members of the family, and the shoes worn were of very rough, coarse, heavy, crudely tanned cowhide, which leaked in many places. Usually these persons did not wear their shoes every day or on all occasions, but some few wore them fairly constantly. We were therefore able to form one group of laborers who never wore shoes in field work, and another of laborers accustomed to using shoes in field work. All other conditions that entered into their mode of living were exactly alike—food, shelter, type of work, etc. The individuals in both groups were chosen from three widely separated localities. A comparison of their infection is shown in Table XII and Chart 9.

It is almost inconceivable that so simple a thing as wearing an old pair of shoes to work in the fields could have a fundamental influence on the well being of a field laborer, but our table of comparison shows this to be a fact. An average of 27 worms per case in adults

36 years of age is not a serious but a mild infection, as we have already shown. The mildness of the infection is, moreover, substantiated by the fact that the average hemoglobin of the shoe-wearing group was 72 per cent, an exceptional hemoglobin for a Brazilian field laborer 36 years of age. The field laborers who worked barefoot side by side with men who wore shoes had an average infection of 251 worms per case, or almost exactly ten times as many worms as their shod companions. The effect of this infection is clearly shown in their hemoglobin index.

TABLE XII.

Hookworm Infection in Adult Field Laborers Who Wore Shoes and Those Who Went Barefoot.

	No. of cases.		Average age.		Average hemoglobin.		Average No. of hookworms per case.	
	Wore shoes.	Went barefoot.	Wore shoes.	Went barefoot.	Wore shoes.	Went barefoot.	Wore shoes.	Went barefoot.
			yrs.	*yrs.*	*per cent*	*per cent*		
Fazenda Magnolia.....	9	50	38	25	71.0	63.6	31	313
Fazenda Chanaan.....	14	58	37	23	68.0	56.0	24	250
Atibaia.....	6	40	33	26	78.0	75.0	27	190
Average for the 3 groups..			36	24	72.3	64.8	27.3	251

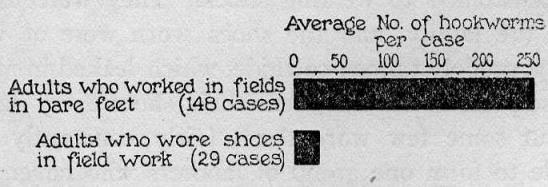

CHART 9. Relative severity of hookworm infection in adult field laborers who wore shoes and in those who went barefoot.

Comparison of Adults and Children in a Single Family.

Another interesting comparison was made in a single family of Spanish colonists, consisting of six adults and four children, all of whom lived under identical conditions and had been working side by side for the same number of hours in the same fields for a number of years past. Theoretically, if all were exposed to the same conditions, all should be equally infected. But there was one difference between the adults and the young members of the family—all the

adults wore a crude home-made half-shoe in the field, whereas the children went barefoot. The reflection of this difference of condition in the infections of adults and children is shown in Table XIII.

TABLE XIII.

Comparison between Adults and Children in a Family of Spanish Colonists.

	No. of cases.	Average age.	Average No. of hookworms.
		yrs.	
Adults	6	31	40
Children	4	15	226

The preceding studies emphasize the fact that hookworm disease is a soil disease and show that very simple means may be successfully employed in combating the disease. They make it clear that any factor, however crude and simple, that prevents the bare skin from coming in contact with infected soil is of definite value in preventing infection with hookworms.

HOOKWORM INFECTION SLOWLY ACQUIRED AND SLOWLY LOST.

It is a common belief that hookworm disease, like typhoid fever, malaria, etc., may follow a single exposure to infection. Frequently individuals have an unreasonable fear that they are infected with hookworm disease because they spent a few days in the country, where they chanced to drink polluted water or ate fruit and other uncooked food. As a matter of fact, while it is theoretically possible to receive massive infection with hookworms from a single exposure, this does not actually occur. In field experience we have found that hookworm infection is very gradually acquired—a worm here and another there, many days and weeks passing without any addition to the number of worms harbored.

Evidence that Hookworm Infection Is Slowly Acquired.

The gradual accumulation of infection is well illustrated in Chart 4 (page 15), showing hookworm infection of children by age-groups. The base line in this chart represents children under 4 years of age with almost no infection at all. Each year the average infection rate rises until at 10 years of age the average Brazilian country boy harbors 60 hookworms. Since he began to acquire the infection 6 years before, and since the average length of life of a hookworm, as shown by previous workers, is probably about 5 to 6 years, these 60 worms may be considered as representing 6 years of accumulated infection, or an average rate of about 10 hookworms a year. Between the ages of 8 and 9 the average boy begins to work in the fields and is at once exposed to the maximum conditions for acquiring infection. But he does not acquire the average degree of infection for adults until he is 20 years of age more or less (see Chart 1, page 7). Chart 6 (page 19) shows that children who begin to work in the fields at 8 years of age have at that time an average infection of about 15 hookworms each. The infection increases at the rate of about 50 hookworms a year, or an average of 1 a week, until the 14th year. Those children who do not work in the fields have an average increase in infection of only 1 new hookworm every 6 weeks, or 8 a year.

Thus we see that the mass infections are not acquired in a week or a month or even a year, but over a long period of years.

The fact that hookworm disease is slowly acquired is also clearly shown in Chart 5 (page 17). 50 per cent of the children under 10 years of age examined for this study had acquired less than 10 hookworms—an average of 1 a year. Not a single child 10 years of age or less, of all those examined, had an infection of 150 hookworms, even though many of them had been working continuously in the fields and had been constantly exposed to heavily infected soil for more than 2 years.

Chart 14 (page 55) shows that a group of Japanese colonists (Group 1) who had been working in heavily infected soil in Brazil for about 2 years had only begun to change their worm formula—that is, to lose *Ancylostoma duodenale* and acquire *Necator americanus*. Countrymen of theirs who had been in Brazil for 4 or more years (Group 2) were gradually losing ankylostomes and acquiring necators, but even after 4 years they had not acquired as many necators as the natives who were working side by side with them in the field.

We studied one young woman of 18 years who had been a servant in a city home all her youth. On marrying a colonist, she had gone to live on a coffee plantation, where for the first time in her life she began to work in the fields. The average infection of the field workers for the fazenda was 176 hookworms which showed a heavily infected soil. Yet when we treated this young woman after she had been working in the field for 4 months, we found to our surprise that she had not become infected with a single hookworm.

Evidence that Hookworm Infection Is Slowly Lost.

All the instances cited above prove that infection with a large number of hookworms does not occur in a few days or even a few weeks but represents the slow accumulation of years. Certain other instances seem to prove that hookworm infection is also slowly lost. We studied one group of people who lived in a village in the State of Rio de Janeiro. The average infection of those persons who did no field work was 28 hookworms. Two members of the group, a brother and sister aged 18 and 21 years, respectively, had worked in the fields since childhood until 3 years previously, when their father had bought

a store, moved to the village, and, becoming prosperous, provided his children with shoes. Despite the fact that these young people had left the fields 3 years before and had been living since under comparatively good hygienic conditions, they harbored respectively 318 and 223 hookworms. The average infection of field workers of the district was 390 hookworms. In the same village there lived a servant girl of 23 years who had left the fields 4 years previously to work in the kitchen of a wealthy landowner. She had been living under splendid sanitary conditions, with good latrines, good food, etc., but she still harbored 369 hookworms.

In another instance we treated a young woman of 21 years, who had always worked in the fields until 3 years before, when she had married. Since that time she had devoted herself to housework and had not come in contact with heavily infected soil. Nevertheless, she still harbored 379 hookworms. Group 1 of the Japanese colonists (Chart 14, page 55) even after 2 years in Brazil still harbored a large proportion of ankylostomes, whereas their neighbors harbored necators almost exclusively.

These instances all tend to substantiate the contention of other workers that hookworms live for years in the intestines of infected individuals. What the average length of life of hookworms is can be proved with accuracy only by carefully controlled experiments over a period of 10 years, but the data which we have, and which might be added to indefinitely, prove that hookworm infection is slowly acquired and slowly lost.

THE HEMOGLOBIN INDEX IN RELATION TO THE NUMBER OF HOOKWORMS HARBORED.

The hemoglobin index of all cases that we studied was estimated with the Dare instrument. All estimations were made with the same instrument, with the same technique, and by the same individual, and all were made 1 or 2 days before the first treatment for the disease was given. There was such a marked variation in individuals that we despaired at first of being able to arrive at any conclusions in regard to the effect of hookworm infection upon the hemoglobin index, but after a large series of examinations was made, certain definite tendencies became evident. Before we can discuss these findings, it is important to decide what should be considered a normal hemoglobin for a rural Brazilian.

Average Normal Hemoglobin of a Rural Brazilian.

The normal adult hemoglobin in temperate zones is usually given as from 90 to 95 per cent, but in tropical climates the average hemoglobin is much lower. In a considerable series of examinations made upon medical students and other healthy city dwellers, both Europeans and natives, we rarely encountered in Brazil a higher hemoglobin than 90 per cent. The average was about 85 per cent. The average for healthy country dwellers, even those of the better class, was lower still. A survey of the hemoglobin of rural Brazilians of the better class gives us the following averages for the various age-groups: for from 5 to 14 years, 67.5 per cent; for from 15 to 39 years, 71 per cent; for 40 years and over, 72.5 per cent. The average normal hemoglobin of the field workers who compose a large proportion of the rural Brazilian population is even less. There were only one or two peasants in our whole series who had no hookworm infection whatever, but we formed a group that was approximately normal out of the cases that harbored less than 10 hookworms each. The average hemoglobin for this "normal" group, according to age, is shown in Table XIV.

This comparatively low normal hemoglobin index is due to various causes. The first is hard labor. The Malaya Board proved that hard labor and underfeeding in the tropics were important factors in lowering the hemoglobin (4), and the same is undoubtedly true in Brazil. One important difference between the better class of rural Brazilians and the field laborer is that the former does not overexert himself, whereas the latter spends from 12 to 14 hours a day in the fields at hard physical toil. There is a corresponding difference between the hemoglobin index of the better classes and the field laborers whom we have considered as normal. A second cause is the insufficient diet of the Brazilian field laborer. The food eaten by the average peasant family is poorly prepared, endlessly monotonous, and at times entirely insufficient in quantity and quality for daily bodily needs. This insufficiency of diet is one of the important causes of a

TABLE XIV.

Average Normal Hemoglobin of Rural Brazilians.

Age.	No. of cases.	Average hemoglobin.	Average No. of hookworms.
yrs.		*per cent*	
5–14	56	67.5	3.8
15–39	50	71.0	3.8
40+	27	72.5	2.8

low hemoglobin index in rural Brazil. It will be discussed in greater detail in another section. The part that excessive drinking plays in lowering the hemoglobin is entirely conjectural. We did not keep data on the alcoholic habits of each case, but when an individual was a noted drunkard, the hemoglobin index was invariably very low. We feel that alcoholism plays an important part in lowering the hemoglobin, but this point needs confirmation.

The studies of the hemoglobin index in hookworm disease made by the Malaya Board were greatly complicated by the intercurrent infection with malaria in a large proportion of their cases. We did not have this problem in our studies. Malaria exists in many parts of Brazil and causes great damage, but there are also many locations which are free from this disease. We purposely chose places for study where there was a minimum of malaria. As a

result, malaria played a very small part in the reduction of the hemoglobin of the cases in our series.

For the reasons mentioned above and for others less important, the average normal hemoglobin of a rural Brazilian is almost 20 per cent lower than the normal hemoglobin of his own class in a temperate climate. Using 72 per cent as an average of the hemoglobin for adults, we can make a rough estimate of the degree of injury caused by hookworm infection in rural Brazil.

The Hemoglobin Index Not a Good Index of the Number of Worms Harbored.

Individual variation is extreme. At times one encounters a young adult worker who has a hemoglobin index of 80, yet who yields 600

TABLE XV.

Hemoglobin in Relation to Number of Hookworms Harbored, by Age-Groups.

5–14 yrs. (186 cases.)		15–39 yrs. (308 cases.)		40 + yrs. (72 cases.)	
Average No. of hookworms harbored.	Average hemoglobin.	Average No. of hookworms harbored.	Average hemoglobin.	Average No. of hookworms harbored.	Average hemoglobin.
	per cent		*per cent*		*per cent*
3.8	68	3.8	71	2.8	73
25	68	28	71	24	65
72	64	76	67	73	68
146	58	145	65	—	—
243	63	234	62	265	55
350	49	351	66	—	—
—	—	672	61	—	—
715	45.5	—	—	773	48.5

hookworms on treatment. His fellow-laborers may have a hemoglobin of 50 and yield only 300 hookworms. The reason for this is that the body is not a reservoir with a certain fixed amount of blood in which a certain given number of blood-destroying units will always cause a certain definite reduction in hemoglobin. Hookworm infection is slowly acquired, the blood-forming elements of the bone marrow are active forces, and the body defenses put up a struggle with the hookworms to retain a normal hemoglobin. In the older

individuals, 40 years of age and over, and in young children, 14 years years old and under, the body defenses have less endurance, and if hookworm infection is heavy, they wage a losing battle. In active youth and young adult life, a heavy infection of even 200 to 400 hookworms does not always produce severe anemia. The hemoglobin index, therefore, is not a good index of the number of hookworms harbored by the individual. Even when hookworms are the only cause of a low hemoglobin, the low index simply represents an

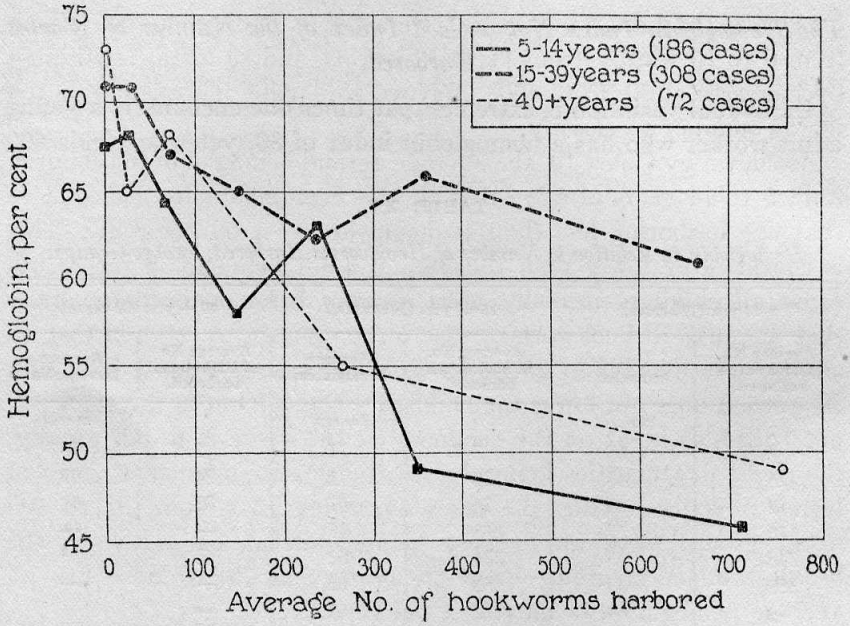

CHART 10. Hemoglobin index in relation to number of hookworms harbored, by age-groups.

end stage of the disease—the amount of ground that has been lost in the body's struggle to maintain a normal working level. This relation is shown in Table XV.

The Hemoglobin as an Index of the Amount of Injury Produced by Hookworms.

Despite the fact that the hemoglobin is not an index of the number of worms harbored by the individual, it is one of the earliest and one

of the best indices we have of the amount of injury that hookworms are producing in any individual case. This is illustrated by Chart 10 (page 40). The cases on which the chart is based were divided into age-groups as follows: children, 5 to 14 years of age; young adults, 15 to 39 years; and those aged 40 years and over. As we have stated before, an individual over 40 years old belongs to the aged group, for he is broken in health and strength. Having begun hard labor at 10 years of age, his force is largely exhausted after 30 years of work. All cases were also classified according to the number of hookworms harbored; that is, they were divided into groups containing from 0 to 10 worms, from 11 to 50 worms, and so forth, continuing by increases of 50 up to 400. Beyond this point the cases were too few in number to classify.

As shown by Chart 10, the average normal hemoglobin for children from 5 to 14 years of age—that is, the hemoglobin for children of that age harboring less than 10 hookworms—is 68 per cent. This is considerably lower than the normal adult hemoglobin rather because all children normally have a lower hemoglobin than adults than because 10 hookworms cause more damage to children than to adults. An average of 25 hookworms per case (Group 2, less than 50 worms) does not lower the children's hemoglobin in the slightest, but from this point on the tendency of the curve is to fall rapidly, the slight irregularities being due to the smaller number of cases of heavy infection. Thus the cases averaging 72 worms (51 to 100 worm group) have an average hemoglobin of 64 per cent; the heaviest infection group—with an average of 715 worms—has an average hemoglobin of only 45.5 per cent.

For adults from 15 to 39 years of age the normal hemoglobin is 72 per cent, with no reduction in those cases that harbored an average of 26 hookworms. A slight reduction occurs in those cases which harbored 70 hookworms each, and from this point there is a slow but very gradual fall in the curve. The resistance to hookworm infection of this age-group is so great that even in the group of highest infection—averaging 672 hookworms—the average hemoglobin is 62 per cent, or only 10 points below normal, whereas children harboring approximately the same number of worms are 20 points below normal.

For the group of the aged—40 years and over—the normal hemoglobin—73 per cent—is slightly higher than that for young adults, but under the influence of hookworm infection the curve declines so rapidly that in the highest infection group—cases averaging 773 hookworms—the average hemoglobin is only 48 per cent, or 25 points below normal. The curve is more irregular for this group than for the others because this group contains fewer members.

We may conclude from these findings that an average of 25 hookworms is not sufficient to break down bodily resistance more rapidly than it can be built up, even under the unfavorable living conditions of rural Brazil. The definite break in resistance in all the age-groups comes when an average of 75 hookworms is harbored. From this point on the reactions of children and the aged to increasingly heavy infections are almost exactly parallel; the hemoglobin decreases rapidly and constantly. That young adults are much more resistant to heavy infections is clear from the chart, for though the tendency of their curve is downward, it falls very slowly.

A separate study of children and youths is presented in Chart 11 (page 43). For this purpose all cases were divided into 5 year age-groups and classified according to the number of worms harbored, exactly as in Chart 10. The normal hemoglobin of the first group —children from 5 to 9 years of age with an average infection of 4 hookworms each—is 64 per cent. An average infection of 25 worms (11 to 50 worm group) does not reduce the hemoglobin of these small children in the slightest degree, but higher infections soon cause a break. Thus for children under 10 years harboring an average of 128 worms the average hemoglobin is 53 per cent, proving that an average of 128 hookworms in young children reduces the hemoglobin to a greater extent than does five times as heavy an infection in youths from 15 to 19 years of age. There was not discovered a single child under 10 years of age who harbored more than 200 hookworms.

The normal hemoglobin for the age-group 10 to 14 years is approximately 70 per cent. An infection of 25 hookworms has no effect, but from this point the curve falls rapidly, with slight irregularities due to the fewer number of cases in the higher infection groups. Children of this age harboring 713 hookworms have an average hemoglobin of only 45.5 per cent.

The normal hemoglobin for the third group—youths of 15 to 19 years of age—is approximately the same as for the preceding group. And, as in both the other groups, it is not lowered in cases averaging 27 hookworms. Indeed, those cases have even a slightly higher hemoglobin than the cases harboring 3.3 hookworms each. From this point the curve falls, but so slowly that the highest infection group, averaging 645 hookworms, has an average hemoglobin of 60 per cent, or only 10 points below normal.

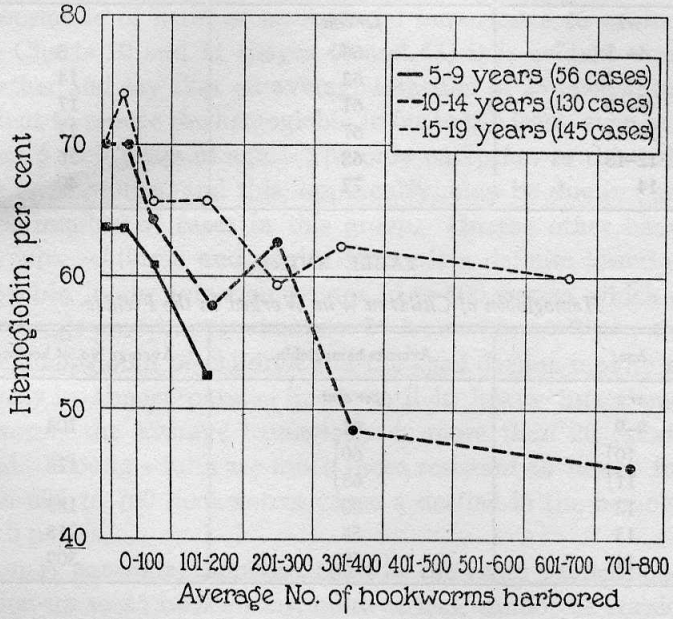

CHART 11. Hemoglobin index in relation to total number of hookworms harbored—children and adolescents.

Chart 6, which is presented in the discussion of hookworm disease in children (page 19), illustrates the fact that small children normally have a low hemoglobin which gradually increases up to about the 14th to the 16th year. Table XVI is taken from that chart.

The effect of heavy hookworm infection in growing children is well shown in a table of hemoglobin of children who worked in the fields (Table XVII).

According to this, a child of 14, who should have an average hemoglobin of 71 or 72 per cent even under the adverse conditions under which he lives, has instead, when infected with large numbers of hookworms, an average hemoglobin of 59 per cent, or 13 points below normal.

TABLE XVI.

Hemoglobin of Children Who Did Not Work in the Fields.

Age.	Average hemoglobin.	Average No. of hookworms.
yrs.	*per cent*	
4– 5	63	3
6– 7	62	14
8– 9	61	17
10–11	67	27
12–13	68	36
14	72	49

TABLE XVII.

Hemoglobin of Children Who Worked in the Fields.

Age.	Average hemoglobin.	Average No. of hookworms.
yrs.	*per cent*	
8–9	61	104
10	60	128
11	63	
12	60	189
13	58	213
14	59	309

Conclusions.

From a review of the tables and charts, certain facts become manifest. It is evident, in the first place, that we cannot make a set formula to the effect that a certain limited number of hookworms are required to lower the hemoglobin index 1 point. One reason is that such a formula would require the compilation of a much larger series of cases than ours, and a second is that there are a large number of factors other than hookworms which enter into the battle for existence and tend to reduce the hemoglobin. Among the most important

of these factors are overwork, poor and insufficient food, excesses, and other infections.

Are we, however, able to decide from these studies what degree of infection with hookworms causes notable injury to the body; what degree of infection can be considered as casual, more or less accidental, and producing little or no harm to the body; and what degree of infection should be considered as actual hookworm disease? Our charts give us definite answers to these questions.

Practically all authorities agree that an infection of from 2 to 3 hookworms is of little or no material importance to an individual. From Charts 10 and 11 (pages 40 and 43) it is evident that we can go further and say that an average infection of 25 hookworms is not sufficient to reduce the hemoglobin index in the least, even in children of from 5 to 9 years of age. The only exception to this rule occurs in the aged groups, and this, apparently, may be due in part to the smaller number of cases in this group. On the other hand, in all age-groups—children and adults—there is a definite lowering of the hemoglobin in the infection groups 50 to 100 worms, which averages for each age-group approximately 75 hookworms. From this point on the hemoglobin of children and the aged decline rapidly and continuously in almost parallel lines, until in heavy infections of 700 hookworms the average hemoglobin is more than 20 points below normal. Young adults are much more resistant to heavy infections —even 695 to 700 hookworms cause a decline in the hemoglobin of only 10 points.

We may conclude, therefore, that, in the cases studied, hookworm infection up to 25 hookworms, more or less, cannot be considered as hookworm disease, for such an infection does not disturb bodily functions seriously enough to lower the hemoglobin even a fraction of 1 point. An average infection of 75 hookworms, however, is heavy enough to disturb the balance; in the average individual it causes a distinct lowering of the hemoglobin. Infections higher than 75 hookworms affect children and the aged very severely, especially children under 10 years, while young adults between 15 and 39 years of age are extremely resistant even to very high infections of 500 or more hookworms.

INFLUENCE OF NUTRITION ON HOOKWORM DISEASE.

We have already shown that there is considerable variation in individual resistance to hookworm disease. In general, young adults are more resistant than people of 45 or more, and much more resistant than young children. 100 hookworms will produce more severe symptoms and cause a more rapid fall in the hemoglobin in a child of 6 years than in a child of 12 years.

The breaking down of resistance against hookworm infection in any individual is due to numerous associated causes, one of the most important of which is poor and insufficient food. The kind of food eaten by individuals is so dependent on their economic situation that it was almost impossible to obtain for comparison two groups of people who were living under exactly similar conditions except in respect to food. People who have plenty of good food have good homes, little work, and shoes; people who have insufficient food work hard in the field, have no shoes, and often drink alcohol to excess.

Comparative Study of Well Nourished and Poorly Nourished Groups.

However, we were fortunate enough to obtain for study two small groups of cases differing only in respect to their food. On a big farm devoted to the production of milk we treated eight individuals who were milkers. These men worked long hours at very laborious work, for they not only milked but also did field work in their spare time. They enjoyed the privilege of drinking all the milk they could; each one estimated that he drank from 2 to 4 liters of warm milk a day, which with the other food eaten gave a good caloric intake. On a neighboring plantation we treated individuals who were comparable to the milkers in every way except that they did not have the privilege of drinking milk. We also included in the study a small third group, which added to the interest. These were men who lived in the hills surrounding the plantation, relatives and friends of the first two groups, small tenants tilling their little bit of land. They were very poor and underfed, being in most cases on the verge of destitu-

tion. A comparative table of these three groups (Table XVIII) is very striking.

TABLE XVIII.

Comparison of Well Nourished and Poorly Nourished Groups.

	No. of cases.	Average age.	Average hemoglobin.	Average No. of hookworms.
		yrs.	*per cent*	
Milkers	8	26	66	350
Field workers	16	31	57	224
Mountaineers	3	32	33	518

The hookworm infection in all three groups was very high, but the milkers had a hemoglobin far above the average for individuals in the same age-group with a similar number of worms (see Chart 10, page 40), whereas the mountaineers had a far lower average hemoglobin than that for all Brazilians of their age-group infected with the same number of hookworms—518. The contrast between the individuals was striking. The milkers were strong, active, ruddy, bright, and animated about their work; the poor mountaineers were waxy yellow in color, weak, discouraged, with edema of faces and feet—typical pictures of severe hookworm disease. The contrast was due almost entirely to the fact that one group had plenty of food while the other group had insufficient food.

Influence of Starvation on Hookworm Disease.

We wish to state here our belief that hookworm edema is closely related to war or starvation edema. Having seen the two conditions side by side, we believe that it is impossible to differentiate them clinically, and that edema in hookworm disease is a late manifestation of faulty nutrition or metabolism, just as is starvation edema. The identity of the two conditions can only be proved when we have discovered the mechanism of production of starvation edema, a subject in which there is so much interest at present. We await expectantly the publication of the methods of research and of the conclusions of the large number of workers who are at present studying war edema, in order that the same experimental methods may be applied to cases of hookworm edema.

A study of the effect of starvation on hookworm disease was carried out on a plantation where there were from 400 to 500 refugees from the famine-stricken district of Ceará. They had all passed through the horrors of the big drought in Ceará in 1920 and had seen their brothers and children drop dead by the roadside from hunger. They finally reached the capital of Ceará, where they were given some food and sent on to São Paulo. When we examined them, they had had 2 months of good housing and of sufficient food, but the effects of the famine were still dreadfully apparent, especially in the children. A comparison between these individuals who had come from Ceará 2 months before and colonists who had been on the plantation for several years revealed some interesting facts. It must be remembered that both groups were now eating the same food, living together in the same houses, and performing the same tasks in the fields. The comparison is presented in Table XIX.

TABLE XIX.

Effect of Starvation on Hookworm Disease.

	No. of cases.	Average age.	Average hemoglobin.	Average No. of hookworms.
		yrs.	*per cent*	
Adults.				
Cearenses	27	29	55.0	243
Other colonists, same fazenda	34	27	60.0	187
Average for all Brazil for the age-group 25–30 yrs	—	—	63.9	236
Children.				
Cearenses	14	11	52.0	99
Other colonists, same fazenda	18	11	58.0	149
Average for all Brazil, same age and similar worm count	—	—	58.0	151

The quality and quantity of food eaten by the original colonists could not by any stretch of the imagination be called a full and balanced ration; it was always very limited, very poor in quality, and very poorly prepared. Nevertheless, it gave them sufficient calories to enable them to spend long, laborious hours in field work. The table shows that this group, despite their highly unsatisfactory but comparatively full diet, had a very much higher average hemo-

globin than the Cearenses, who had suffered from both hookworm disease and starvation. This is particularly evident in the children, for whereas the old colonists' children harbored 149 worms each and had an average hemoglobin of 58 per cent, the Ceará children harbored only 99 worms each and yet had the much lower hemoglobin of 52 per cent. These few cases, though inconclusive, tend to prove what seems an obvious fact, that as ample food builds up resistance against the ravages of hookworm disease, starvation markedly increases the effects produced by the worms upon the body. Unfortunately, the individual who is heavily infected with hookworm disease is so weakened that he cannot do a full day's work. He is thus unable to earn the food which he so urgently needs to combat the ill effects of the disease.

DISTRIBUTION OF ANCYLOSTOMA DUODENALE IN BRAZIL.

The presence of *Ancylostoma duodenale* in Brazil was discovered many years ago, but the prevalence and distribution of the worm has not been studied. Since *Ancylostoma duodenale* is larger in size than *Necator americanus*, causes greater injury to the intestinal mucosa, and is on the whole more harmful, it is of great importance to know the prevalence and distribution of this type of hookworm.

Macroscopic Differences between Ancylostoma and Necator.

Formerly the differentiation of *Ancylostoma duodenale* and *Necator americanus* was a slow and difficult process, for the *microscopic* characteristics were used as the indices of differentiation. Thanks to the work of Lane (2), we now have a rapid and easy method of *macroscopic* differentiation which greatly simplifies the task. A brief description of these macroscopic differences may be of interest. A few small details have been added by us to the points noted in the Malaya report.

In order best to bring out all their characteristic differences, one should take hookworms that have been freshly picked out from washed stools and treat them with boiling 65 per cent alcohol. This process is not absolutely necessary but is of aid to the beginner. The chief differences to be noted are as follows:

Ancylostoma duodenale.	*Necator americanus.*
Female.	Female.
Size.—Slightly longer than *Necator* and very much thicker.	Slightly shorter than *Ancylostoma* and decidedly thinner.
Shape.—Always assumes a curve in the form of the letter *C*, sometimes slight, sometimes accentuated.	Assumes the form of the letter *S* owing to the posterior curve of the head.
Posterior extremity.—The posterior extremity terminates in a broad blunt point.	The posterior extremity terminates in a slender tapering point.

Ancylostoma duodenale. Female.	*Necator americanus.* Female.
Color.—White—with sometimes a black spot in the region of the esophagus. Fresh blood is very frequently seen in the body of the worm.	Distinctly brownish in color; the red color of blood is almost never seen in the body of the worm.
Texture.—In rolling the worm under a needle, one notices that it has a tough resistant feeling like cartilage.	The worm is soft when pressed with a dissecting needle.

The above-mentioned characteristics apply to the males as well as to the females, and in males the following additional variations are to be noted:

Ancylostoma duodenale. Male.	*Necator americanus.* Male.
Size.—Much larger than *Necator* male; the diagnosis can almost always be made on this point alone.	Much smaller than *Ancylostoma* male.
Shape.—The shape is almost exactly that of a nail—sometimes curved slightly in the form of a *C*.	The shape is always that of an *S*, with the characteristic dorsal curvature of the head.
Posterior extremity.—The posterior extremity terminates in an open bursa which appears like the petals of an open flower.	Posterior extremity terminates in a bursa which is closed like the bud of a flower.
Color.—Same as *Ancylostoma* female.	Same as *Necator* female.
Texture.—Same as *Ancylostoma* female.	Same as *Necator* female.

The microscopic differential characteristics are not given here, for they are too well known to need repetition. They are used only in confirmation of macroscopic examination results.

With a little practice it is possible to differentiate the two species with great rapidity: 10,000 or more hookworms, if properly prepared, can be easily classified in an hour without a single error. One should never depend upon one factor of differentiation alone but should consider all factors. The most valuable differentiating points are the size and characteristic shape.

Factors Influencing Distribution of Ancylostoma.

The use of the macroscopic method made our studies of the prevalence of *Ancylostoma duodenale* in Brazil a simple matter. We simply included the problem in the course of other work, noting the relation of the prevalence of *Ancylostoma duodenale* to age, sex, race, nationality, type of work, mode of life, type of soil, and geographic location. We were able to prove readily that the factors of age, sex, soil, type of work, and mode of life, though they greatly affect total infection with hookworms, do not affect the relative prevalence of *Ancylostoma* and *Necator*. Nor did we find any racial immunity to *Ancylostoma;* given equal exposure, the black, white, yellow, and copper-colored races were alike infected. This fact was shown extremely well in some of the experiments.

There were two factors, however, which had a marked effect upon variation in the proportion of *Ancylostoma duodenale* infection to *Necator americanus* infection; namely, nationality and geographical location. As Dr. Darling has already noted, *Ancylostoma duodenale* is the prevailing hookworm in southern Europe, including lower Italy, Spain, and Portugal, and in Egypt and Persia (5). It is the predominating species in China and Japan. The original home of *Necator americanus* is Central Africa, whence it has spread eastward to Ceylon, southern India, and the East Indies, and westward, with the slave traffic, to North and South America. Theoretically, therefore, we should expect to find the northern part of Brazil where almost all field labor is performed by descendants of African slaves, to be infected almost exclusively with *Necator americanus*. States that imported Italian and Spanish colonists to do the field work after the days of slavery were ended should have at least a slight infection with *Ancylostoma*, and plantations that have employed Japanese colonists should have a comparatively heavy *Ancylostoma* infection. Let us see how our prediction agrees with fact.

Experiment 1.—Fazenda Magnolia was a large plantation divided into two parts. One part, the home settlement, consisted almost entirely of Brazilians born on the fazenda and living there quietly all their lives. The population of this part of the plantation underwent little change. Colonia Santa Maria, a mile away, was an immigrant colony made up almost entirely of Italians and Spaniards

who had been from 4 to 20 years in Brazil. 2 years ago many Japanese had lived in the colony, but only for 1 year. The distribution of *Ancylostoma* and *Necator* in these two settlements is shown in Table XX.

TABLE XX.

Distribution of Ancylostoma and Necator on Fazenda Magnolia.

	No. of cases studied.	Ankylostomes per case.	Necators per case.	Proportion of ankylostomes to necators.	Percentage of cases infected with ankylostomes.
Group 1. Native Brazilians.....	55	2.2	242.0	1:110.0	62
Group 2. Italian and Spanish immigrants.....	26	12.0	241.8	1: 20.1	81

It may be seen that the immigrant colony had five times as many *Ancylostoma* as the home colony, though soil conditions, food, housing conditions, labor conditions, etc., were the same (Chart 12).

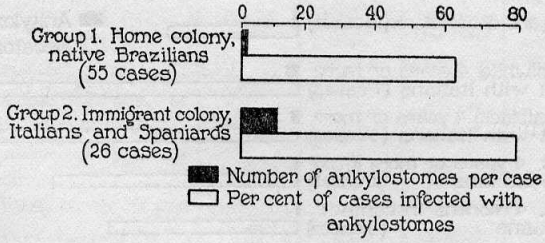

CHART 12. Per cent of total cases infected with ankylostomes and average number of ankylostomes per case in different groups on Fazenda Magnolia, State of São Paulo.

Experiment 2.—Fazenda Chanaan, São Paulo. This fazenda proved a splendid place for study, for it contained a large number of people from different states and of different nationalities, all living together under exactly the same conditions. A few were natives of the State of São Paulo—both white and black; some were Italians and Spaniards, who had been on the fazenda many years, who had, in fact, previously made up a large part of the fazenda population. The most interesting groups were from Bahia and Ceará. The Bahianos had arrived 4 months previously; the Cearenses were divided into two groups—those who had arrived 4 years before and had lived since in the same colony with the Italians and those who had arrived only from 1 to 2 months before. The results of our study are shown in Table XXI and Chart 13.

TABLE XXI.

Distribution of Ancylostoma and Necator in Various Groups on Fazenda Chanaan.

	No. of cases.	Ankylostomes per case.	Necators per case.	Proportion of ankylostomes to necators.	Percentage of cases infected with ankylostomes.
Italians and descendants	38	15.1	152	1:10	87
White Paulistanos	7	10.2	271	1:26	70
Spaniards* and descendants	10	3.2	109.6	1:34	90
Cearenses, 4 yrs. on fazenda	10	5.3	200.2	1:38	70
Black Paulistanos	5	6.4	298	1:46	100
Bahianos, 4 mos. on fazenda	5	2.0	156	1:78	60
Cearenses, 2 mos. on fazenda	34	1.2	235	1:154	35

* The relatively low average of hookworm infection in the Spaniards was due to the fact that all adults wore shoes.

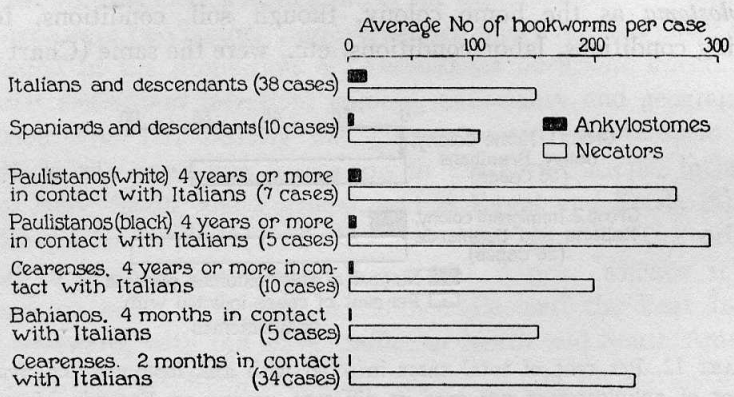

CHART 13. Ankylostomes and necators harbored by different groups on Fazenda Chanaan, State of São Paulo.

The table of comparison shows clearly that the type of infection contracted on this fazenda—the type of hookworm larvæ with which the fazenda soil was seeded—was in a considerable proportion of cases *Ancylostoma* infection, *Ancylostoma* larvæ. It is more than probable that the fazenda was infected with ankylostomes by the Italians and Spaniards, who still had the heaviest infection. The Paulistanos, white and black, who had been associated with the Europeans for from 8 to 10 years, were moderately infected with *Ancylostoma*, as were also the Cearenses who had been on the fazenda

for 4 years. The Bahianos, who had been on the fazenda 4 months, and those Cearenses who had come only recently had almost no ankylostomes at all.

Experiment 3.—Fazenda Bom Jardim. On this fazenda the colonists were all Japanese. We divided them into two groups according to the length of time they had been in the country. Group 1 consisted of colonists who had emigrated from Japan less than 2 years ago and who had not yet come into intimate contact with local conditions. Group 2 consisted of those who had been in Brazil 4 years or more and had been in close association with Paulistanos, Bahianos, and Italians, living in the same houses, eating the same food, etc. A third group was formed of a colony of Italians who lived less than 300 yards away from the Japanese. These had all been in Brazil for from 10 to 30 years. The results of our comparative study are shown in Table XXII and Chart 14.

TABLE XXII.

Distribution of Ancylostoma and Necator on Fazenda Bom Jardim.

	No. of cases.	Ankylostomes per case.	Necators per case.	Proportion of ankylostomes to necators.	Percentage of cases infected with ankylostomes.
Group 1. Japanese, 2 yrs. or less in Brazil.....	20	9.6	14.1	1: 1.4	65
Group 2. Japanese, 4 yrs. or more in Brazil.....	8	2.3	233.0	1:98.0	75
Group 3. Italians, 10 to 30 yrs. in Brazil.....	30	3.5	161.0	1:46.0	72

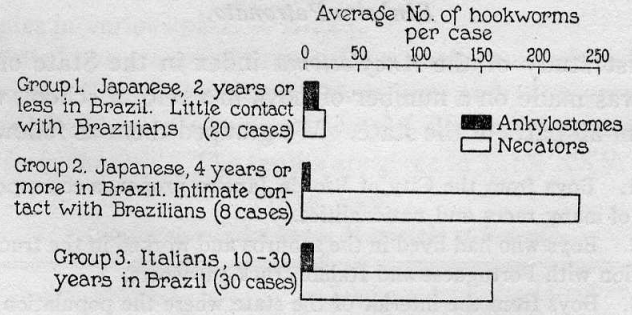

CHART 14. Ankylostomes and necators harbored by different groups on the same coffee fazenda.

The experiment demonstrates that an exchange of intestinal parasites was going on; the Japanese were losing their ankylostomes as they were losing their national customs and acquiring the São Paulo worm picture as they were acquiring Brazilian manners and habits of toil.

Normal Ancylostoma Index of São Paulo.

All the studies described above were made on the newly developed large coffee fazendas of São Paulo, to which during the past 20 years there has been a great immigration of field workers. The normal *Ancylostoma* index of São Paulo was studied in one of the older settlements, which was made up almost entirely of pure Brazilians who had lived all their lives in the community. The study included coffee fazendas, small farms, and villages. The results are shown in Table XXIII.

TABLE XXIII.

Ancylostoma Index in Old-Established Community in São Paulo.

	No. of cases.	Ankylostomes per case.	Necators per case.	Proportion of ankylostomes to necators.	Percentage of cases infected with ankylostomes.
Atibaia; typical São Paulo community.....	112	0.4	52	1:194	10

Studies of the Ancylostoma Index of the State of Rio de Janeiro. Pinheiro Patronato.

Our first study of the *Ancylostoma* index in the State of Rio de Janeiro was made on a number of boys in a reform school, who had come from all parts of the state. We grouped them as follows:

Group 1. Boys from the City of Rio de Janeiro proper, a cosmopolitan city composed of many races and nationalities.

Group 2. Boys who had lived in the suburbs and worked in the truck gardens in association with Portuguese and Italian truck gardeners.

Group 3. Boys from the interior of the state where the population is almost purely Brazilian.

Table XXIV gives our findings.

TABLE XXIV.

Ancylostoma Index of the State of Rio de Janeiro.

	No. of cases.	Ankylostomes per case.	Necators per case.	Proportion of ankylostomes to necators.	Percentage of cases infected with ankylostomes.
Group 1. Rio, city.....	30	2.2	61.7	1:28	50
Group 2. Rio, suburb.....	29	8.5	171.0	1:20	93
Group 3. Rio, interior of state...	15	2.2	193.0	1:87	87

The experiment showed that boys who worked in contact with Italians and Portuguese had four times as many *Ancylostoma duodenale* as the interior boys who were not in contact with immigrants. The proportion of *Ancylostoma* larvæ to *Necator* larvæ in the soil in and about the City of Rio de Janeiro was demonstrated to be about 1 to 25, and in the interior about 1 to 100.

Municipio of Rezende.

Material for another interesting comparison was furnished by the Municipio of Rezende. The Municipio, or County, of Rezende was formerly a great coffee-raising center, where the field labor was done by slaves. With the freeing of the slaves, coffee culture was abandoned, and the slaves settled on the hillsides where their descendants now live. There has been almost no immigration of foreigners. The City of Rezende, however, has been used in years past as a depot for European colonization—a distributing center where the immigrants, mainly Italians, remained for from 3 to 4 months until assigned to the colonies in various parts of Brazil.

We studied two groups of people: (1) a small group which had lived in or near the City of Rezende all their lives and (2) a group of field workers and village dwellers on two old slavery plantations 12 or 15 miles from the city. The results are given in Table XXV.

TABLE XXV.

Ancylostoma Index in the Municipio of Rezende.

	No. of cases.	Ankylostomes per case.	Necators per case.	Proportion of ankylostomes to necators.	Percentage of cases infected with ankylostomes.
Group 1. Rezende.....	5	26.5	446	1: 16.9	60
Group 2. Itatiaia.....	58	1.6	160	1:100	25

This experiment showed that the soil of the City of Rezende had a heavy proportionate *Ancylostoma duodenale* infection, and that the old slave fazendas had very light *Ancylostoma duodenale* infection.

Study in the State of Matto Grosso.

The only other group study made was in the State of Matto Grosso, in a colony of pure-blooded, semicivilized Indians who were entirely separated on their reservation from contact with either blacks or whites. In the past there had been some communication with both Brazilians and Paraguayans. Their life was pastoral, though they lived in rude houses in a village and planted some cereals. The results of our study are shown in Table XXVI.

TABLE XXVI.

Ancylostoma Index among the Indians.

	No. of cases.	Ankylostomes per case.	Necators per case.	Proportion of ankylostomes to necators.	Percentage of cases infected with ankylostomes.
Indians.....	34	1.7	87	1:57	62

Distribution Judged by Individual Cases Treated.

We had opportunity from time to time to treat cases from almost every state in the Union but could draw no conclusions from a single case or scattered group of cases except the information as to whether or not *Ancylostoma* were to be found in the region from which they came. In general, we may conclude from our data that individuals from the interior of the states of Para, Rio Grande do Norte, Pernambuco, Ceará, Bahia, and Minas may, and usually do, harbor large numbers of *Necator americanus* but almost never harbor *Ancylostoma duodenale*. Individuals from any of the cities along the northern littoral may have a few *Ancylostoma*, but we never found them in these individuals in the proportion that we found them in persons from the states of Rio and São Paulo. The few cases that we studied from Paraná, Santa Catharina, and Rio Grande do Sul had few hookworms of any variety. Unfortunately, we had no opportunity

to study recently arrived immigrants from Portugal, Spain, and Italy because scarcely any came from those countries after our studies began. The one recently arrived Portuguese who was treated had a worm count of *Ancylostoma* 13, *Necator* 56. A comparison of all groups is given in Chart 15.

DESCRIPTION OF THE GROUPS REFERRED TO IN CHART 15.

1. Rezende group. This group was taken from a city of 8,000 inhabitants which was formerly a center of Italian colonization. The group is small, but 12 other incompletely studied cases from the same city show the same relative proportions.

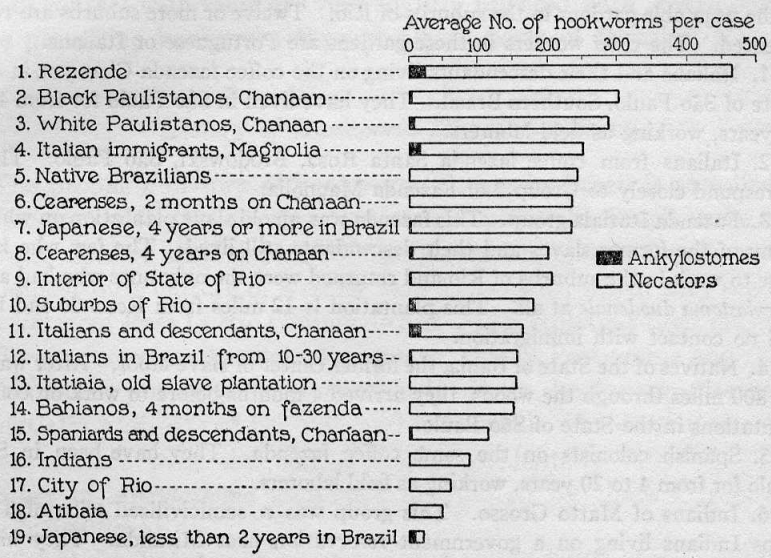

CHART 15. Ankylostomes and necators harbored by various races and groups in Brazil.

2. Black natives of Fazenda Chanaan. They have always lived in the State of São Paulo.

3. White natives of Fazenda Chanaan. They have always lived in the State of São Paulo.

4. Fazenda Magnolia (coffee): Group 2 lived in a separate colony about 1 mile away; they were nearly all Italians who had been in Brazil many years.

5. Fazenda Magnolia (coffee), Brodowski, State of São Paulo: Group 1 were almost all pure Brazilians who had lived all their lives on or near the fazenda and had not come into contact with foreigners.

6. Group B on Fazenda Chanaan, from the State of Ceará, Northern Brazil. They came as refugees to São Paulo 2 months before, because of the severe drought in their own home.

7. Japanese colonists on the same fazenda who have been in Brazil for from 4 to 6 years and have adopted Brazilian customs.

8. Group A on Fazenda Chanaan, from the State of Ceará, Northern Brazil. They came as field laborers to the State of São Paulo after the drought in Ceará in 1915.

9. Boys from seventeen different places in the interior of the State of Rio, where there is little immigration.

10. Boys from the suburbs of Rio. This group consisted of boys who worked in the vegetable gardens in the suburbs of Rio. Twelve or more suburbs are represented. The chief workers in these gardens are Portuguese or Italians.

11. Italians and their descendants living on the coffee fazenda Chanaan, in the State of São Paulo, Southern Brazil. They have lived in São Paulo for from 4 to 20 years, working as field laborers.

12. Italians from coffee fazenda Santa Rosa, Brodowski, São Paulo. They correspond closely to Group 2 of Fazenda Magnolia.

13. Fazenda Itatiaia group. This fazenda was an old slave plantation on which many of the former slaves and their descendants still lived. The few who had gone to work in the suburbs of Rio and returned were the only ones who had any *Ancylostoma duodenale* at all. This plantation is 12 miles from Rezende and has had no contact with immigration.

14. Natives of the State of Bahia, the former center of slave labor. After walking 800 miles through the woods, they arrived 4 months before to work on coffee plantations in the State of São Paulo.

15. Spanish colonists on the same coffee fazenda. They have been in São Paulo for from 4 to 20 years, working as field laborers.

16. Indians of Matto Grosso. This group was a semicivilized tribe of Terrenos Indians living on a government reservation near Miranda. They have had little contact with whites, though they fought in the Paraguayan war.

17. Vagabond boys from the City of Rio. The street was their home, and undoubtedly they sometimes went to the country. They are not a true index of the degree of infection of the city but probably represent the type of infection that may be acquired in the city.

18. Atibaia group. This was a large group made up of field workers, villagers, and town dwellers. They lived in an old settled part of the State of São Paulo and were not in contact with immigration. They were almost all pure Brazilians.

19. Japanese colonists on the coffee fazenda Bom Jardim, an estate in São Paulo, Southern Brazil. They have lived in Brazil less than 2 years and have retained their national customs.

Influence of Immigration.

Our experiments show clearly that wherever there has been extensive immigration of field laborers from Southern Europe or Japan into Brazil, there has been a corresponding increase in the number of *Ancylostoma duodenale*. The immigrants have not only reinfected themselves but have infected the natives who have been in close contact with them. Infection of Brazilians consequent on seeding of the soil with *Ancylostoma* has been closely limited to places where the contact with immigrants has been intimate, where natives and newcomers have lived in the same houses or groups of houses and worked in the same fields. Natives living 2 or 3 miles from immigrants and not in contact with them are very slightly infected with *Ancylostoma*. The prevailing hookworm throughout all parts of Brazil is *Necator americanus*.

History of Hookworm Disease in Brazil.

The probable history of hookworm disease in Brazil is as follows: Coincident with the development of agriculture in Brazil came the introduction of slave labor. These slaves brought to Brazilian soil an almost pure culture of *Necator americanus*,with which they seeded the soil from Para to Rio Grande do Sul. It is true that their masters and overseers were Southern Europeans, chiefly Portuguese and their descendants, but as we have previously shown, hookworm disease is essentially a disease of the soil, and individuals who do not come in close contact with the soil are only incidentally infected. The number of *Ancylostoma duodenale* distributed by these Europeans was insignificant.

With the end of slavery in 1887 entirely new conditions arose. The coffee industry in the State of São Paulo began to develop rapidly, and there was in consequence a great lack of field laborers. 25 to 30 years ago colonization from Southern Europe began—an influx of field laborers and peasants. Wherever these colonists went to work in the fields, they seeded the soil with *Ancylostoma;* the worms found ideal conditions for development and infected both their former hosts and the natives who were associated with the Europeans in the field

work. Within the past 6 years there has also been an influx of Japanese, whose hookworm index is largely *Ancylostoma*, and where these colonists have gone, the *Ancylostoma* infection index is proportionately high. In the older, more backward states of Brazil almost the only hookworm to be found today is *Necator americanus*. In fact, one can judge very well whether a community is progressing or not by its hookworm index. If it is active and progressive and has good colonists, it will have a high proportional number of *Ancylostoma duodenale*. If it is backward, undeveloped, poverty-stricken, the hookworm infection will be almost entirely *Necator*. Though *Ancylostoma* are an index of progress, they are not at all a necessary part of progress; on the contrary, they are a severe check on the progressiveness of an otherwise active community.

There is one very good and simple method for combating *Ancylostoma*. Every immigrant from Southern Europe or Japan should have a microscopic stool examination before he embarks, and if hookworm disease is discovered, he should be given thorough anthelmintic treatment. This is a conservative, reasonable recommendation and has ample precedent. We believe that the Brazilian Government should give the matter careful consideration.

VALUE OF THE ROUTINE MICROSCOPIC EXAMINATION OF STOOLS IN FIELD TREATMENT.

A summary of the results of our experiments to test the value of the routine microscopic examination of stools in field treatment for hookworm disease has appeared in a previous monograph (6). The findings were very striking but were based on a rather small number of cases for so important a subject. Since then we have investigated 131 more cases and wish to summarize here the results of all our experiments to date.

Two Kinds of Experiments. Summary of Results.

The 1920 experiments, like those of 1919, were of two kinds:

1. Treatment and worm counts of cases that were negative to the routine microscopic examination of the stools (in 1920, 22 cases).
2. Treatment and worm counts of cases in which the microscopic stool examinations had been made and the results withheld (in 1920, 109 cases). After the experiment was completed, the microscopic results and worm counts were compared.

All our experiments of the first kind are summarized in Table XXVII.

TABLE XXVII.

Results of Treatment of Cases Negative to Microscope.

	No. of cases.	Without hookworms.	With hookworms.	Total No. of hookworms.	Average No. of hookworms per infected case.
Adults, over 14 yrs.....	29	4	25	891	35
Children, under 14 yrs.....	25	7	18	192	10.6

From this we see that of the negative cases only 14 per cent of the adults and 28 per cent of the children were correctly diagnosed by the microscope. Cases that were definite microscopic failures—that is, that harbored more than 10 hookworms each—were divided as follows: 7 adults with an average of 116 hookworms and 5 children with an average of 33 hookworms. From these results taken by

themselves, the microscope would seem to be a very uncertain and unreliable aid in the diagnosis of hookworm disease.

In 109 cases in 1920 the results of the microscopic examinations were withheld until after the cases were treated. When all worm counts had been made, the microscopic results and the actual worm counts of the cases were compared. A summary of these results and the results obtained in similar experiments in 1919 is given in Table XXVIII.

TABLE XXVIII.

Comparison between Microscopic Results and Worm Counts.

No. of cases studied, all harboring hookworms.	No. of cases diagnosed as negative by microscope.	Percentage of cases correctly diagnosed by microscope.	No. of microscopic failures, cases harboring more than 10 worms.
269	15	94	8

This table gives the microscope a reprieve, since 94 per cent of accuracy is not at all a bad showing. The test is a fair one, representing typical routine field conditions.

These experiments were small but characteristic portions of the whole fabric of the field laboratory technique—as if one made a cross-section of the work of each individual in the post. They were the result of the work of six different laboratories in widely scattered localities and of more than fifty individuals—nurses, persons who collected specimens of stools, microscopists, chief nurses, etc. Thus, though the series is small, it is representative.

We have also made a compilation of all cases treated by us during the past 2 years in which the microscopic examination of the stools was negative. The results of treatment are shown in Table XXIX.

TABLE XXIX.

Results of Treatment of All Cases Negative to Microscope.

No. of cases negative to microscope.	Cases yielding no hookworms.	Average No. of hookworms per treated case.	Cases yielding more than 10 worms.	Average No. of hookworms in cases which yielded more than 10 worms each.
104	16	31	18	152

It is evident from this table that one's judgment on the success or failure of the microscope depends upon one's point of view. If

one believes that the microscope has failed if it does not diagnose correctly every single case harboring hookworms, then the microscope is indeed a failure, for out of 104 negative cases it diagnosed correctly only 16. But if one expects from the microscope only relative accuracy, and if one believes that it has not done the slightest injustice to any one in diagnosing as negative those cases harboring less than 10 hookworms, then the routine microscopic examination has been a failure in only 18 cases out of more than 600 studied.

Recommended Use of Microscope.

Another point is of interest. Of the 18 cases harboring more than 10 hookworms which were diagnosed as negative by the microscope, not one was under 8 or over 50 years of age. The greater proportion of the 86 positive cases harboring less than 10 hookworms were small children or old people. As we have shown in a previous section, hookworm disease is a disease of the soil, and children under 8 and adults over 50 years of age are only incidentally, and usually lightly, infected. When in the course of a hookworm campaign the microscope reports a case under 8 or over 50 years of age as negative, the result may be accepted without question as relatively correct. When, however, the microscope reports a field worker between the ages of 8 and 50 years as negative, the result should be looked upon with extreme suspicion, and a second stool specimen should be obtained. If this rule had been followed in the 600 cases that we studied, there would probably not have been one failure by the microscope, for every single one of the 18 cases reported as negative but in fact harboring more than 10 hookworms were field workers between the ages of 8 and 50 years. As the average number of hookworms harbored by these 18 cases was 152 worms, the failure was probably due, in the majority of cases, to faulty collection or labeling of stool specimens.

We believe, therefore, that if we make this slight modification in microscope technique—namely, reexamination of all field workers between 8 and 50 years of age whom the microscope reports as negative—we shall find the microscope to be a very accurate and valuable aid in the campaign treatment of hookworm disease. We must, however, thoroughly understand the limitations of the microscope; we must realize that it cannot be expected to diagnose accurately

cases harboring 10 hookworms or fewer. The microscope may or may not give a positive diagnosis for a case harboring 10 hookworms or fewer, but even if it fails, it is doing a favor to the individual, for 3 or 4 or even 10 hookworms do not cause any one sufficient injury to warrant the inconvenience and discomfort of two full treatments for hookworm disease.

EFFICIENCY OF THE UNDIVIDED DOSE OF CHENOPODIUM IN FIELD TREATMENT.

In a previous monograph we showed that the undivided 2 cc. dose of chenopodium preceded by a purge the evening before treatment and followed in 2 hours on the morning of treatment by a saline purge gave excellent results in the elimination of hookworms (6). The advantage of the method is that as the purge is given only a short 2 hours after the drug, the patient absorbs less of the drug and hence suffers much less inconvenience. 2 cc. of chenopodium in an individual dose can be given with fewer resulting symptoms than 1.5 cc. given by the divided dose method. We also stated in the previous monograph that the 2 cc. undivided dose was far less effective when no preliminary purge was given.

The series studied as a basis for our conclusions was rather small, 56 cases, and the experiments were performed under ideal conditions. We were waiting for the opportunity to try out the experiment in the field when quite by accident a field experiment was delivered gratis into our hands. By mistake a field director had misunderstood orders from the head office and was giving the undivided dose of chenopodium. He prescribed the same dosage as other laboratories, but instead of giving the drug in two equal doses 2 hours apart, he gave it in one single dose and followed the treatment in 2 hours by a saline purge. We seized this opportunity and gave a third treatment to those cases which had been given two treatments by the nurse. A single group of 26 cases was studied first, with results so startling that we thought that possibly the technique of the nurse was at fault. We then carried through a second series, checking up the work of another nurse, and obtained similar results. The results of our experiments are compiled in Table XXX.

Group 1 of the table consists of those who received the undivided dose of chenopodium. The nurse gave 1 to 1.5 cc. of chenopodium in a single dose at 6 a.m., following the treatment in from $1\frac{3}{4}$ to 2 hours by a saline purge. No preliminary purge was given. No children were included in the series. Group 2 consists of patients at Fazenda Santa Maria who received the divided dose of chenopodium. The

nurse gave 1 to 1.5 cc. of chenopodium to adults, with graded dosage for children. No preliminary purge was given. The drug was divided into two equal doses, one given at 6 a.m. and the other at 8 a.m. At 10.30 to 11 a.m. a saline purge was given.

From the table we can conclude at once that the 1.5 cc. undivided dose of chenopodium without the use of a preliminary purge is a very unsatisfactory method of treatment for hookworm disease. We had already suspected this fact, for we had found in previous experiments that an undivided dose of 2 cc. of chenopodium without the employment of a preliminary purge gave slightly less efficient results

TABLE XXX.

Efficiency of the Divided and Undivided 1.5 Cc. Dose of Chenopodium without the Use of the Preliminary Purge.

	Group 1. Undivided dose of chenopodium.	Group 2. Divided dose of chenopodium.
No. of cases	51	56
No. of cases cured by treatment	3	23
Percentage of cures	5	41
Percentage of total worms removed by nurse's treatment (estimated)	72	96
Average No. of worms remaining per case	51	5.8
Percentage of failures; 10 or more worms remaining after treatment by the nurse	60	21.4

than the smaller divided dose of 1.5 cc. The summary of these latest results proves this fact conclusively.

We also learn from these experiments that the technique in hookworm treatment is all-important; when the same amount of the drug was given in two slightly different ways, one yielded good results and the other very poor results. Thus, a drug may be condemned as inefficient when in reality the fault lies wholly in the method of administration. It hardly seems possible that so slight a modification of technique as that described above could lower the effectiveness of the drug more than 25 per cent, but that it does is proved consistently by the results of the comparative experiments. We recommend, therefore, that field laboratories stick closely to the treatment technique that has been found most efficient; otherwise results will be poor, and the campaign work will rapidly fall into disrepute.

GENERAL DISCUSSION OF FINDINGS.

Distinction between Hookworm Infection and Hookworm Disease.

We believe that our studies have shown that we should make a distinction between incidental hookworm infection and hookworm disease. It is not necessary to split hairs as to the exact degree of infection required to produce disease. Every one will agree that a person harboring 100 hookworms or more has hookworm disease and we believe that we are perfectly justified in the contention that a person who harbors 10 hookworms or less has simple infection. Certainly, our hemoglobin results show that even in the case of a child of from 5 to 9 years, infection with 25 hookworms does not affect the hemoglobin index in the least.

Hookworm Disease an Occupational Disease.

We believe, also, that hookworm disease is an occupational disease and should be considered as such from the point of view of prophylaxis and treatment. An analogous occupational disease, encountered in work in industrial hygiene, is anthracosis. Anthracosis is a chronic disease of coal miners caused by the inhaling of large amounts of finely pulverized carbon particles. The pathological process which is produced in the human lungs by fine carbon particles is not limited to coal miners, however, for every individual who lives in an industrial community incidentally inhales considerable amounts of fine carbon particles. The infecting agent, smoke, is so widely disseminated that every city dweller is incidentally infected, but anthracosis, as a disease, is occupational and is limited to coal workers. The infection in both cases is due to the same agent, and the difference between incidental infection and disease is one of degree.

The analogy between anthracosis and hookworm disease is almost perfect. In rural Brazil hookworm larvæ, like smoke in an industrial community, are so widely disseminated that despite our special efforts we found only 18 persons out of about 600 cases studied who were entirely free from the infection. Hookworm disease, however, was limited to soil workers. Just as we successfully use general

prophylactic measures to limit the dissemination of carbon particles in a large city, so we should be able to prevent the greater part of the incidental infection with hookworms by the adoption of general measures for limiting the dissemination of material infected with hookworm larvæ. The analogy breaks down when we consider the disseminating agent, for city dwellers are not disseminators of coal dust, whereas cases incidentally infected with hookworms may disseminate hookworm larvæ. Nevertheless, we believe that the use of general preventive measures would be sufficient in this type of infection.

The knowledge that hookworm disease is an occupational disease and that we can make a distinction between incidental infection and disease is of great importance in a campaign. Without it much effort, money, and time might be wasted in treatments of casual infections, which would not greatly benefit the individuals and would, therefore, react unfavorably upon the benefactor, so that in the end all similar efforts would be discredited. A good example of such wasted effort in public health work is found in the "swat-the-fly" campaigns that have been carried on in some of our large cities, in which a tremendous amount of organized effort and a large amount of money have been wasted in fruitless endeavors to eliminate flies by wholly illogical methods. As no results have been achieved, both the work and the workers have been discredited. So, in any group of people in which 50 per cent of the individuals harbor less than 10 hookworms each, with an incidence-of-infection curve similar to that of the age-group 6 to 9 years (see Chart 4, page 15), we believe it to be extremely doubtful if an intensive anthelmintic campaign will accomplish much more in the end than to discredit the work and its directors.

We should attack the disease where it exists in all its destructive virulence, using the common methods which are familiar to health officers in combating any industrial disease whether it be litharge poisoning, industrial arsenical poisoning, methyl alcohol poisoning, or hookworm disease. These methods, in the order of their importance, are as follows:

1. General methods to prevent dissemination of infecting material. These prevent the acquiring of the disease by the worker and also prevent casual or accidental infections.

2. Special methods to protect the worker while at work; for example, masks in litharge poisoning and shoes in hookworm disease.

3. Treatment to eliminate the infecting agent in those workers who have the disease.

Special Preventive Measures Recommended.

Let us consider under the preceding general heads the special measures which should be most useful in preventing hookworm disease.

1. Prevention of dissemination of infecting material.

(*a*) Latrines. We recommend that the construction of latrines be insisted upon as a prerequisite to all campaign treatment.

(*b*) Popular education as to the mode of infection and the means of preventing the disease—personal hygiene, etc. The lantern slides and chalk talks have been both popular and profitable in the prophylactic campaigns against hookworm in Brazil.

2. Special methods for the protection of the worker while at work.

(*a*) Construction of latrines in the fields. This is an important and entirely neglected means of preventing hookworm disease. Curiously enough, Dr. Mario Pernambuco, director of hookworm campaigns in the State of São Paulo, working independently of us and having only practical experience to guide him, arrived coincidentally with us at the same conclusion—namely, that one of the best methods of hookworm prophylaxis is the construction of simple latrines in the fields. This method can be used most successfully when conditions approach those of São Paulo, where laborers spend long hours in the fields far from their houses.

(*b*) The use of shoes. This should be stressed as a splendid means of preventing hookworm disease. We found that the use of a crudely made pair of half-shoes reduced infection to less than 0.1 the usual rate of those who did not wear shoes. We realize that many workers would refuse to wear shoes even if provided with them by the employers, but we also know that litharge workers sometimes refuse to wear masks. This fact, however, is not an argument against the use of a mask, nor the use of shoes.

3. Treatment of infected individuals.

(*a*) Limit the work, so far as practicable, to field workers.

(*b*) Omit from the census all cases under 5 and over 55 years of age, because their infection is entirely unimportant.

(*c*) Carry on field campaign work along the same general plan as previously, using the present admirable methods of house to house canvas, census, examination by the microscope, etc.

(*d*) All field workers who are reported negative by the microscope should receive a second feces examination.

(*e*) All cases in the census which the microscope reports positive should receive two routine treatments of chenopodium 10 days apart. 1.5 cc. of chenopodium should be given to adults, with graded dosage for children—2 drops for each year of age down to 8 years, the dropper being graduated so that thirty drops equal 1 cc. Children between 5 and 8 years should receive only 1 drop for each year of age. The treatment should be given in two divided doses, one capsule at 6 a.m. and one at 8 a.m. A final saline purge should be given at 10 a.m. No preliminary purge is necessary. No food should be eaten from 8 p.m. of the day before treatment until the treatment is completed and the bowels have acted well. A small cup of black coffee may be permitted at 7 a.m.

This routine of treatment in field work gives the best results with fewest symptoms and should be rigorously adhered to in every detail. Slight modifications in the treatment interfere greatly with the efficiency of the drug.

It seems unnecessary to enter into a defense of these recommendations since they represent logical conclusions from experiments which are discussed at length under individual topics. As it is more than possible that future experiments will demonstrate that the conditions of hookworm infection in other countries are quite different from those we found in Brazil, owing to different working conditions, local customs, mode of life, etc., we must limit our recommendations to conditions as they exist in Brazil.

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