

HOOKWORM DISEASE AND PREGNANCY

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HOOKWORM disease, caused by *Ankylostoma duodenale* or by *Necator americanus*, is found, according to Dock and Bass,¹ in all parts of the tropics, in many subtropical countries, and also in some temperate regions. It has, in all probability, existed from time immemorial, though its exact identity has been established and the causative agent isolated only in the past half century. It is characterized chiefly by an anemia of varying intensity, dependent upon the severity of the infection, with a concomitant state of mental and physical languor, rendering the subject more or less incapable of performing properly his appointed tasks, and hence is directly responsible for a great deal of economic inefficiency and waste. It is essentially a soil pollution disease, and thus affects particularly those whose work brings them into intimate relations with the soil, such as farmers and farm laborers, miners, etc. In our country it is found chiefly in the southern states, and in some areas it is responsible for severe economic losses. Some patients are heavily infected and are incapacitated, the majority have mild or moderate infestations and are not acutely ill, but are tremendously handicapped, while those with very light infestations are of considerable importance as carriers.

The disease may be contracted by ingestion of the ova with the food, but it is well established that the chief route of infection is through the skin, generally that of the feet, the initial lesion being commonly referred to as "ground itch." Going barefoot in infested areas is hence the usual way in which the malady is acquired. The infested mud is particularly prone to lodge between the toes; the encysted larvae dig their way into the skin and deeper tissues, reach the blood stream, then are carried to the right heart and thence to the lungs. Here they are entrapped in the capillaries because of their size, penetrate the tissues, and get into the bronchial tubes. Next they reach the mouth and pharynx, being carried there by the constant outward current of the mucous membrane or by coughing, and are swallowed. An astute Mexican observer, P. H. Lira,² has described this cough as a symptom of hookworm disease, and has reported cases erroneously diagnosed as tuberculosis in this stage of the infection. Dock and Bass also mention this cough as one of the symptoms. Reaching the small intestine, the larvae undergo further metamorphosis, and anchor themselves by means of their hooks, to the mucous membrane, chiefly of the duodenum and upper jejunum. Loss of blood ensues from the bites of the

worms; some of this blood is ingested by the parasites, some can be found in the feces by appropriate tests. There is some evidence suggesting that the worms also feed on intestinal mucus and on the mucosa. Bacterial infection of the bites occurs, and plays an important part in the pathology of the disease. Some observers believe that a specific toxin is in some way elaborated and absorbed. Ova produced by the female worms are constantly being cast off, but do not hatch into larvae in the intestine of the host; this occurs in the warm, moist soil after the eggs are passed in the feces. The persistence of the disease is maintained in great part by reinfection; Chandler³ believes "that there is a rapid loss of the parasites and an equally rapid replacement by new ones." Both he and Bass believe, however, that some parasites may live in the intestine of the host for as long as six or seven years. One of my patients had been living in the city for five years, with little or no opportunity for reinfestation in the usual manner, but still harbored the worms.

The symptomatology naturally varies with the degree of the infestation. The severe cases present objective symptoms, the milder ones frequently do not, so that these patients do not realize that they are subnormal, hence many individuals of this type are overlooked unless one is on the alert. The mass surveys that have been made in this country and in others have revealed that in some localities 50 per cent or more of the inhabitants have been infected, with only a small proportion actually complaining of the subjective symptoms of the disease. Anemia is the chief characteristic, the hemoglobin being 30 per cent or less in the severe cases. The patients have a peculiar sallow, muddy complexion, differing from that of pernicious anemia or of ordinary secondary anemia. In the advanced stage we may encounter edema of the feet and legs, dyspnea, a hemic heart murmur, and at times albumin and casts in the urine, so that a mistaken diagnosis of cardiovascular disease may easily be made. The patients do not perspire so freely as do normal individuals. If the infection is acquired in childhood, as is common, growth is abnormally slow and the patient is "stunted," the hair development is scanty, the appearance of the secondary sexual characteristics is delayed, and in girls, as pointed out by Stiles,⁴ the establishment of menstruation is retarded and it tends to be scanty and irregular. No definite information as to a possible increase in the percentage of sterility is available. Stiles, in 1910, on a visit to New Orleans, called our attention to some characteristics of the hair. It is frequently of an indefinite sandy color, neither blond nor brunette, is deficient in oil, and hence of a peculiar dull, dry appearance. This, with the rather characteristic anemia, has often led me to make a tentative diagnosis on inspection alone. The blood shows the usual picture of secondary anemia, plus an eosinophilia of varying intensity. The

final diagnosis, of course, is made by the finding of the ova or the worms in the feces. Two or three examinations may be necessary, and at times special concentration methods are employed.

Naturally, many thousands of pregnant women have suffered from this complaint, yet comparatively little attention has been paid to this combination, either by obstetricians or by public health workers. It goes without saying that a condition which may so profoundly affect a woman's general health would exert its influence on her reproductive life. Lambert,⁵ writing of his experience with the disease in the Fiji Islands, states that in pregnancy "the dire effects of hookworm disease are dramatized most vividly," and is of the opinion that in this region there occurs each year, from this cause, a number of deaths of mother or child, or both. Dock and Bass state that "abortion is likely to occur, and it, as well as birth at term, may be fatal in anemic patients; lactation is imperfect in hookworm patients, but improves promptly under thymol treatment; the offspring of hookworm patients are likely to be poorly developed and marantic." And again, "When hookworm patients become pregnant, the tendency to dropsy is very much increased by the disease, and in severe cases the swelling is often great. The swelling of the labia is especially troublesome as the patient approaches term."

Cinselli,⁶ in 1878, reported the case of a woman dying of putrid infection after delivering a dead baby. Autopsy showed marked anemia and hookworm infestation. Cinselli thought that the uncinariasis so lowered her resistance that the puerperal infection could not be combated. Bruni,⁷ in 1891, reported a patient with marked anemia due to hookworm disease (diagnosed only the day before death), who died a few weeks after the delivery of a normal child. Tridondani,⁸ in 1900, reported ten cases of severe hookworm disease in pregnant women, only one of whom went to term. Six of the others spontaneously delivered prematurely, and in three instances premature labor was induced because of maternal indications; one of these three mothers died on the eighth day of the puerperium, and one on the twenty-sixth. Six of the babies were lost, one being stillborn, the others dying shortly after birth. He thought that the loss of the infants was due partly to the anemia, the hydremia, and the anoxemia, but chiefly to a toxic action of the parasites, possibly to a specific toxin elaborated by them. Pinetti,⁹ in 1899, reported a case terminating in premature delivery at seven and one-half months; he felt that this outcome was due to a specific toxin, to which the patient had not had time to adjust herself, as she had been infected for only two months. He quoted Mangiagalli,¹⁰ who reported a patient in much worse general condition who did not deliver prematurely, probably because she had had time to adapt herself to the gradually developing toxemia. Raineri's¹¹ patient had a severe double infection with hookworm and bothriocephalus; she delivered a living, premature baby at the seventh month. Bolli,¹² in 1905, reported the case of a woman with severe infestation and delivery at term of a child weighing 2800 gm. He found that the blood of this child was subnormal in many respects as compared to the blood of a normal newborn infant. Saechi,¹³ in 1909, found 38 patients with ankylostomiasis in the course of a routine study of the feces in a series of 200 pregnant women; 37 of these 38 occurred in the 152 peasant women of the series, an incidence of 24.34 per cent, showing that the disease was at that time common among the

country people of Italy; the rice growers were particularly liable to the infection. His cases were mild or moderately severe, and did not show the heavy incidence of premature interruption of pregnancy noted by Tridondani. There was spontaneous or induced abortion in three instances, six patients delivered prematurely, and in one patient it was found necessary to induce premature labor because of renal damage. Eight of these 10 patients suffered from nephritis in varying degrees (fatal in one instance), two had severe chronic bronchitis, and the majority of these 10 had developed various other debilitating conditions before or during their pregnancies. Hence he felt that the hookworm infestation was only a contributing factor, but one of considerable importance in some instances. Sinnemtamby,¹⁴ of Ceylon, in 1905, related some experiences with a series of 32 pregnant women who were seriously ill because of this complication. There were six maternal deaths, due, he felt, to cardiac failure subsequent to dilatation of the heart caused by the anemia. He stated that premature labor was the rule, but gave no details. Wilson,¹⁵ of South Carolina, in 1918, reported three cases, two with associated toxemia; there was one fetal death on the twelfth day postpartum. Isfrán, of Paraguay, in 1926, in the course of the mass treatment of 100,000 persons, encountered 205 pregnant women who volunteered the diagnosis of pregnancy complicating their hookworm infection. He felt sure that many other such patients were also treated, in whom the pregnancies were undiagnosed. Soper¹⁷ treated 63 women who were from two to eight months pregnant.

The incidence of renal lesions in severely infected pregnant patients is high, as noted by these various observers, and is generally thought to be due to a specific toxin elaborated by the parasites. The occurrence of eclampsia in hookworm patients has been reported by Rowan,¹⁸ of Mississippi, Turberville,¹⁹ of Florida, and Opocher,²⁰ of Italy. Rowan stated that southern Mississippi, at the time of his report (1911), was a highly infested area, and that the native white women were peculiarly subject to the toxemias of pregnancy. In 19 cases of eclampsia he could eliminate only 2 as being possibly free from hookworm disease. A number of his patients who were treated for this complication had no trouble in subsequent pregnancies. Kitrell, in discussing this paper, stated that he knew of several instances in which the combination of hookworm disease and pregnancy resulted in the death of the mother from convulsions. Turberville felt that hookworm infestation, by preparing the ground for the operation of the causative factor, had an indirect rôle in the abnormal frequency of eclampsia in his section of Florida. He encountered 7 cases in 300 pregnant women, while 2 neighboring physicians reported incidences of 6 to 200 and 15 to 350, respectively; the average ratio being estimated as about one to 500. The author felt that he had in several instances prevented the development of eclampsia by the eradication of the hookworm infection; one patient developed eclampsia before the treatment could be completed, and in another instance the combination resulted in the death of the patient. In Opocher's patient eclampsia supervened in the seventh month of the first pregnancy; labor was induced, thymol was administered, and a macerated fetus was delivered.

For several years, in a rather casual manner, I have watched for patients presenting clinical manifestations of hookworm disease in my obstetric service at the New Orleans Charity Hospital, and up to January 1 of this year I had thus detected 22 cases, each diagnosis confirmed by stool examination. Since that date, I have had a routine examination of the feces made on each patient admitted, and have thus discovered 12 infected women out of a total of 180 admitted. On one occasion there were four such patients in the ward simultaneously. All of these

Bass tells me that this statement was based mainly on theoretic considerations. Carbon tetrachloride, in 3 c.c. doses, together with 30 to 40 gm. of magnesium sulphate, was given to some patients. Soper and Isfrán used this drug in doses of 2.4 c.c. The usual treatment at present employed in hookworm eradication campaigns is a mixture of carbon tetrachloride and oil of chenopodium, the best proportions, according to E. C. Faust, Professor of Parasitology, Tulane University,²¹ being 1.8 and 0.7 c.c., respectively. Lambert states that oil of chenopodium is claimed by some to be contraindicated in pregnancy, but in Isfrán's opinion this idea is erroneous. If carbon tetrachloride is used, it is highly important that it be absolutely pure. Lambert treated 42,000 persons with this drug without untoward developments, but in the next 8,000 he had three deaths, due to impurities in the preparation used. At present, in the Charity Hospital, thymol is preferred, because of the occasional occurrence of toxic manifestations following the use of carbon tetrachloride. The treatment, whatever drug be used, should be repeated several times, as one treatment usually fails to remove all the parasites. It is well to check the thoroughness of the treatments by repeated stool examinations. Reinfestation is very common, hence the patient should be cautioned as to its possibility, and should be instructed as to the methods to be pursued in avoiding its occurrence.

Practically all observers agree that treatment during pregnancy does not cause abortion or premature labor. Lambert stated that he had treated hundreds of pregnant women with carbon tetrachloride with no abortions as a result. Isfrán, as well as Soper, had similar experiences. The former noted five abortions occurring from eight to twenty-nine days after treatment in the 63 cases followed up by him, but did not think that the drug was responsible for any of these interruptions. In Soper's series of 63 cases, two abortions occurred on the tenth and twelfth days, respectively, but the author did not think that these occurrences were due to the treatment. My experience has confirmed these observations, and the majority of my patients were treated so soon as the diagnosis was made, with no deleterious effect on the pregnancies. The three spontaneous interruptions of pregnancy, noted above, occurred in untreated patients, delivering shortly after admission, before the diagnosis was made. It would appear that treatment should tend to prevent these spontaneous premature deliveries that are liable to occur in the severer cases.

It is evident, then, as recently stated by Gamble,²² that hookworm infestation is still a public health problem in the southern states, though the surveys and mass treatments so diligently pursued have reduced the percentage of infected persons markedly. Its occurrence in conjunction with pregnancy is not at all uncommon, as is shown by the fact that, in a city hospital, I easily detected these 34 cases. There

can be little doubt that this disease predisposes to the development of toxic states in severely infected pregnant women, and that it is a potent factor in increasing the percentage of premature interruptions of pregnancy in such patients. Treatment along accepted lines is well borne, does not cause interruption of pregnancy, and is of distinct benefit to both mother and child.

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MAISON BLANCHE BUILDING.

Hookworm Disease Complicating Pregnancy, by DR. EDWARD L. KING,
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DISCUSSION

DR. M. PIERCE RUCKER, RICHMOND, VA.—When you consider how widespread hookworm infection has been in the South, it is evident that any one who has practiced obstetrics in the South must have had many cases associated with pregnancy, but to have recognized it is another matter. The first Rockefeller survey in Virginia showed that in many counties as much as 66 per cent of the population had this disease. A little later, the second survey showed that the incidence of hookworm disease was reduced 2 per cent to 8 per cent. Inquiry of the Health Department and also of doctors practicing in rural Virginia has failed to show any very evident difference in the obstetric results obtained in these counties.

In 1921, at the Spring Street Home, an institution for unmarried mothers, we had a patient with edema and anemia. We found hookworm eggs in the stools, and this led us to make a survey of the population of the institution. We found 25 per cent infected with hookworm. I thought this possibly might have been a factor in their delinquency. We found these girls coming from rural Virginia. Later we had a city crowd and the hookworm infection disappeared. None of these cases was severe. The lowest hemoglobin was 65 per cent, and there were no obstetric complications. All of them went to term and had live babies. Looking up their histories later, I found that all these patients in the puerperium complained of headache and most of them had red lochia for several weeks. That seemed to be the only clinical difference between this group and the other cases.

In regard to treatment, I am glad to hear Dr. King say that it is safe to treat them during pregnancy. I did not treat any of them until after they were confined for fear of producing abortion. I do not think that the mild infection plays any rôle in obstetrics.

DR. B. P. WATSON, NEW YORK, N. Y.—I had my first experience with hookworm disease just two weeks ago in New York City. The patient had been delivered in the Sloane Hospital two years ago by cesarean section. At that time she had been very anemic with only two million red cells and 40 per cent hemoglobin. When she returned to the clinic in her second pregnancy she was still anemic. We are making a special study of the anemias of pregnancy, and in the course of the routine stool examination the hookworm eggs were discovered. The patient came from the West Indies but has lived in New York during the last six years. The patient is now seven months' pregnant and requires another cesarean. We have been afraid to carry out any treatment for the hookworm disease for fear of dire results. I am glad to have the assurance that treatment can be carried out safely during pregnancy.

DR. E. L. KING (closing).—At first we hesitated to treat these patients. We had one or two instances where the patient aborted or delivered prematurely and lost the baby, but this was not due to treatment. Since we have adopted the procedure of treating them as soon as they are admitted, sometimes several times before delivery, our results have been better. Our system is to treat them every eight or ten days. It takes about that long for the thymol to disappear, and thus we avoid the possibility of thymol poisoning. Since doing that we have had no trouble from abortion or miscarriage. Lambert said he had treated several hundred cases without abortion. Isfram had followed 60 cases, with several abortions, but he felt that the treatment was not responsible. The same experience is reported by Soper.

We had taken it for granted that hookworm disease had been eradicated, and then in New Orleans picked up about 30 cases in a ward that was not a medical ward. The patients came in solely for the pregnancy. It does appear that there is an increased frequency of toxemias in these very ill women.