HOOKWORM DISEASE

A

B

Intestinal lesions in uncinariasis. *A*, the intestine from a case of uncinariasis (uncinaria duodenalis), showing patches of congestion with elevated centers, to one of which a parasite is attached, and in the center of another of which a tiny hole exists—formerly the seat of attachment of another parasite. *B*, the intestine showing ulcerations in uncinariasis. This is a composite drawing representing the lesions repeatedly observed in uncinariasis of man and dog. For the use of this valuable plate we are indebted to the author, Dr. Allen J. Smith, of Philadelphia.

HOOKWORM DISEASE

ETIOLOGY, PATHOLOGY, DIAGNOSIS, PROGNOSIS, PROPHYLAXIS, AND TREATMENT

BY

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ILLUSTRATED WITH FORTY-NINE SPECIAL ENGRAVINGS AND COLORED PLATE

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TO

CHARLES WARDELL STILES, Ph. D., D. Sc.,

Chief of the Division of Zoology in the Hygienic Laboratory, United States Public Health and Marine Service,

Whose brilliant conceptions and untiring labors have enlarged our knowledge of hookworm disease, and thereby opened up one of the most important fields of preventive medicine,

this volume is dedicated by

THE AUTHORS.

PREFACE.

Few diseases surpass the subject of this work in the strangeness of its history, the importance of its ravages, or the theoretic ease of its extinction.

It probably existed from remote antiquity among tropical peoples, and, although attempts have been made to trace it back to a very early period, these efforts fail for lack of the careful clinical methods of diagnosis that are necessary for the recognition of such diseases. For almost fifty years after the disease was made known in Italy, and after it had been the subject of many important investigations in diagnosis, biology, and treatment, it remained for us in America chiefly an interesting, but remote, fact, devoid of practical relations. Its absence was accepted as evidence of the greater personal cleanliness and superior mode of life of our citizens, and at most it was feared that among recent immigrants cases might be imported and even spread in less favorable localities. No more striking example of the transitory state of medical knowledge can be advanced than the proof brought within the last few years, not only that hookworms exist as human parasites in a large part of the country, but that they may with reason be looked upon as among the most important causes of diseases of the South in extent, in destruction of life, and in leading to physical and mental degeneration. The fact that the parasites in the United States belong to a new species is a most important one and very suggestive in its bearing on medical zoology.

In many parts of Europe hookworm disease is one of the most important economic problems. Immense labor and expense have been devoted to the measures for its repression in Belgium and Germany especially, where it seriously affects the mining industry.

The study of hookworm disease in America has shown the heavy load that endemic disease lays upon a country. Largely due to it, a region that should be most fertile lies relatively uncultivated; a population derived from the best colonizing blood ekes out a miserable existence, and is doomed to extinction unless it is soon relieved of its infection. Thanks to the painstaking labors of zoologists and physicians, much has been learned of the disease and its parasite. Physicians and hygienists have realized that the evil, preventable as it is, must stop, and medical men, administrative officers, and private philanthropists are now working actively to that end.

In the widespread effort at extermination many forces must co-operate. Physicians will be called upon to treat the disease in its various forms, as well as to assist in its prevention. For them primarily this book has been written, for the authors have for a long time been interested in the medical features of the disease. Hygienists, employers of labor, and others interested in sanitation may also find information of practical value. How well we have succeeded we leave to our readers. We take pleasure in thanking many well-known authorities for the use of material and illustrations, especially Dr. C. W. Stiles, Allen J. Smith, Claude A. Smith, and H. F. Harris. Many others whose works we have drawn upon freely, and who have accomplished important work on the subject, are mentioned in the following pages.

We have avoided bibliographic references, except in rare instances, believing that those who wish to consult original sources will have to use the "Index Medicus" in any event. We have also repeated certain statements in order to make easier the use of the book for reference by those who wish to gather practical lessons from it.

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CHAPTER I.

DEFINITION.

Hookworm disease is due to certain species of hookworm (ankylostoma duodenale, sometimes called uncinaria duodenalis, and necator Americanus) which live as parasites in the small intestine. It occurs especially in warm countries and in certain regions in temperate latitudes where the climate in the summer, or other features—such as warm mines—offer favorable conditions; chiefly in persons who come in contact with damp earth, or with water containing larvæ of the parasites. It is characterized by the discharge of the ova of the worms with the feces; by a progressive anemia, weakness, impaired development in young subjects, and by various symptoms on the part of the circulatory, digestive, and nervous systems, in varying degrees and combinations; occasionally fatal, it is capable of cure by removal of the parasites and of prevention by hygienic measures.

The term "hookworm carrier" is applied to persons in whom hookworms live as parasites, but who, either from small number of worms, from race immunity, or other causes, do not develop obvious symptoms.

The importance of this class in the dissemination of the disease is very great, and will be considered in the following pages.

Synonyms.

Ankylostomiasis; anchylostomiasis; ankylostomasie (French).

Anchilostomanemia (Italian).

Ankylostomo-anæmia (Latin).

Ankylostomen-Krankheit (German).

Anquilostomiasis (Spanish).

Uncinariasis.

Dochmiosis.

Egyptian or tropical chlorosis.

Tunnelworker's anemia; tunnel disease; tunnel anemia.

St. Gothard tunnel disease.

Brickmaker's anemia.

Mountain cachexia; mountain anemia.

Miner's anemia; miner's cachexia; anémie d'Anzin.

Anémie des pays chauds; anemia of Ceylon; Porto Rican anemia.

Anemia intertropicalis.

Hypoæmia intertropicalis.

Malarial anemia.

Cachexia Africana; cachexia Americana; cachexie aqueuse.

Mal d'estomac (Père Labat, 1742).

Mal de cœur.

Geophagia (in part).

Allotriophagia (in part).

Dirt eating (in part).

Negro consumption.

Rihagan (in Egypt the "yellows," Sandwith).

Opilaçao (Portuguese).

Amerellao (i. e., "icterus").

Cançaçao (i. e., "tired feeling").

Pica (in part).

Malnutrition (in part).
Tun-tun.

The synonyms of hookworm disease indicate the wide range of symptoms, as well as the extensive geographic distribution, as shown by the diversity of languages.

Historical.

The efforts to interpret certain statements in the Ebers papyrus (1550 B. C.) as proof of the knowledge of hookworm disease on the part of the ancient Egyptians are purely fanciful. We may admit that the disease occurred in Egypt then as it does now, and we may also accept the ingenious suggestion of Sambon that its suspected causation was related to the veneration of the dung beetle, the sacred scarab, by the Egyptians. But even if the symptom picture was clearly recognized then, and even if the existence of the parasites was known, no information came down to assist later generations in the recognition, prevention, and treatment of the disease.

The history of hookworm disease is identical, as we now know, with that of cases described in various tropical countries during three centuries—viz., Piso in Brazil (1648), Father Labat in Guadeloupe (1748), Bryon Edwards in Jamaica (1799), under various names as given in the list of synonyms, and characterized by severe abdominal symptoms, anemia, dropsy, and weakness, often causing death, chiefly among negro slaves, but also affecting other classes of the population. At the time the true nature of the conditions described was not understood and often wholly misinterpreted, and the misinterpretation continued to a recent period. This is particularly true as regards the supposed relation of malaria to the anemia, and hardly less so to the relation of dirt eating, warm climates, and poverty.

The discovery of the first hookworms in 1782 and 1789 had no influence on clinical study.

Certain diseases of miners in temperate latitudes, described by older writers, can also be explained now by hookworm infection. Anemia was a striking symptom, and the "miner's anemia" sometimes occurred in epidemics. In 1786 such an epidemic broke out in Schemnitz in Hungary, and more than 1,200 miners were affected. There were similar epidemics between 1802 and 1820 in the French mines of Anzin, Fresnes, Vieux-Condé, Avize, Escarpelle, and Graissesac. In 1875 the Medical Society of the Loire Basin investigated the epidemic anemia. Sporadic cases were observed and reported in Hungary and Bohemia. Hammerschmid noted that the disease differed from ordinary anemia or chlorosis, that it represented a disease *sui generis*, and that the explanation by the mine climate or vitiated air was not satisfactory.

In 1838 Dubini, in Milan, found what he thought were previously undescribed worms in the intestine of a woman dead of pneumonia. Four years later he found some more worms of the same kind in the body of a woman dead of hydrothorax, and on a third occasion in the body of a man dead of jaundice. In these three cases he saw only female worms, but in another case he discovered males, and later found similar worms in many subjects, either free in the duodenum and jejunum, or hanging on to the mucosa by their mouths. On the whole, he found them in at least 20 percent of bodies examined, and sometimes in company with other worms. He thought the worms not without effect on the body, though not causing special accidents; that their seat was especially in the duodenum or upper half of the jejunum; that an unusual amount of mucus was essential for their existence; that the mucosa in the parts affected was either normal, or injected, or punctate, red or black, and that the parasites occurred especially in cachectic, emaciated persons, ultimately dying from diarrhea and dropsy. The late discovery of the worms he attributed to the failure of earlier observers to examine the intestinal mucosa without washing the adherent mucus away with water. He described the parasites accurately as small, bent, partly transparent in the fore part, partly yellowish, reddish, or brown worms, with a dark elevated point in the middle, and the stomach filled with black material. He gave a clear description and pictures of the microscopic features, especially the rounded mouth with four curved hooklets rising from conical elevations, the flask-shaped esophagus, the blunt tail of the female, the fan-like tail of the male inclosing the genitalia. He proposed the name agchylostoma—from ἀγκύλος, bent, and στομα, mouth. The other details do not seem necessary to cite now.[1]

Though Dubini thought he had discovered a new worm, he had been anticipated to a certain extent. In 1782 Goeze discovered some worms in the intestine of a badger (Meles taxus). Although he gave it the name ascaris criniformis (on account of its hair-shape), he suspected it belonged to a different genus from the ordinary ascaris. He saw the membranous expansion of the tail of the male, and in it two rib-like structures, which he called hooks.

In 1789 Frölich found similar worms in the intestines of foxes. He also observed the membranous expansion and hooks, and proposed the name hookworm (Haakenwurm) or uncinaria for the genus. The fact that other members of the family strongylidæ possess similar "hooks" in the bursa does not interfere with the retention of the name.

Dubini, besides describing the caudal hooks, noted the hook-like teeth and the bent shape of the body. As Stiles

[1] Dubini was ill advised in the construction of the new word. In translating from the Greek he should have changed the γ to n and the κ to c for Italian usage. In other languages the κ would be c, ch, or k.

well points out, the feature that led to the common name was the result of a misinterpretation; the "hooks" in the mouth are not present in all species, and the curvature of the body is not always distinct, but nevertheless the common name is likely to be retained by reason of the rules now followed in zoologic nomenclature.

Von Siebold (1845) gave the parasites a place in zoology among the strongylidæ. Castiglioni and Pruner soon after described the occurrence of the worms in the bodies of dropsical and cachectic individuals, but, like Dubini, did not realize the actual relations. Bilharz (1853) and Griesinger (1854) in Egypt recognized the relation of the parasites to the extremely prevalent "Egyptian chlorosis," the cause of more than one-quarter of all deaths in that country. But although Griesinger especially was emphatic in his statements, practically no attention was paid to them for more than ten years. In 1866 Wucherer, in Bahia, again called attention to the subject, based upon its frequency among negro slaves in Brazil. His statements were confirmed by other Brazilian physicians, and gradually reports began to appear from various other tropical regions. In Italy many additions to the knowledge of the occurrence of hookworms were made, the most important being the suggestion by Paletti and Maliverria (1877—1878) that the anemia of brick workers, long known in Italy, was caused by hookworm, and the discovery by Grassi (1877) and Parona of the diagnostic value of the ova in the feces of hookworm subjects.

The migratory habits of Italian laborers led to a striking epidemic of hookworm disease. In the digging of the St. Gothard tunnel (1879—1880) a large number of workmen showed signs of intense anemia. Perroncito and Concato, Bozzolo, Colomiatti, Parona, Sonderegger, and others showed that not only did the parasites occur in the anemic cases, sometimes in enormous numbers, but that they were often the only discoverable causes of disease. These results were confirmed in other places, notably in Switzerland, by Immermann and others, and in Freiburg by Bäumler in tunnel workmen.

These discoveries led to the proof that the so-called "miners' anemia," ascribed to deprivation of light and air, in the mines of France and Hungary was also due to hookworms, and in the mines of Sardinia measures to check the development and spread of hookworm eggs were followed by diminution in the number of cases of anemia.

The conclusions regarding miners' anemia were rapidly extended to other countries. In 1869 Leuckhart thought ankylostomiasis did not occur north of the Alps. In 1882 it was discovered in brick workers in the Rhine country, who had no relation to Italian workmen. In fact, the anemia of the brick workers in the Rhineland and Prussia had been recognized, but not correctly explained, for more than twenty years before. The prevalence of hookworm disease in the region of Cologne gave Leichtenstern opportunities for making some of the most important contributions to the subject, including the discovery of the disease among the Belgian miners ("Walloons"), who worked in the coal mines of Mons, Liége, etc., in winter and in the Rhenish brick fields in summer.

It does not seem necessary to describe the discovery of hookworms in various parts of the tropics. The present conditions there will be mentioned in the next chapter. Suffice it to say that the evidence points to the tropics, and especially Africa, as the original home of the disease. It is not easy to trace the routes the parasites followed to Europe, but it is highly probable they entered from Egypt by way of Italy or Hungary, and spread from there to Switzerland, the Rhine, and Belgium, from Hungary to Germany, and from various parts of the tropics to Cornwall.

The history of hookworm disease in the United States is of great interest. From an early period reports were published on the dirt eating and anemia of negroes in several southern states, and Hirsch (1883) and other European writers based upon these reports the statements that hookworm disease existed, "although only in slight extent, among the negro population of some parts of the southern United States." That Hirsch does not deserve particular credit for the accuracy of his statement appears from the fact that he thought there was little hookworm disease in Asia.

It is worth while recalling some of the early American accounts, for from these it is obvious that the disease existed, but the accurate diagnosis was not to be expected at the time, as the presence of hookworms—in many cases even intestinal worms in general—was not suspected, and the significance of the disease was wholly missed.

Stiles quotes Joseph Pitt (1808) as the earliest author he has found to refer to the disease in this country. Pitt described dirt eating among the poor white people and negroes, and thought it was due to deficiency of nourishment. The author most frequently quoted abroad is Chabert (Réflexions médicales sur la maladie Spasmodico-lyperienne des Pays Chauds, vulgairement appelée Fievre Jaune. J. L. Chabert, Dr. en méd. de la Fac. de Montpellier, a. m. ord. des arm. Franc., etc., Nouvelle-Orleans, de l'imp. de l'Ami des lois. 1821). He referred to dirt eating as a habit contracted by many slaves, and described the resulting lesions and the means of recognizing and curing them. His words are worth quoting more fully (p. 188 *et seq.*): "For most of the negroes, doing nothing is the supreme bliss. Some of them carry love of idleness to such a point that they employ, in order to escape work, every means suggested by sloth, notwithstanding the certainty of injury to health. Among these, earth, the internal use of which causes a species of poisoning, is most common of all, if I may judge by my own practice. Under the influence of this bizarre food there develops in those who use it symptoms and accidents like those produced by poison in the living organism—i. e., yellow complexion, dry scaly skin, puffy face, swelling of the legs, engorgement of the abdominal viscera, atrophy of the muscles, palpitation, dyspnea, and at last obvious signs of aneurism (i. e., dilatation) of the heart from thinning of its walls, which, when well marked, always ends the case.''

Chabert made an autopsy in the case of a dirt eater, but described no worms, and thought a perforation he found in the stomach was due to an old ulcer. It can hardly be doubted that he was dealing with genuine cases of hookworm disease, but wholly unaware of the fact.

Geddings, in 1834, doubtless saw cases in the anemic and cachectic ''sand lappers'' of Carolina. Little, in 1845, gave an interesting account of dirt eaters in Florida, in which the descriptions of the subjects leave no doubt they had hookworm disease. Sir Charles Lyell (1849) also made observations during his travels in the South, and noted cases of dirt eating in Alabama.

James B. Duncan (Report on Topography, Climate, and Disease of the Parish of St. Mary, La., Southern Medical Reports, edited by E. D. Fenner, New Orleans and New York, vol. 1, p. 190, 1849) gave a very accurate description of cases. He speaks of a very common anemia among negroes on plantations, ''very often attributed, and perhaps justly so, to the pernicious habit of dirt eating.'' The proportion of severe cases was not large. Duncan says (p. 194): ''Almost every large plantation has three or four, and sometimes more. Until the vital powers of the system are beginning to be undermined, no marked symptoms of the disease being visible to the eye of the planter, they are generally suspected of laziness or malingering. After this condition has existed for some time, the skin presents a paler hue than natural, or, if the subject is a mulatto, an ashy white; the lips, tongue, lining membrane of the mouth, and palms of the hands white, lacking the reddish tinge of health; the legs edematous; abdomen distended; pulse full, soft, and frequent; action of the heart violent; if blood is drawn, it is pale and watery; respiration on the slightest exertion anxious and hurried; in fine, all the symptoms that characterize chlorosis in females. We find this condition of things in subjects of both sexes. Many of these cases are, doubtless, produced and aggravated by the deleterious habit of dirt eating. But I never heard a negro admit that he was addicted to the habit. Some admit that formerly, years ago, they ate dirt, but do not now; and others, trusty, truth-telling negroes on all other subjects, on this will lie most pertinaciously to the last, unless detected in the act." Duncan thought that in many cases "dirt eating was a symptom only of a diseased condition of the digestive organs and of the system generally. With them dirt eating is the same propensity to which white females resort to relieve a disordered acid condition of the stomach by eating quantities of chalk, magnesia, etc. This condition of system is often, in my opinion, produced by a deficiency of suitable nutriment. The diet of negroes on most plantations being mostly salt pork, corn bread, and molasses—rarely eating fresh meat and vegetables—a condition of the system is thus produced closely allied to scurvy." (He noted spongy gums, and functional and organic disease of the heart.) Duncan reported cures by the use of nutritious foods, fresh meats, vegetables, and greens, porter and wine, iron, stomachics, and tonics, laxatives when indicated, and out-door exercise. He throws a curious light on the seriousness of the condition so briefly described by speaking of the use of tin masks, iron gags, and chaining to the floor to correct dirt eating. "By using these means," he says, "it is true the habit can not be indulged in, but the cause that produced the propensity still exists. Restore the healthy tone of the system, invigorate the subject, put rich blood into his veins, clothe him well, feed him well, and do not overtask him; arouse his feelings of pride, teach him to feel that he is a reasonable being, and in a majority of cases success will attend our efforts, and we shall have the satisfaction of rescuing a valuable servant from the grave."

It is impossible to tell how much of this belief was founded on actual treatment. It may be that mild cases then improved without direct causal treatment, but it is difficult to imagine that reinfection did not occur.

Heusinger wrote an interesting work on dirt eating ("Die sogenannte Geophagie oder Tropische—besser, Malaria—chlorose als Krankheit aller Länder und Klimate, dargestellt von C. F. Heusinger, Cassel, 1852), but showed great lack of critical insight. He asserted dirt eating was common also in the region of the great lakes, based largely on statements of Bartlett, Wood, and Drake. He properly considered dirt eating a symptom and not a cause of disease.

None of these writers give the impression they were dealing with a widespread disorder. This is probably due to the fact that then, as now, many negroes were immune to the severe effects of the infection, that the white population was scattered and was relatively small, and many of the whites probably escaped infection. None of the medical writers we have consulted speak as if the disease was communicable, but we have found a suggestive statement in the account of an excellent lay writer, Mr. Thomas Affleck, of Washington, Miss., author of the "Southern Rural Almanac," who had been an extensive planter, and wrote an interesting chapter for Fenner's "Southern Medical Reports" (vol. 2, p. 429—436, 1851) "On the Hygiene of Cotton Plantations and the Management of Negro Slaves." He confirms what others say of the diet: "The general allowance of meat being three and a half to four pounds per week of sound mess pork, or its equivalent in bacon, to each working hand over 10 years old, with bread, hominy, vegetables, etc., *ad libitum.* Fish and molasses are given occasionally. Not nearly enough of vegetables are grown and fed to negroes." He also said (p. 433): "Dirt eating is frequent among young negroes, and always kills them if not cured. The constant use of molasses is said to induce it, but I can not say how correctly. Those under the best care are liable to it. Seems to be occasioned by a morbid state of the stomach, and should be so treated. *One dirt eater upon a plantation will infect the whole. Mostly infected at from two to ten years.* Say, one child in forty eats dirt." [Italics ours.—D. and B.]

On the whole, the reports from the South in the first half of the nineteenth century could not easily convince one that ankylostomiasis existed there, and in the latter half, for a long time, no accurate observations seem to have been made. Moreover, during this part malaria acquired a new interest and importance, so that its occurrence was easily exaggerated.

In 1886 Dr. Joseph Leidy made an interesting remark apropos of some specimens from anemic cats sent by Belfield, of Chicago. He noted the worms had the same structure of mouth as had ankylostomum duodenale; thought they might be able to infect man, and be one of the previously unrecognized causes of pernicious anemia. This idea had been expressed before, and was then repeated more or less distinctly by various writers for the next ten years. In 1891 Dolley called the attention of American physicians, especially those of the southern states, to the "fact," as per Hirsch, that ankylostomiasis was long since reported in the South.

In 1893 Blickhahn, of St. Louis, reported a case in the person of a brickmaker from Oberhausen, near Essen, in Westphalia. In 1897 Möhlau reported several cases in Buffalo, and it seemed that some of the patients became infected in this country from Italian or Polish immigrants. Through the courtesy of Dr. Joseph Collins, Dock was able to cite a case observed in New York by Dr. Joseph Fränkel in the person of a foreigner who had long lived in the United States, and seemed to have acquired the disease here, "perhaps handling hides." (Article on Anchylostomiasis, Loomis and Thompson's System of Practical Medicine, vol. 3, p. 337 *et seq.*, 1898.)

To this transition period belong the reports of Herff (1894), who found worms in a Mexican and asserted their existence in this country; Dabney (1898) and Tebault (1899), who both found them in New Orleans; Gray (1901), who found them in Richmond, Va.; Claytor (1901) in Washington, D. C.; and Boston, Allyn, and Behrend (1901) in Italians in Philadelphia; Dyer in St. Louis; and Hall and Yates in Baltimore.

The era of productive discovery began at the same time. Allen J. Smith, in 1895, found ova of hookworm in the feces in a water closet in Galveston, Texas, but could not fix upon the individual from whom they were derived. On February 17, 1901, Dr. Smith recognized ova in the stools of a sailor born in Melbourne, Australia, who first became ill while acting as overseer of a plantation in southern Mexico, where there was an epidemic disease of a very fatal type, which led to pallor, emaciation, and dropsy. The patient also had amebic dysentery. Dr. Smith recognized differences in the worms expelled from the patient as compared with ankylostoma duodenale, and thought they might be uncinaria stenocephala of dogs. The dogs in the laboratory, however, had only uncinaria canina, so that comparisons could not be made. Later, Charles Wardell Stiles showed the existence of a new species in man, and Dr. Smith was able to demonstrate that his patient had both old world and new world hookworms. Stiles had for years pointed out the probability of the frequent occurrence of hookworm in America. In 1901 he published his views (*Texas Medical News*, July), stating that hookworm in man must be more or less widespread in the United States. Soon after that, Smith's case was published by Dr. Charlotte Schaeffer, who also mentioned the finding of ova in the feces of two (later increased to eight) out of eighty-odd medical students in the Galveston school. Stiles (1903) shows clearly the great value of Smith's work in the development of our knowledge of hookworm in the United States. "To the clinician it did not mean very much, since no record existed that the students exhibited any very severe symptoms. To the zoologist, however, it meant a practical demonstration that uncinariasis was more or less common in the South. Here were eight students in a city (Galveston); the chances that the infection took place in Galveston did not seem very great; as the students came from different places, the infection must be more or less widespread; and, since light cases occurred among medical students, heavier infections must naturally occur among persons who come more regularly in contact with the dirt."

From a study of the worms in the case of A. J. Smith and Claytor, and some from Porto Rico, Stiles was able to show that they were not uncinaria stenocephala or any other known species, and on May 10, 1902, he described a new species, uncinaria Americana. In a paper published in the

Eighteenth Annual Report of the Bureau of Animal Industry (September 25, 1902) he declared there was an endemic of hookworm in the United States which had been generally overlooked. In the months between the statements both Claude A. Smith and H. F. Harris had reported cases in Georgia, and a little later Harris made the important assertion that the greater number of cases of anemia in certain southern states were due, not to malaria, as universally believed, but to uncinariasis, and that it was "the most common of all the more serious diseases of the entire South. In no other disease does the victim suffer so long, in no other condition is he for such a period a menace to those about him, and in no other malady of such gravity is treatment so rapidly and surely successful." W. F. Arnold complains, with justice, that the subject was neglected after the striking announcements just described. Some of the subsequent communications will be referred to in the next chapter.

The work of Bailey K. Ashford and his colleagues on hookworm disease in Porto Rico furnishes one of the most interesting and instructive chapters in the history of endemic disease.

In 1899, soon after a destructive hurricane in the island, Ashford established a hospital for the care of those who could not be accommodated in the hospital at Ponce. "Fully three-fourths of those admitted were suffering from anemia, which was then believed to be due to faulty diet, but, as iron, arsenic, and full diet failed to cure, it was attributed to malaria, climate, lack of hygiene, etc., all of which proved upon investigation to be inadequate." In studying the blood as an aid to exact diagnosis, Ashford was struck by the high eosinophilia. He suspected ankylostoma, and "examination of feces made the suspicion a certainty." R. Blanchard had concluded that the disease was present in Porto Rico, but no exact observations had been published and no immediate general attention followed Ashford's first report, though it had official recognition.

In 1902 Drs. Ashford and King made a further study of ankylostomiasis, and reported on one hundred cases in 1903. (*American Medicine*, September 5 and 12.) This aroused much interest, not only in medical circles, but also in the administration of the island. In 1904 a commission was formed for the study and treatment of anemia, consisting of Dr. Ashford, Captain and Assistant Surgeon, U. S. A.; Dr. W. W. King, Past Assistant Surgeon, Public Health and Marine Hospital Service; and Dr. Pedro Gutierrez, health officer of Bayamon. With comparatively slender resources this commission carried out an immense campaign of diagnosis, treatment, and scientific research. It proved beyond question that the anemia so prevalent in the island was only a symptom of uncinariasis, which affected the rural population to the extent of 90 percent. Still more, it published most valuable reports upon the work, and upon hookworm disease in general. (Report of the Commission for the Study and Treatment of "Anemia" in Porto Rico. San Juan, P. R., 1904 *et seq.*)

Even before the time the parasites were receiving so much attention in America, Looss (1898), in Cairo, Egypt, made the important discovery of the penetration of the skin by the larvæ, a discovery that has made the pathology and especially the prevention of the disease much more exact than it was before. This part of the history will be discussed in connection with the "Modes of Infection."

CHAPTER II.

DISTRIBUTION AND ECONOMIC IMPORTANCE.

Hookworms have an extensive range, being found in all parts of the tropics, where they may be said with truth to be the greatest enemies of the human race, and in many countries with subtropical climate, as well as in some regions properly classed as temperate. The extreme range of latitude is from 51° N., or the latitude of Belgium, to nearly 40° S. Altogether it is one of the commonest disorders, and in the tropics one of the most important. It is in all probability the chief cause of the so-called tropical anemia, which has been looked upon as due to climatic conditions rather than disease factors in the usual sense.

In Europe the disease has been found chiefly in Belgium, France, England, Germany, Hungary, the Balkan peninsula, and Italy. In Italy, Sicily, and Sardinia, where ankylostoma was first discovered as a human parasite, it occurs in various parts and sometimes in great intensity. Previtera found 75 percent of miners infected in Catania, in a district (Muglia) where almost 100 percent had oxyuris. In Spain it occurs in miners, and probably other classes also.

In Austria, Hungary, the plains of the Danube and Theiss, Servia, and Bulgaria it occurs, especially in the mining regions, but also elsewhere and in other classes of the population. In some parts of Hungary up to 95 percent of miners have been found infected, but, owing to precautions taken and treatment, this has been reduced to about 30 percent. Many are so severely affected that they are unable to work on account of swelling of the feet and shortness of breath. The great heat in many Hungarian mines, up to 104°—113° F., favors the development of the larvæ.

In Belgium the disease has been very prevalent in the last quarter of a century. The parasites were first discovered in Belgium by Firket in 1884, but, as said before, the disease probably existed among miners long before that. It was reintroduced by miners from St. Gothard and became epidemic about 1884, but subsided apparently, only to break out afresh in a most virulent form, with a high death rate. Little attention was paid at first, but, after it became serious in the mining districts of Liége, Mons, and Charleroi, active measures for its repression were begun by the government. At the International Congress of Miners in 1903 it was said that 10,000 miners in the Liége basin were infected. So great was the extent that sick benefit societies had to refuse membership to men working in some mines, the proportion of affected workmen being from 25 to 75 percent, with in some places a very high death rate.

In France the miners in many localities are also seriously infected, especially in Anzin, Valenciennes, Lyons, and St. Etienne (2 percent), and the Loire basin (5 percent).

In the Dolcoath mines in Cornwall, England, where a severe form of anemia had been noted in the miners for about eight years previously, Boycott and Haldane, in October, 1902, showed its occurrence, and traced it to miners who had lived in the tropics.

Stockman (1903) reported the case of an infected miner in Scotland who had been in India.

In Germany it is especially in the Rhineland and Westphalia that the parasites abound, but many cases occur in the vicinity of Berlin and a few cases have been found in Saxony, introduced by Polish miners, and in Silesia. On the Rhine, Cologne, Bonn, and Aix-la-Chapelle, and in Westphalia, Essen, Dortmund, and Bochum are important foci.

The possibilities for harm of the disease, outside of the tropics, are well illustrated by the conditions in the Westphalian mines. Infection there was brought about by Italian, Hungarian, and Polish miners, and was favored by certain factors. One was the rapid increase of the mining industry, which led to the importation of 20,000 new miners in a single year. (In the year 1902 there were 289 mines, with 256,000 miners.) But the most important cause was the introduction of spraying the mines with water for the purpose of preventing explosions of coal dust. On February 17, 1898, there was a tremendous explosion. On July 12, 1898, regulations for spraying were passed, and put into execution from July 1, 1899, to January 1, 1900. The effect of this can be seen in the following table after Oliver, a slight decline being followed by a notable increase:

Year.	Number of infected mines.	Number of cases.	Per 10,000.
1896	15	107	6.4
1897	31	113	6.2
1898	23	99	4.9
1899	26	94	4.4
1900	40	275	11.7
1901	63	1,030	40.6
1902	66	1,355	52.9

In 1901, out of 63 infected mines, 57 of them were watered, and showed 1,021 cases. The other 6 infected mines were not watered, and gave only 9 cases. At one time in Westphalia there have been 25,000 cases of hookworm disease.

In Africa, Egypt (90 percent in Cairo, 20—30 percent in other places), and the Mediterranean countries, the east and west coasts to the Cape, Uganda, Mombosa, Mozambique, Zanzibar, Madagascar, Mauritius, and the Comoro Islands are all infected, but, as Zinn and Jacoby first pointed out, the African negro races are not so likely to show severe symptoms as many other races. In Cameroon, Külz found

70 percent of the population affected, and, although in adults the symptoms, especially anemia, were less marked than in children, many even of the former had severe palpitation of the heart. The less civilized the tribe the greater was the extent of the infection. In Kimberly, Mathias discovered the disease in miners in 1896. In the Transvaal, Posnett found 32 percent of native miners affected.

In Madeira, Goldschmidt discovered two foci, apparently due to returned emigrants from Brazil. The infection, severe at first, became milder.

In Asia there are many severely infected areas, including most of India, where it was first found in 1879 by McConnell (Calcutta), China, Cochin China, Burmah, Siam, Ceylon, the Malay Archipelago, Java, Borneo, Formosa, and Japan. In Japan the parasites were first found by Baelz in 1877. The infection is very prevalent among country people, but as a rule not severe. Cases have been found in Siberia, derived from the Japanese. In the tea gardeners of Assam, Dobson found ova in the stools of 454 out of 574 immigrants from all parts of India.

Manila and the Philippines, Guam, Australia, New Guinea, Fiji, and the Sandwich Islands are also severely affected. In Manila, Strong found 52 percent infected among 4,016 Philippine prisoners. Among the returned soldiers are many cases, most of whom, fortunately, in returning to the United States live in places not favorable for the development of the larvæ.

In South America the disease is still very extensive, especially in Brazil, where Wucherer and Lutz made such important observations. It occurs also in other parts of the continent, as far as Argentine, and in the islands along the coast. Daniels found parasites in 52 percent of autopsies in Demerara. Law (1908) found 45 percent of the population infected in British Guinea.

In Mexico, Manuel discovered the worms in 1902 in the southern states of the republic. Alvarez found none in the north (Sonora), but some in lower California and Sinaloa.

In Central America the disease is common in all parts, especially in the coast countries and the foot hills. According to Prowe, legends tell of its existence—symptomatic, of course—in Guatemala and San Salvador for centuries.

In all parts of the Antilles the disease is present. In Cuba it was first shown to exist by Agramonte (1902). Guiteras finds it less prevalent in Cuba than the Porto Rico Commission found it in the latter island.

In Panama, in the pathological laboratory of the Ancon Hospital, Whipple found, in autopsies, old world hookworm in 17 percent, the new world variety in 21 percent of bodies. In about half the cases of the latter the old worm was present, but necator Americanus predominated in all heavy infections. Brem, in Panama, found hookworms in 36.1 percent of 277 patients from various parts of the tropics.

United States.

No systematic investigation has been made of the territory known to be infected. Dr. C. W. Stiles has made several reconnoissances, including a large part of the South. These have stimulated many valuable observations by physicians in various parts of the country. The extent and the intensity of the infection in the whole population can be surmised from the data present, but a systematic and extensive search is very much needed.

It is clear that the country from Virginia, at the Potomac river, to Florida and Texas is infected. In Virginia, Claytor's early case furnished Stiles with the first specimen of uncinaria Americana. Bagly (1910) believes there are 80 percent of infected work people in the cotton mills.

In North Carolina the disease is even more frequent, as shown by the valuable work of Nicholson and Rankin (1904). They found that 37 percent of 140 students of Wake Forest University were infected, usually in a mild form. Sometimes every man from a given district was infected.

In South Carolina the conditions are doubtless equally serious, as shown by Stiles' investigation, but extensive observations are lacking.

In Georgia the assertion of Harris that the disease is one of the commonest of the serious diseases was found justified by C. A. Smith (Atlanta), Warfield (Savannah), A. G. Fort, and many others.

In Florida extensive observations do not yet exist, but the disease is frequent, as Stiles pointed out in his early survey. Kinyoun (1908) found very many hookworm carriers, especially among negroes. At present active efforts are being made for repression of the disease.

In Alabama, Bondurant, of Mobile (1903), first called attention to the extent of the disease. Harrison, of Talledega (1904), made an important addition to our knowledge. Perry (1910) reports 15 to 20 percent in the white population infected, and Cole and Winthrop (*vide infra*) show even more.

In Mississippi, Bass found from his own observations and those of correspondents that up to 50 percent of the population were affected, and concluded that practically all the rural population of the southern half of the state have or have had the infection.

In Louisiana, Lemann and Guthrie called attention to the importance of the disease in 1903, and many cases have been observed since then, but no extensive series of cases has been reported. The conditions in country localities are doubtless about the same as in adjacent states. Gage and

Bass have examined 90 students in the Tulane University who were living in the state; 42.4 percent of those from the country, and 2.5 percent from the city were found infected, or a total in the whole state of 20.7 percent of young male adults were hookworm carriers.

In Arkansas, Deaderick found comparatively few cases, and the same will probably hold good in Tennessee.

Texas is widely affected, as Allen J. Smith showed early. Investigations are now being made by the State Board of Health, and fully confirm the wide range and intensity of the infection.

Valuable information appears in a report by Dr. Stiles to the Bureau of Labor. (Annual Report of the Surgeon General of the Public Health and Marine Hospital Service of the United States for the fiscal year 1908, Washington, 1909.)

The investigation shows that 12.67 percent of cotton mill employees are hookworm suspects. The percentage varies with sex and age.

	Percent suspects.
Over 20 years	8.4
16 to 20 years	19.2
Under 16 years	27.2
Females	16.1
Males	15.2
Boys under 16 years	29.4
Girls under 16 years	18.7
Boys 16 to 20 years	20.7
Girls 16 to 20 years	18.1
Males over 20 years	5.8
Females over 20 years	13.

Interesting observations have been made on recruits in the United States Army. Siler (1909), in an examination of 105 recruits from the southern states, found 93 infected, or 88.5 percent, and 85 percent in a total of 140 cases.

Chamberlain (1909) found 60 percent of infected men among southern recruits.

The observations of Gage and Bass on 296 university students are interesting in comparison with those on recruits, for they deal with young men of about the same age, presumably equally free from obvious symptoms, probably belonging to families in better circumstances than those of the recruits, and not so much exposed to the danger of infected soil. The figures are small, but no selection was made. The number of worms recovered from the subjects varied from 3 or 4 to 200, so that the men were worm carriers of real danger under conditions favorable to the dissemination and development of the ova.

Locality.	Positive.	Negative.
Alabama	14	19
Arkansas	4	9
Florida	1	4
Georgia	7	7
Illinois	..	2
Kentucky	0	1
Louisiana, outside New Orleans	27	51
Louisiana, in New Orleans	1	39
Massachusetts	..	1
Mississippi	14	38
Missouri	0	3
Oklahoma	1	3
Pennsylvania	0	1
South Carolina	0	3
Tennessee	2	6
Texas	7	7
Canada	..	1
Porto Rico	1	0
Roumania	..	1

Out of the subjects from the southern states outside of New Orleans we get a percentage of infected students of 32.8.

Winthrop and Cole, in examining 66 Alabama medical students, found 33, or 50 percent, infected.

Further facts bearing on the economic aspects of hookworm should be noted. Among the females of child-bearing age, 13 to 18 percent are unable properly to nourish infants. Of males of military age, 5.8 to 20.7 percent are relatively inefficient. Among children of school age, 18.7 (females) to 29.4 (males) are unable properly to profit from study. "Taking all the statistics together, 12.6 percent of the mill population are affected with a disease which materially inhibits their normal working powers, and hence inhibits the economic development of the community in which they live."

It should also be noted that in some of the mills the proportion of hookworm cases is as high as 80 percent among the children.

Stiles has also pointed out the part the negro has in the perpetuation and spread of hookworm disease. Relatively immune to the disease, the negro is an extensive worm carrier, and is even more careless as regards soil pollution than his white neighbor.

In general, the parasite found in old world cases is ankylostoma duodenale; that in America, necator Americanus; but Leiper found the latter widely distributed in the tropics, especially in Africa. It has been found in returned immigrants in Italy, from Brazil as well as from the United States (Schifone), and also in other localities, but apparently has not yet spread beyond the immigrants. Necator Americanus has also been found in patients from various parts of Asia, Ceylon, the Philippines, and Australia, in the Hamburg Sailor Hospital (Rodenwaldt), and by Noc in Cochin China. Looss found it in pygmies in Africa, and Fülleborn in Cameroon. Da Silva Pinto finds necator more frequently in the state of Sao Paulo in Brazil than ankylostoma. Branch thinks necator may be the original and more common tropical hookworm. The conditions of work and travel at the present time are such as to cause even greater mingling of the two species than occurs now.

Climate.

The chief factors in the existence of hookworm infection, given the presence of the parasite, as by fresh importation, are high temperature and moisture. The extent of the disease in the tropics makes this clear, and the intensity of the disease in the tropics even clearer. Outside the tropics, mines offer the best conditions for the disease to exist. Not all mines are equally affected, even when miners carrying worms are employed. In the mines of Pas-de-Calais, for example, Bréhon found only two infected miners, and they had come from a mine near Mons, in Belgium. The mines at Pas-de-Calais have neither high temperature nor great moisture. So also in Bohemia no cases were found until 1903, and since then only a few. But the mines are not very deep and the temperature, accordingly, not very high. Wainwright and Nichols (1904) made a large series of observations in the anthracite coal mines of Pennsylvania, but found hookworm in only one case.

Tenholt gives an instructive table showing the relation of temperature in mines to infection in Westphalia.

Temperature.	Number of workmen.	Percentage of infected.
Below 17°C.=62.6°F.	36,033	0.6
17°—20°C.=62.6°—68°F.	68,604	0.4
20°—22°C.=68°—71.6°F.	43,710	2.5
22°—25°C.=71.6°—77°F.	39,836	11.7
Above 25°C.=77°F.	9,853	39.9

(The most favorable temperature for the development of the larvæ is from 25° to 35° C., or 78.5 to 95° F. Below 22° C. or 71° F. few ova develop.)

The hot season in countries with temperate climates may assist in the development of hookworm larvæ in permanent or temporary water or in damp earth, but, owing to the length of time the larvæ require in order to reach the infecting age, such regions are rarely intense seats of the disease.

The relation of moisture to hookworm infection has been noticed by all who have studied the disease. In the tropics, in brickyards, and in tunnels and mines (coal, tin, sulphur, gold, diamond, etc.) a certain degree of wetness of the soil has been found to obtain wherever the hookworm disease occurs. This agrees with facts regarding the life history of the parasites, which will be discussed in another place. Turner explains the absence of ankylostomiasis in certain South African mines by the acidity, from sulphuric acid, of the water. Deep, warm, wet, and alkaline mines are especially affected.

Stiles has shown that in the southern states sandy soil is more favorable than clay for the production of the disease. This is probably due to the fact that in wet sand the larvæ can easily avoid drying and at the same time obtain oxygen. On dry soil the larvæ soon die, and among dwellers of such places, as the Arabs of the Sahara desert and the Soudanese, the disease is rarely seen. Deaderick has pointed out that alluvium offers favorable conditions for the larvæ, and that all the ground conditions are not yet known. The Porto Rico Commission has also shown that not only alluvium, but also clay soils, offer numerous foci, but Leichtenstern could find no larvæ in the clay of brickyards. It is important to distinguish between pools of water that may long remain on clay and earth free from water. The life history of the larvæ (see Chapter III) will throw much light on the subject.

Shade is an important element, and will have to be considered in connection with the life history of the larvæ and the modes of infection. Elevation is of no importance if the other conditions are favorable; mountains, as the St. Gothard tunnel, over 3,000 feet above sea level, as well as coast lands, are involved.

Occupation and social position of hookworm subjects.—Hookworms affect especially those who have intimate relations to the soil. In the tropics it is especially the poorer classes, the agriculturists and their families, that are affected. According to the Porto Rico Commission, for example, 85 percent of the nearly one million inhabitants are poor and 75 percent are agriculturists. "The poorer the man, the more exposed is he to heavy infection. Coffee pickers and laborers on coffee estates are the most exposed of all laborers on the island. Infection on sugar plantations is not so common, but is nevertheless frequent, especially in the irrigating ditches." Washing at the edges of streams and banana culture are other occupations leading to infection. One of us has observed many instances in charcoal burners and turpentine "dippers." The people come from infected regions, and their occupations offer favorable conditions for the spread of the disease.

Gardening is a possible means of infection in the well-to-do, as also in professional gardeners.

In many regions outside the tropics, hookworm disease is rather a trade disease than an endemic. Mining and brick-making have frequently been alluded to. The details of the mode of infection are discussed in Chapter IV, but it may be said here that in many places the wives and families of miners and brickmakers, and sometimes gardeners, do not share the disease.

Barefooted children.—In certain occupations infection takes place through the hand, the bare feet, or through defective boots. An important cause in the southern United States is the habit among children, even of the better classes, in the country of going barefoot. Not only country children, but city children, in the summer vacations have ground itch, and later hookworm disease, as we have ascertained in dozens of instances. Even adults occasionally get infected by wading in pools, yielding to what Claude A. Smith aptly calls "the joy of going barefoot." In heavily infected regions persons of all kinds of classes and occupations, and of all ages, occasionally get the disease. In some of these the method of infection is obscure. Dirty vegetables or fruit, or skin infection by larvæ-containing water, are the most probable.

CHAPTER III.

ZOOLOGIC FEATURES.

Hookworms belong to the class of nematodes, the family strongylidæ and subfamily strongylinæ.

The nematodes form a very large class of worms, usually long and narrow, from 1 millimeter to 40 to 100 centimeters in length, round on section, and sometimes hair-like in their proportions. The sexes are usually distinct; the males usually smaller than the females, and generally distinguished also by the shape of the tail end, which is sometimes rolled in a circular, spiral, or cork-screw manner; sometimes, as in hookworms, spread out like an umbrella, or funnel-shape. The length of the body is sometimes marked, as in ascaris, by four longitudinal bands. There are in some species circular striations, and in others the bodies are smooth, or furnished with papillæ or other appendages. The mouth end varies in shape in different genera, is generally narrower than the body beyond it, and possesses six papillæ. It passes into a muscular esophagus, that also varies in shape and proportion in different genera, and this in turn is followed by the chyle-gut and the rectum, which opens near the tail end of the worm. The nerves of nematodes are made up of scanty groups of ganglion cells and fibers, especially well developed around the esophagus. The parasitic species have no special sense organs. Some free-living ones have two reddish eyes, furnished in some species with lenses. The excretory organs consist of a system of tubes, ending in an excretory pore. The genital organs are tubular. That of the male opens in common with the rectum, and that of the female is separate from and usually anterior to the anus. All male nematodes have preanal and postanal papillæ, which are used in specific differentiation. The eggs are so-called "simple ova," containing only one kind of cell, and, though varying considerably, are usually characteristic for each species. Some species are oviparous, and others viviparous. The development of nematodes is simpler than that of tape-worms or flukes. In many cases, as ascaris, trichocephalus, and oxyuris, there is no intermediate host; in others, as dracunculus and filaria, there is. In some, as strongyloides, there is reproduction outside the definitive host. In the case of hookworms, as we shall see, part of the development of the larvæ takes place outside the host. Very few nematodes (strongyloides) reproduce outside the definitive host.

Round worms live partly in fresh or salt water, in earth or mud, in decomposing matter of all kinds, partly parasitic in various organs of animals, and very often in plants. Familiar examples are the common intestinal round worm, ascaris lumbricoides, the "vinegar eel" (anguillula aceti), and the trichina spiralis (trichinella); one of the most interesting is the "hair-worm" (gordius), popularly supposed to develop from horse-hair put in water for that purpose, and in rare cases found as a parasite in man.

The nematodes are subdivided into eight families:

1. Enoplidæ. Live free; many species in sea water.

2. Anguillulidæ. Characterized especially by a double swelling of the esophagus ("rhabditic"); live free, especially in fresh water or in earth, or in decomposing material ("vinegar eels"); many are parasites of plants, and a few of animals. Many are very minute.

3. Angiostomidæ. Developing by heterogeny, containing the genus strongyloides.

4. Gnathostomidæ. A small family, often parasitic in wild animals, but very rarely in men.

5. Filaridæ. Very long, narrow worms, represented by several species of important parasites, including filariæ.

6. Trichotrachilidæ. Containing several important parasites, especially trichina (trichinella) and trichocephalus, or the whipworm, a common parasite of man in warm countries.

7. Strongylidæ. A very large group subdivided into several subfamilies. Besides hookworms, eustrongylus, strongylus, and sclerostoma belong to this family.

8. Ascaridæ. Containing the common parasitic round worms and pinworms, and some others.

The strongylidæ form a very large family. They are characterized by long, cylindrical bodies, rarely filiform; the possession of six oral papillæ—two lateral and four submedian—generally projecting in the form of nodules or conical points; a mouth capsule with or without teeth, either in the body axis or turned dorsally or ventrally. The esophagus is more or less swollen in the posterior part. The males have a "bursa copulatrix" and one or two spicules; the females have one or two ovaries. The eggs are usually deposited in segmentation, sometimes containing the embryo. The sexes are distinct. Important members are the "colic worms" of horses and the kidney worms of hogs (but not the kidney worms of dogs and man—Stiles), the "gape worms" of chickens, and the hookworms. Many others are frequent parasites of various lower animals, and occasionally of man. The members of the family have undergone many changes of nomenclature, not necessary to describe fully in this place. There is also much difference of opinion regarding the nomenclature and classification of the hookworms. The following list shows some of the most important synonyms in chronological order:

1789: uncinaria—Frölich.

1843: agchylostoma duodenale—Dubini.

1845: ancylostoma duodenale—Creplin.
1850: anchylostoma duodenale—Dubini.
1851: ancylostomum duodenale—Diesing.
1851: strongylus quadridentatus—von Siebold.
1851: sclerostoma duodenale—Cobbold.
1861: dochmius anchylostomum—Molin.
1861: monodontus—Molin.
1866: strongylus duodenalis—Schneider.
1876: dochmius duodenalis—Leuckart.
1879: anchilostoma duodenale—Bozzolo.

Ankylostoma Duodenale.

The generic name above, or ankylostomum duodenale, or ancylostomum duodenale (French, anchylostome; German, ankylostomum or anchylostomum; Italian, anchilostoma) is preferred in England and the continent for the old world hookworm. No matter how spelled, Dubini's name seems justified by the accuracy of his description. The spelling "agchylostoma," passable in Italian, would have to be latinized for international nomenclature, "ancylostoma" being the correct spelling.

The name uncinaria was widely adopted in America by reason of the important work of Stiles, though Looss from the beginning objected to the change on account of the fact that the genus uncinaria of Frölich agrees with the type criniformis (Göze) more than with ankylostoma duodenale (Dubini). More recently (1907), Stiles states that "the old genus uncinaria (type vulpis = criniformis) must be divided into at least four smaller groups: uncinaria (type vulpis), agchylostoma (type duodenale), necator (type Americanus), bunostomum (type trigonocephalum), and probably into several additional units. . . . Evidence is accumulating to the effect that they should be given generic rank." The recent (1909) classification of Railliet and Henry shows the same tendency. Besides the two human species of ankylostoma and necator, there are several species of the genus uncinaria which are found in lower animals—e. g.:

Uncinaria canina, Uncinaria stenocephala, Uncinaria trigonocephala, } in dogs.

Uncinaria (ankylostoma) tubæformis, or Uncinaria perniciosa, Uncinaria Balsamoi, } in cats.

Uncinaria trogocephala, in sheep.

Uncinaria radiata, in cattle.

Uncinaria Lucasi, in seals (thought by Looss to be the cause of the great mortality—17 percent—of suckling seals on the Pribiloff Islands).

Uncinaria os papillatum, in elephants.

There is no proof that any of these infect man, and among lower animals each genus infested seems to have its own species of hookworms. The worm supposed by Rathonyi to be a hookworm in mine horses in Hungary has been shown to be a sclerostoma.

In order to make clear the anatomic features of human hookworm, it seems best to describe at length the one longest known, and to mention more briefly the points of difference in the new world parasite. In this we follow the more exhaustive descriptions, especially of Looss, Stiles, and Allen J. Smith.

The old world hookworms are small and almost cylindrical, the male about 10 millimeters long and 0.45 millimeters wide, the female 12 to 18 millimeters long and 0.60 millimeters wide. (Frontispiece.) In both sexes the anterior end tapers gradually. In the female the posterior end tapers to a fine point or spine. (Fig. 1.) The posterior end

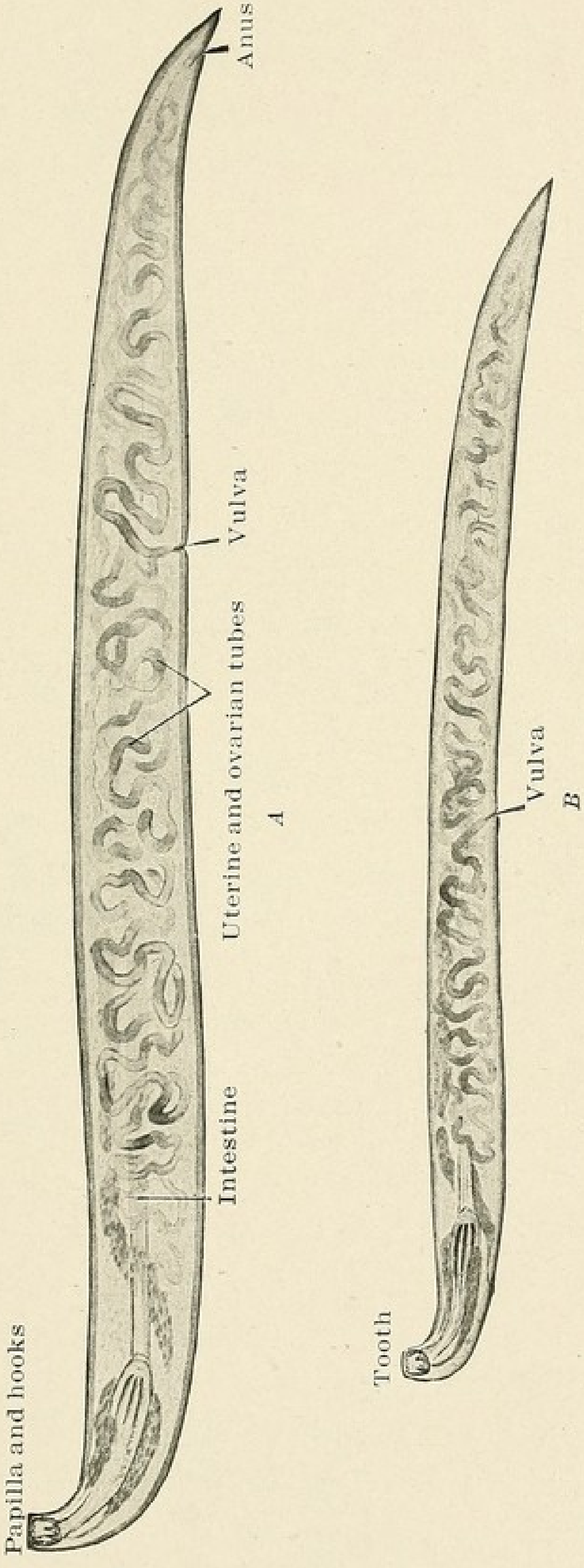

Fig. 1. Females. *A*, uncinaria duodenalis. *B*, uncinaria Americana. Showing comparative size and position of sexual opening. (After Allen J. Smith.)

of the male tapers in about the last quarter of its length, but the tip of the tail is concealed by the bursa, which flares out to a width equal to that of the thickest part of the body, or even more, giving the tail end a square or sometimes concave appearance at the end. The color when alive is somewhat flesh-red or cream color; when dead, duller, gray or grayish white. The posterior two-thirds are often brown or reddish brown, from blood in the intestine. The skin is smooth, delicate, with fine transverse striations. With the bending of the worm transverse folds are formed, especially about the head. The name hookworm is often supposed to be due to the bending of the head backwards, and this is so striking a feature that the supposition is natural, though the name was given on account of other "hooks," as has been mentioned before. Eight (Smith)—Looss, four—muscular bands, most plainly defined on the sides, symmetrically arranged, run the length of the body, merging together laterally to form a fairly continuous body wall, and in the male help to form the bursal ribs.

Besides the proper skin muscles, Looss describes certain special muscles, such as the anal muscles, in female worms only; the vulvar muscles; the cephalo-esophageal muscles, which pass from the top of the nervous ring to the surface of the esophagus, and, extending obliquely forward through the body cavity, are inserted partly in the skin and partly in the mouth capsule. They probably assist in the movements of the head, as well as in those of the buccal capsule. The end of the chyle-gut is surrounded by a network of muscles, especially well developed in males. In both sexes there is a sphincter muscle of the rectum. Finally, there is a complicated system of muscles in connection with the tail end of the male.

The body cavity is divided by a membranous septum attached dorso-ventrally, in the folds of which, as in a mesen-

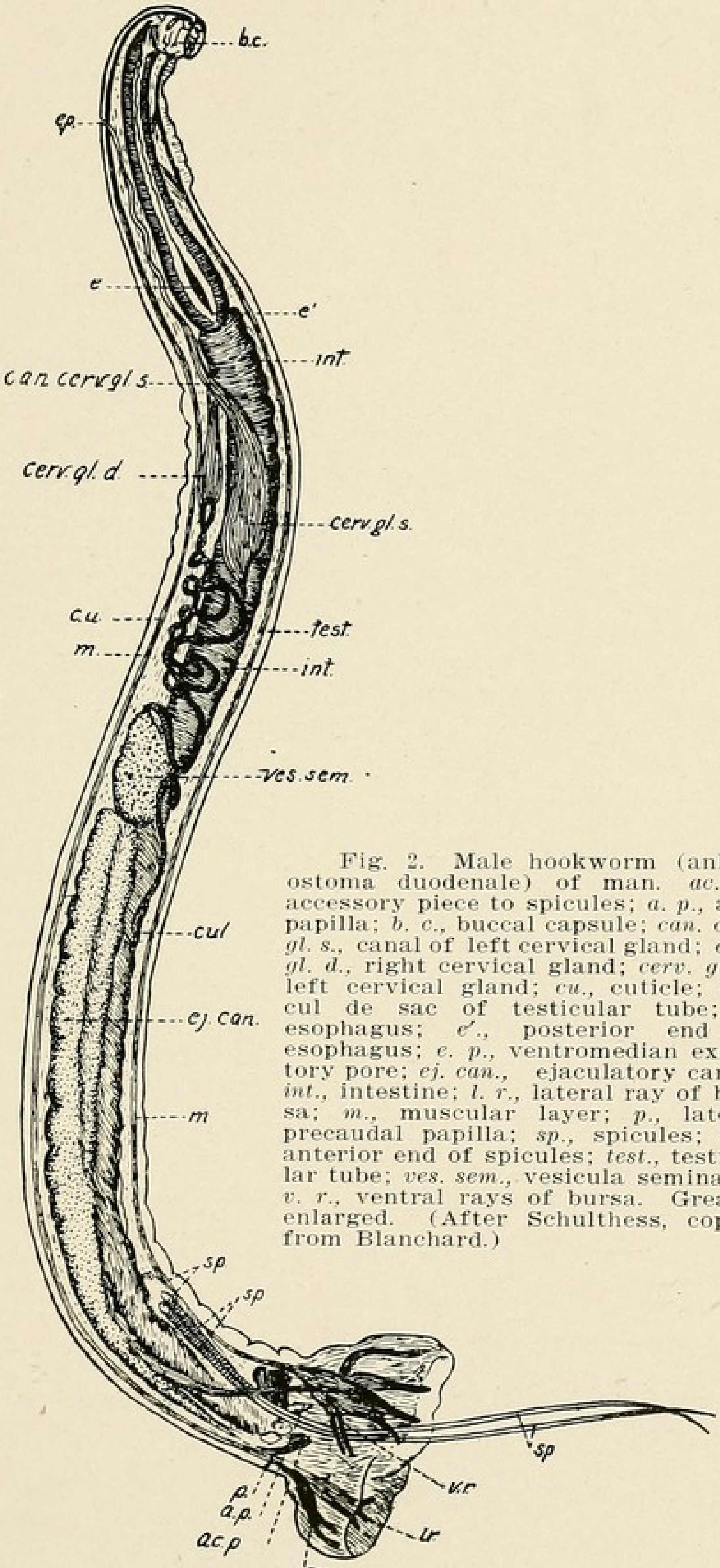

Fig. 2. Male hookworm (ankylostoma duodenale) of man. *ac. p.*, accessory piece to spicules; *a. p.*, anal papilla; *b. c.*, buccal capsule; *can. cerv. gl. s.*, canal of left cervical gland; *cerv. gl. d.*, right cervical gland; *cerv. gl. s.*, left cervical gland; *cu.*, cuticle; *cul.*, cul de sac of testicular tube; *e.*, esophagus; *e'.*, posterior end of esophagus; *e. p.*, ventromedian excretory pore; *ej. can.*, ejaculatory canal; *int.*, intestine; *l. r.*, lateral ray of bursa; *m.*, muscular layer; *p.*, lateral precaudal papilla; *sp.*, spicules; *sp'.*, anterior end of spicules; *test.*, testicular tube; *ves. sem.*, vesicula seminalis; *v. r.*, ventral rays of bursa. Greatly enlarged. (After Schulthess, copied from Blanchard.)

tery, the alimentary canal is supported. In the two divisions of the cavity are the cervical and esophageal glands, the sexual tubes and glands, and the anal glands. (Fig. 2.)

The alimentary apparatus consists of the mouth and its appendages, the esophagus, and the straight intestinal canal, which extends to the posterior end in each sex, terminating independently in the female, but in the male forming a cloaca with the sexual apparatus.

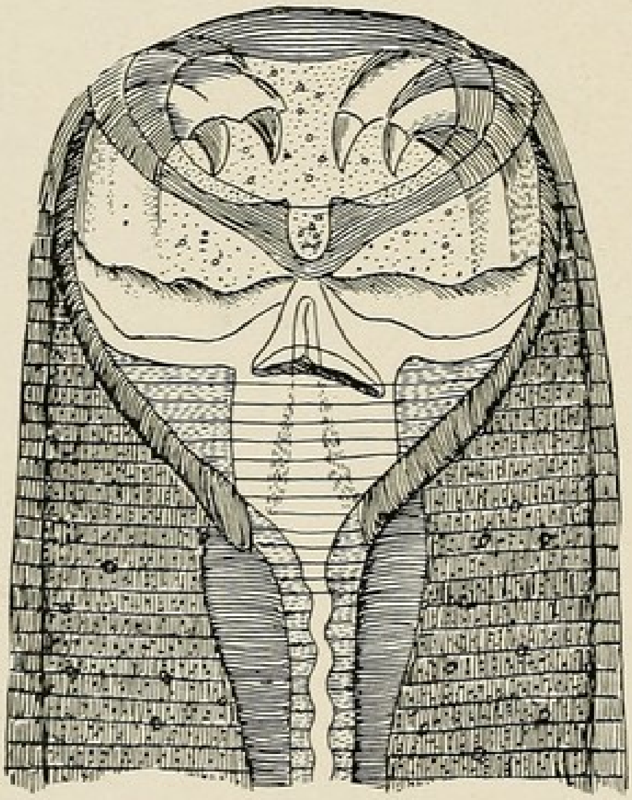

Fig. 3. Dorsal view of anterior end of the old world hookworm (ankylostoma duodenale) of man. Greatly enlarged. (After Perroncito.)

The mouth parts of a hookworm are remarkable and complicated, and furnish important features for the specific diagnosis of the worms. The mouth in the old world worm opens toward the back of the parasite, on account of the dorsal bend, so that the rim of the mouth is nearly or quite parallel to the long axis of the body of the worm. (Fig. 1.) The mouth capsule, or "buccal capsule," is of half-oval or cup shape, the anterior axis curved and long, the posterior shorter and nearly straight. The bottom of the mouth cavity is flat, uneven, and nearly transverse to the long axis of the animal. (Fig. 3.) Seen from the front, the mouth is somewhat longer dorso-ventrally than laterally. The framework of the mouth is made up of a number of chitinous plates, or, according to Looss, a continuous plate with suture-like depressions, giving it rigidity, but permitting changes of shape, such as are demanded by the function of the mouth, and especially holding on to or letting go the mucosa of the host. The shape of the opening varies much with the degree of dilatation of the orifice at the time of examination or fixation. On the ventral side of the capsule, just within the cavity, are two pairs of sharp-pointed, curved, hook-shaped teeth; at the base of the capsule, on the ventral side, two triangular pointed teeth, or "lancets," and on the front of the dorsal part two tooth-like structures separated by a fissure. "Beneath the buccal rim the lining of the cavity is thrown into six papillary prominences, characteristic of the entire group." (Smith.) In the middle of the dorsal wall of the mouth capsule is the orifice of the duct of the dorsal esophageal gland. From the hook-shaped ventral teeth the so-called cervical glands extend almost to the middle of the body. (Fig. 8.)

The esophagus begins at the base of the buccal capsule, and extends as a thick-walled, long flask-shaped organ, 700 to 800 microns long and 150 to 175 microns wide at the widest (posterior) part. Its lumen on transverse section is triangular or triradiate. At the lower end, above the narrower intestine, is a trilobed valve. Looss says the muscles along the three angles of the esophagus can be distinguished optically and chemically from the ordinary muscles along the lumen. Between the esophagus and the body wall are the well-developed nervous system and the esophageal glands. The former appears to communicate directly with the nervous ring, and consists of three longitudinal nerves which run the whole length of the esophagus in the middle line of the three sectors. At three places are annular commisural fibers, from which finer fibers pass in different directions.

Lying in the three grooves along the esophagus are three small glands, called the esophageal glands (Figs. 8, 9), which become continuous toward the posterior part of the esophagus. Their ducts pass forward and empty into the buccal capsule. According to Looss, the ducts of the lateral glands open close to the rim of the mouth, outside the lateral hook-shaped teeth, and that of the posterior gland in the dorsal wall of the capsule. Smith is not able to differentiate the cephalic or head glands of Looss from the anterior ends of the esophageal glands.

Near the level of the posterior end of the esophageal glands, about midway in the length of the esophagus, or 500 to 600 microns from the front of the head, on each side, is a small conical papilla. Through this opens the duct (sometimes called the ''excretory canal'') of the cervical gland, a large glandular structure lying along the caudal end of the esophagus and the cephalic end of the intestine. (Figs. 8, 9.) The chyle-gut is made up of two rows of cells, surrounded by a muscular wall.

On each side of the anus in each sex are several small bodies formerly called ganglion cells or ''anal glands,'' which open into the intestinal canal. Their function is unknown.

The sexual opening of the female in ankylostoma duodenale is at the posterior third of the body. Mink (1909) reported an anomaly in an old world worm—the vagina opening at the junction of the anterior and middle thirds. The short vaginal tube passes in and divides into an anterior and posterior uterus, each one continuous with the narrow ovary which lies in transverse folds along the intestine. According to Looss the length of each genital tube is five to six times the length of the body of the worm, the total length therefore being ten to twelve times as long. The beginning of the uterus in all mature females contains masses of spermatozoa, and is sometimes called the "receptaculum seminis." The ovary of the posterior uterus coils upon itself and passes forward, to terminate with the anterior ovary in the anterior half of the body of the worm. At the end of the vagina is the complicated "ovijector," surrounded by a dense layer of muscle cells. Looss gives the two parts of this organ the names "pars haustrix" and "pars ejectrix."

Within the uteri the characteristic ova are seen in great numbers, and in varying degrees of segmentation. Smith speaks of some with embryos in the uterus, but does not say whether these were in recently passed worms. We have never seen this, and think it probable the embryos had developed after the worms left the body of the host in old specimens.

The male sexual glands have an appearance analogous to that of the female, and consist of a long plicated tube along the intestine on each side of the worm, reaching as far as the cervical glands, opening into a sac, the seminal vesicle, about the middle of the body. From this a tube, the ejaculatory duct, passes to the cloaca, which opens in a papilla on the ventral side of the tip of the tail, within the bursa. (Fig. 2.) The duct is covered by the "cement gland," the secretion of which serves to fasten the male to the female during copulation. The opening of this is guarded by a chitinous forked process, the point directed toward the tail, and the intercornual space occupied by a delicate valve-like layer. From the opening two long slender "spicules" (Fig. 2) extend. They vary in length, but are almost two millimeters long generally. Each one has at its base an "exsertor" muscle and two retractor muscles.

The bursa is an umbrella-like expansion of cuticular folds, supported by extensions of the muscular body wall, spoken of as rays. The dorsal lobe is not divided, and the dorsal rays are united to about two-thirds of their length

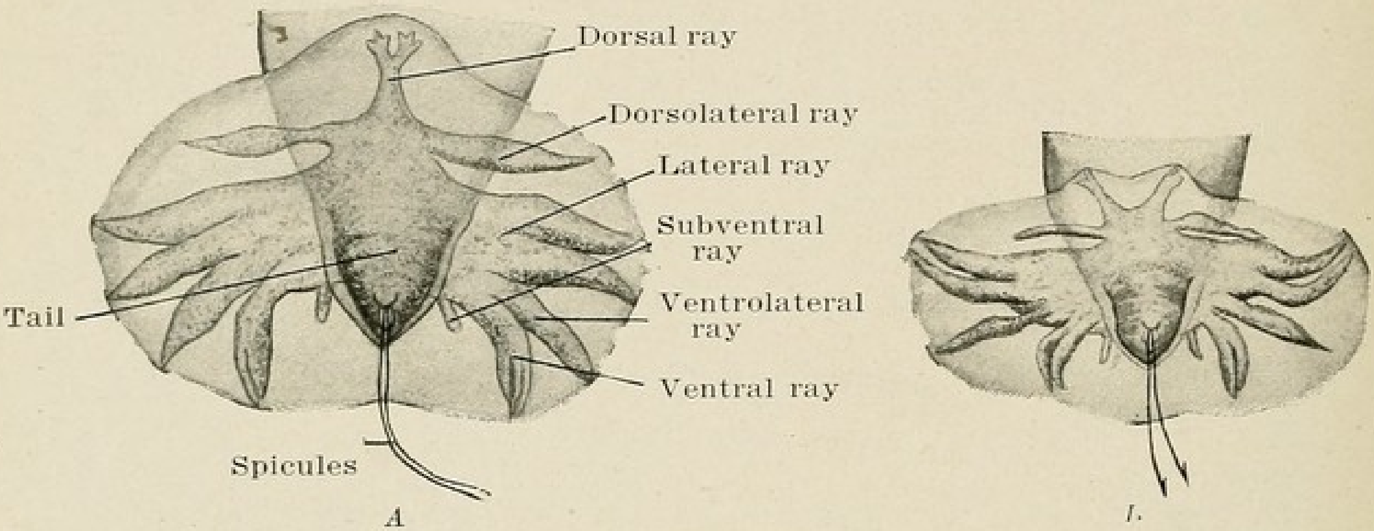

Fig. 4. *A*, caudal bursa and tail of male uncinaria duodenalis. *B*, caudal bursa and tail of male uncinaria Americana. Drawn to scale to show difference in size. (After Allen J. Smith.)

from the base. Each division is tripartite. There is no ventral lobe. The bursa and its muscular rays enable the male in sexual contact to grasp firmly the body of the female and properly coapt the sexual parts. (Fig. 4.)

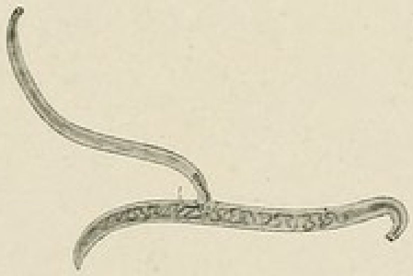

Fig. 5. Ankylostoma duodenale in copulation. Drawn by Dr. J. H. Gage from specimen presented by Dr. Walter Brem.

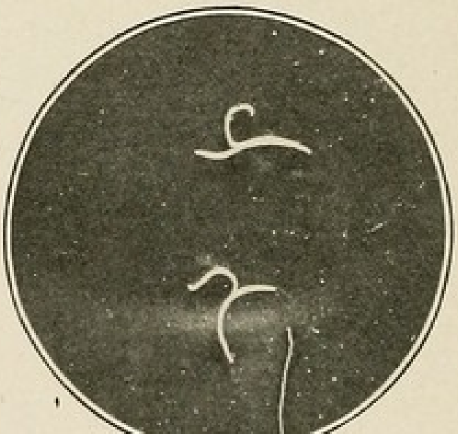

Fig. 6. Copulating hookworms from dog.

The eggs are oval, with broadly rounded poles; the shell is colorless, measuring 0.056 to 0.061 millimeters in length and 0.034 to 0.038 millimeters in width. (Fig. 11.) In fresh stools the eggs are usually in four segments, rarely in fewer or more, and with a broad space between the segments and the shells. (See Chapter VII.)

Necator Americanus.

Synonyms.—Uncinaria Americana—Stiles, 1902; ankylostomum Americanum—von Linstow, 1903; uncinaria (necator) Americana—Stiles, 1903; uncinaria hominis—Ashford, King, and Gutierrez, 1904.

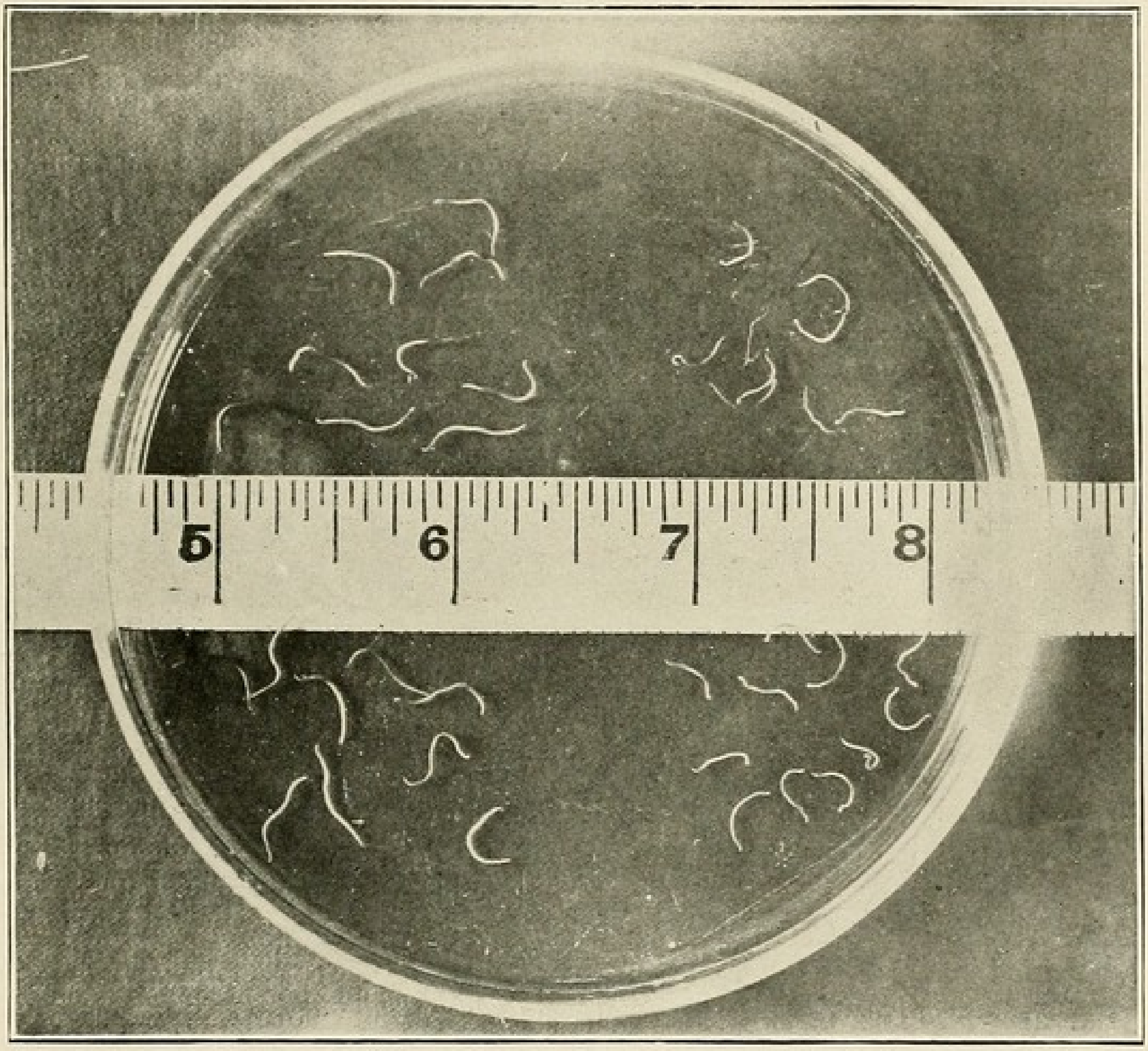

Fig. 7. Necator Americanus. Upper half males, lower half females. Inch measure.

The name (necator = murderer) given by Stiles to the species first shown by him to have generic characters. Stiles first named it uncinaria (1902), having clearly described the differences between uncinaria duodenalis, but believing the worm to belong to the same genus. It is interesting to note that Lutz, in 1888, stated that the Brazilian hookworm did not have hook-shaped teeth. Leuckart's description of dochmius duodenalis (1876) was based on new world specimens. Looss suggests the latter were sent by Wucherer or Lutz from Brazil, but the original material could not be found. Allen J. Smith also recognized the difference between this and the old world species. Both terms of the name have been criticised—"necator" because the parasite is not more murderous than its old world congener, and "Americanus" because it has a world-wide extent. The objections are invalid from the standpoint of zoologic nomenclature.

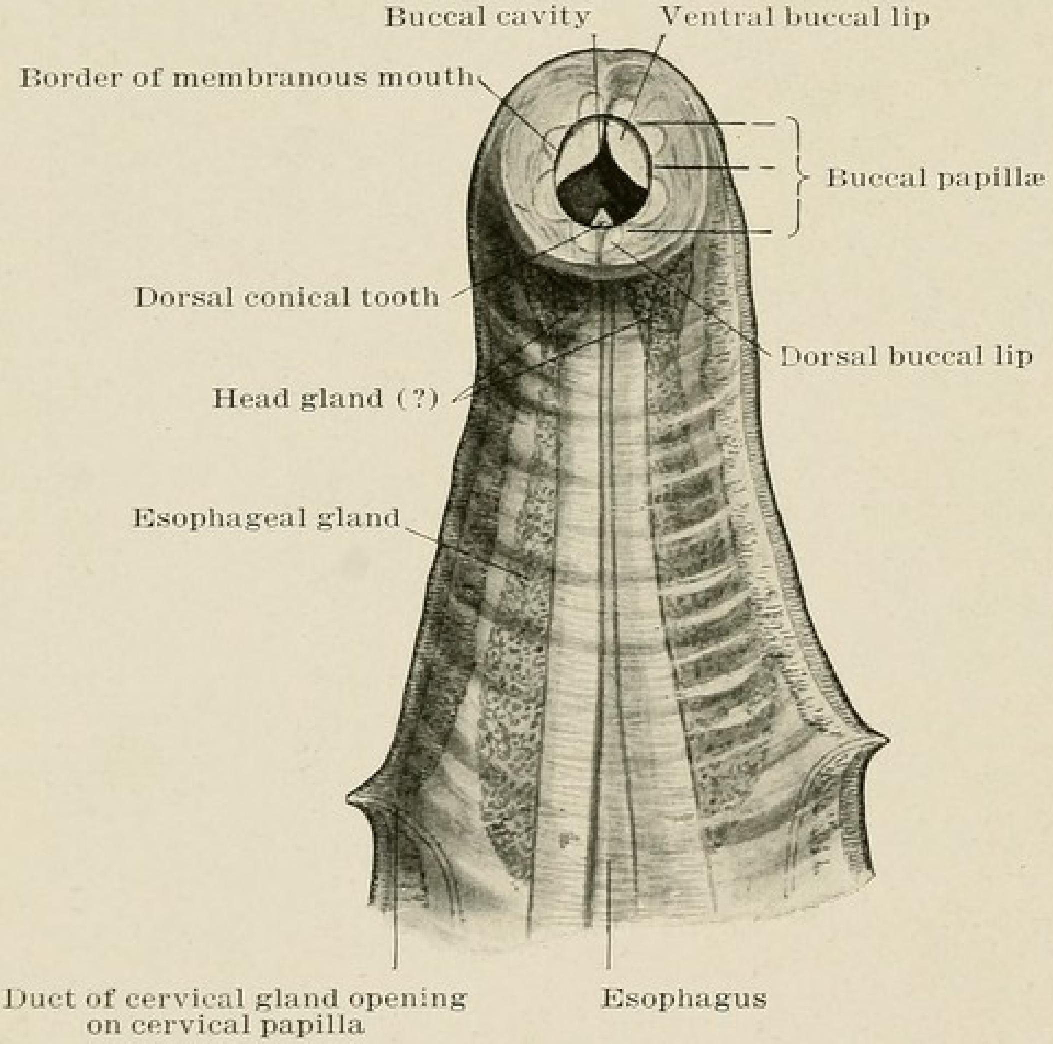

Fig. 8. Dorsal aspect of head end of uncinaria Americana. (After Allen J. Smith.)

This worm is almost as long as, but more slender than, ankylostoma. The males measure 6 to 10 millimeters and the females 8 to 15 millimeters. (Fig. 7.) The mouth capsule is small and globular and its orifice rather quadrate. (Fig. 10.) There are no teeth on the free edge, but two broad lips—dorsal and ventral—extend inward to or beyond the edge of the membranous lip. The base of the larger of the lips reaches from the ventromedian line to

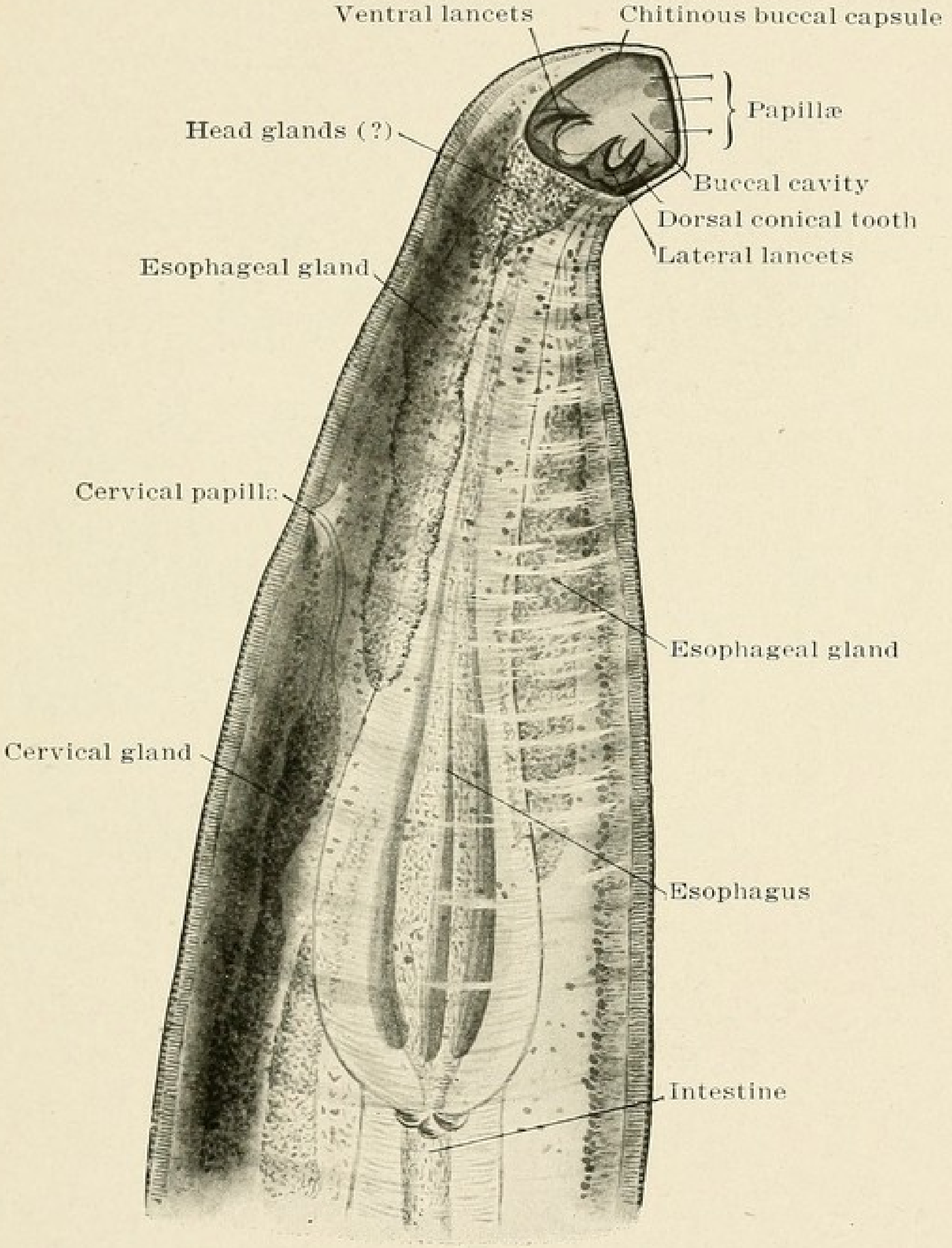

Fig. 9. Lateral aspect of head end of uncinaria Americana. (After Allen J. Smith.)

about the middle of the lateral aspect of the rim; the smaller one from the dorsomedian line about two-thirds of the distance to the ventral lip. They cover two cutting plates. (Figs. 8, 9.) There are two pairs of ventral teeth—the lower pair small and conical, and a blunt, conical, dorsal tooth (Fig. 8), projecting into the capsule. Through it passes the duct of the dorsal esophageal gland. Near its base, on each side, is a chitinous plate.

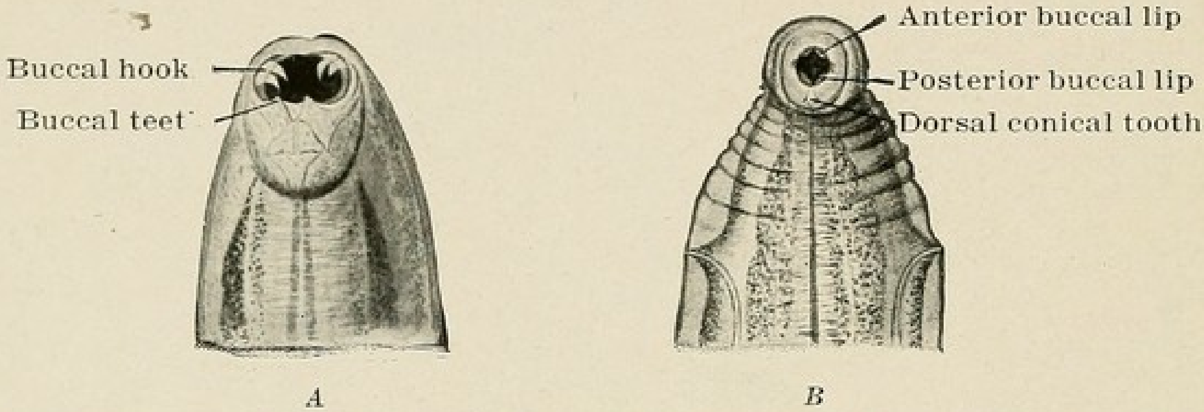

Fig. 10. *A*, dorsal view of head end of uncinaria duodenalis. *B*, dorsal view of head end of uncinaria Americana. Drawn to scale to show difference in size. (After Allen J. Smith.)

The sides of the bursa are very long, so that the bursa seems as if two-lobed. (Fig. 4.) The female genital opening is in front of the middle of the body. The eggs resemble those of the old world hookworm closely, but are

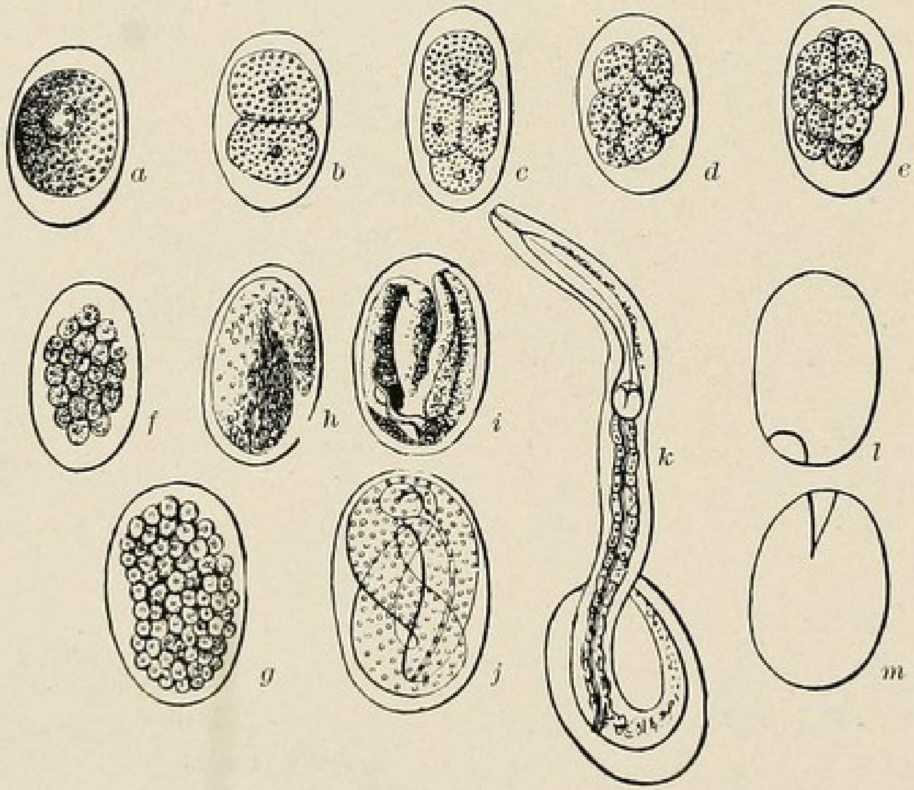

Fig. 11. Embryology of the old world hookworm (ankylostoma duodenale) of man; *a, b, c, d, e, f, g*, segmentation of the egg; *h, i, j*, the embryo; *k*, a rhabditiform embryo escaping from its eggshell; *l, m*, empty eggshells. Greatly enlarged. (After Perroncito.)

slightly larger (0.054 to 0.072 millimeters long and 0.036 millimeters thick), and tapering toward the poles. (Fig. 13.)

The vital characteristics of necator Americanus have not been so closely investigated as those of ankylostoma, but are the same so far as examined. Experiments by Claude A. Smith and Pieri (though the latter rejected the conclusions) prove the skin infection to take place in the same way.

Ankylostoma and necator have been found only in human beings. Von Linstow (1903) reported the occurrence of necator in a chimpanzee (simia troglodytes) in West Africa, but Looss doubts the diagnosis.

Development of Ankylostoma Duodenale.

The females lay their eggs in the intestine of the host, and the ova are expelled with the feces, and under proper conditions develop. The rapidity of development depends upon the temperature, moisture, and available oxygen, as also perhaps on absence of light. Development is most rapid at 25°—35° C. (77°—95° F.). A few develop at 22° C. (71° F.), and Tenholt found that some developed in mines at 20° C. (68° F.) from eggs to larvæ in fourteen days. Freezing often kills ova, and low temperature prevents segmentation, but the possibilities of the development of these worms appear very strikingly from some experiments of Oliver (1910). He froze feces until hard, but after gentle thawing larvæ appeared on the sixth day. Kept in a cold cellar at 15°—17° C. (59°—62.3° F.) for ten weeks, there was no segmentation, but when raised to a moderate temperature segmentation went on and gave rise to stronger and more vigorous larvæ than those hatched immediately. Exposure to light snow does not kill eggs or larvæ. Temperatures of 50° C. (122° F.) kill larvæ, probably from drying. Complete desiccation is one of the most certain causes of death. Deprivation of oxygen also checks development,

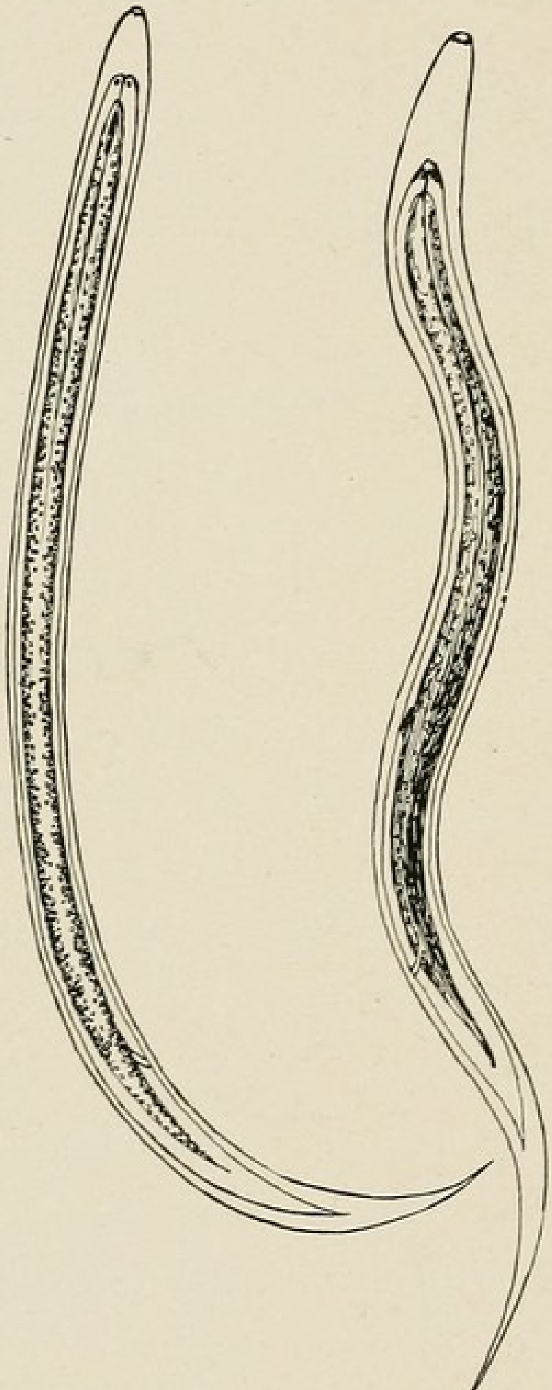

Fig. 12. Two larvæ of the old world hookworm at the end of the second stage ("encysted larvæ"), representing the young worms retracted from their skin. (After Perroncito.)

and, if continued sixteen days, the eggs die. It is the presence of oxygen that makes eggs on the surface of stools develop more rapidly than those in the depths, which either die or develop only when the mass becomes loose. (See Chapter V.) Direct sunlight kills the ova, diffuse daylight checks development, and darkness favors it.

The eggs resist adverse conditions very much at times. Lambinet and Boycott and Haldane found they could be kept from air nine to ten days and then develop.

Fig. 13. Ova of (*A*) uncinaria duodenalis and (*B*) uncinaria Americana. Drawn to scale to show comparative size. (After Allen J. Smith.)

Eggs also die usually in water or in watery stools, but, on the other hand, larvæ can often be cultivated under such conditions. Larvæ can be raised sometimes either in the natural stool or one made into a thick paste with water, but, as Looss pointed out, acid fermentation of stools may kill all the larvæ, even before they escape from the egg-shells. Boycott and Haldane, however, found that larvæ grew for them in acid stools. Looss also points out that the constituents of the feces are important in this connection. In his own infection (experimentally produced) he found that pure vegetable diet produced a less favorable medium for the ova than mixed diet, especially if stools from the latter were mixed with equal part of moderately finely pulverized animal charcoal (made from bones, not blood) and made into a thick, tenacious mass with water. Diarrheal stools mixed with animal charcoal also permit all the ova to develop.

While complete desiccation kills both eggs and larvæ, encysted larvæ resist drying for a long time. There is much divergence in regard to the effect of drying on ankylostoma larvæ, but the differences of opinion probably depend upon errors in technic—sometimes perhaps on mistakes in the diagnosis of the larvæ.

The larvæ, after escaping from the eggs, feed on the feces and grow. They measure 0.2 to 0.25 millimeters long and 0.01 to 0.017 millimeters thick. They are at first rhabditiform—that is, the esophagus shows three parts. It becomes narrow beyond the middle, and then swells out again in an onion shape. In the interior of the swelling are three small valves, that can sometimes be seen to open and shut. (Fig. 11, *k*.) Characteristic of the hookworm larva is a long, cylindrical mouth cavity, with a globular dilatation at the posterior part, lined by a highly refracting membrane. The tail end is sharply pointed; in front of it is the anus, and still farther in front the anlage of the sexual organs, showing as a small oval body.

Four moults are passed through during development of the larvæ, making five stages after incubation, including full development. The first shedding of the skin, or ecdysis, takes place usually within two to five days after incubation, depending upon the temperature and other conditions. In this there is no change of shape. The new skin is formed under the old one. After this moult, again with a lapse of time depending on the temperature, the larvæ grow and change their shape. The body becomes longer (0.7 to 0.8 millimeters) and thinner, and the characteristic shape of the mouth and esophagus are lost. The second ecdysis is prepared for, and reached in five to nine days usually, but the old skin is not shed as soon as the new one is ready. On the contrary, the old skin surrounds the body as a delicate sheath, in which the larva has room to move forward and back. This is the (falsely) so-called "encysted" stage. (Fig. 12.) The larvæ are now called "ripe." Growth and feeding cease, and the free stage of the larvæ is ended. They now endeavor to leave the feces and to get into moist earth, moist wood, or water. As Looss discovered and reported in 1897, they bore through filter paper on which feces are incubating, and in that way can be easily obtained free from fecal contamination. They also pass through a sand filter, even if the water is not running. In various media they may live a long time, and show remarkable tenacity of life. Belger and Oliver found them alive in water sealed in vaseline four months. One of them wriggled into the vaseline and lived nearly to the end of the fifth month. Looss kept them alive in water three hundred days, and Oliver more than eleven months. Perner found them alive in mine sludge ten months after the mine had been closed. In distilled water they live only two to nine days. During this time they live upon certain granular particles in the glands of the intestine, the latter becoming in time almost transparent, instead of granular and opaque as before. In water they are not able to move freely, but sink if the water is still. On the other hand, if the temperature is not too low, they have a strong tendency to migrate, and especially to crawl up on all sorts of objects kept moist by water. Looss found that if he put a piece of wood in the culture glass, with one end out of the water, all the larvæ in a short time would crawl up to the top of the stick, which was kept moist by the water below. Tenholt reports an observation in which larvæ that developed from ova in feces at the lower end of a wet mine timber reached a height of one meter above the ground in twenty days, or not more than sixteen days after reaching the larval stage. The same observer found larvæ in the cracks between the boards of a bath-house. Hermann and Galli-Valerio observed penetration of elder pith by larvæ over night. It is in this stage that the larvæ are infectious. Eggs or young larvæ are not capable of infection, even if swallowed.

Leichtenstern formerly believed that ankylostoma could develop by heterogeny—that is, the larvæ developed outside the body into males and females, the offspring of which in turn were infectious. Leichtenstern later abandoned the view, but it was put forward also by Giles in Assam, and later by Ozzard, Annett, and Ross. As has been pointed out by Looss and other observers, and recently (1909) by Leiper in criticism of Ozzard, the idea depends upon confusion of ankylostoma larvæ with those of other nematodes, especially strongyloides stercoralis, sometimes free living nematodes, of which there are so many species, and failure to sterilize the sand used for culture medium.

As an example of the necessity of extreme care in such work, Leiper cites an observation in which a stool was kept in a glass bottle in the laboratory for a year. The bottle had formerly contained an alcohol preparation. Later the bottle was found to contain forms resembling free adult strongyloides intestinalis, but it became certain later that they were the larvæ of free living nematodes. Leiper also points out that, while the ova of hookworms as found in human feces are diagnostic, they can not be distinguished from the larvæ of all other nematodes.

As Looss has shown, the picture of Giles, purporting to represent the development of the male rhabditis of ankylostoma, shows three different species, as indicated by the shape of the tails.

The larvæ, like the eggs, are easily killed by drying. Galli-Valerio and also Pieri, however, found that they could be dried, but revived up to twenty-four hours after. Differences in the results of various experimenters are to be explained by the difficulty of perfect desiccation within the capsule. Galli-Valerio found that, while noncapsulated larvæ die at 40° C., encapsulated ones could resist a temperature of almost 50° C. He also found encapsulated larvæ alive in a bottle of feces kept nearly a year. The feces were still moist, and the larvæ only on the surface.

Chemical disinfectants.—The larvæ are resistant to chemical agents. Schüffner kept them alive almost four months in water with two or three drops of 1-percent quinine solution to 10 cubic centimeters. Oliver found that sea-water killed them in thirty-seven minutes.

Stronger disinfectants kill both eggs and larvæ, as is mentioned more fully in Chapter IX.

An interesting light was thrown on the possible modes of dissemination of the eggs and larvæ of hookworms by Galli-Valerio (1905). He placed eggs and larvæ of ankylostoma duodenale in a bottle with flies, and on washing the flies found many eggs and encapsulated larvæ which had adhered to their bodies, but none in the flies' intestines.

Having been taken into the body in any of the various ways described in Chapter IV, the larvæ undergo two other moults before becoming mature. The details of these stages are not known, but certain facts are established. Both in the mouth infection and in some cases of skin infection, as in Looss' experiments on young dogs, the larvæ appear in the intestine in ten days.

In skin infection in guinea pigs, larvæ reach the trachea in fourteen days. They have not grown appreciably, but are perfectly agile. They evidently do not all travel with the same speed. Doubtless many are kept back for a time or permanently by the lymph glands. Looss, however, found eggs in the feces after skin infection in thirty to thirty-five days. Tenholt's assistant found a few eggs in his stools forty-seven days after skin infection, and then they rapidly became more numerous. In the accidental infection in himself Looss did not find eggs until the seventy-first day, the same period that elapsed in Pieri's case, but in young dogs Looss found a few adult worms at thirty to thirty-five days.

CHAPTER IV.

MODES OF INFECTION.

Two modes of infection with hookworms are known and have been proved experimentally—i. e., through the mouth directly and through the mouth indirectly by way of the skin. For reasons that will appear below, direct mouth infection, though it may occasionally occur, is of minor importance in the production of hookworm disease. Skin in fection, we believe, is practically the only source of the disease. Different species of hookworms have been found parasitic in various lower animals—namely, dogs, sheep, cattle, horses, pigs, cats, foxes, seals, badgers, etc. These are distinct from those infecting man, and have not been found in man. Two species infect man—ankylostoma duodenale and uncinaria Americana—both of which have been found experimentally to be capable of entering the skin of lower animals, but they have not reached adult life in the intestinal canal of any animal besides man, except possibly the chimpanzee, the gibbon, and the gorilla. They reach adult life or the reproductive stage only in the intestinal canal of man, where they lay eggs, which pass out with the feces. The eggs can not hatch in the intestinal canal for lack of oxygen and possibly for other reasons, such as the presence of acids, gases, etc., produced by the intestinal bacterial flora. Moreover, it has been shown conclusively by Looss, working with the old world hookworm, by Claude A. Smith, working with the American species, and by others, that the young worms can not infect until they have reached a certain stage (the encysted stage) of their life, which requires at least four or five days after they are hatched out, which itself requires eighteen hours or more after the feces have been expelled. The above stated facts—that the reproductive stage of the parasite is reached only in the intestinal canal, that the species infecting man do not infect other animals, that the eggs do not hatch in the intestinal canal, and that the larvæ are not infectious until they are at least four or five days old—show that the feces of infected persons are the real sources of every hookworm infection, and, further, that a man can not directly infect himself.

The number of eggs passed with each stool of a heavily infected person is enormous. Leichtenstern estimated the number passed daily in one of his cases of ankylostomiasis to be over 4,000,000. Bass counted the eggs in one decigram of feces from a severe case of uncinaria Americana infection, originating in Louisiana, and calculated the number in the entire stool to be 4,490,000. We estimated that the daily stool of a patient with apparently only a moderate infection, and 70 percent of hemoglobin, contained 1,700,000 eggs. Remembering that the average number of worms in the severe cases in this country ranges between 1,000 and 4,000, it is obvious that it would not require more than one-thousandth part of the eggs in one such stool to give rise to a severe infection if all developed. In the light of these figures, the wonder is that the disease is not far more destructive of human life than it is.

Requirements for Hatching.

Hookworm eggs do not hatch in the intestinal canal, as has already been stated, nor do they hatch in undiluted feces, except under certain special conditions. We have often kept feces containing hookworm eggs in the laboratory for months at a time in liquid condition without any hatching whatever. In fact, we have kept them in this condition in the bacteriologic incubator at body temperature for a month and have never seen hatching occur in such specimens. If, on the other hand, pure feces are exposed to drying, many of the eggs near the partially dried out surface of the fecal mass will hatch out, but the eggs deeper in remain undeveloped. Claude A. Smith noted that if feces containing uncinaria eggs were exposed to flies that infect them with their larvæ, the constant mixing and aeration (oxygenation) by the larvæ crawling through the mass permits rapid and complete hatching. We have had occasion to confirm this observation in several instances. Though hatching in undiluted feces may occur under the favorable circumstances mentioned, the larvæ die out before they are twenty-four to forty-eight hours old and before they are infectious, except that a few may sometimes live longer in the partially dried out feces. Dilution of the feces with one or more times their bulk of almost any inert porous substance —like charcoal, sand, dirt, etc.—puts them in the most favorable condition. The best results we have ever seen were obtained with equal quantities of charcoal and feces. Looss found animal charcoal the most satisfactory diluent. We have seen nearly as good results from using sand. We made the following experiments for the present work:

Feces containing many uncinaria eggs were mixed with each of the following materials about in the proportion of one part feces to two of diluting material: powdered charcoal (pine), white sand, sand plus about 5 percent slacked lime, sandy soil, black clay soil, and pipe clay, all sterilized before mixing. All were thoroughly mixed and contained about the same amount of moisture. An accident occurred to the specimen which the limed sand entered into and it was lost. The remaining five specimens were placed in glass dishes without covers and put in a bacteriologic incubator (at 37° C.), in which several sponges saturated with water were placed to keep up moisture and prevent undue drying out of the specimens. After fifty-four hours in the incubator the cultures were carefully examined and the following results noted:

Feces plus charcoal: many larvæ, a few empty shells, and no eggs found.

Feces plus sand: many larvæ, a few shells, and two segmenting eggs found.

Feces plus sandy soil: many larvæ, a few segmenting eggs, and three containing embryos were found.

Feces plus black clay soil: in slides made from near the surface a very few larvæ were found and many more eggs, many of which contained dead embryos. Deep in the mixture no progress toward hatching appeared to have been made.

Feces plus pipe clay: no larvæ could be found, but near the surface of the mixture a few dead embryos could be seen in the egg shells.

The charcoal, sand, and sandy soil specimens remained porous and friable, but the clay soil and pipe clay specimens ran together and were sticky. In spite of the precaution to prevent it, all of them dried out considerably, and the clay specimens were coated with a thin hard crust. The experiment shows that best hatching follows dilution of feces with material producing a porous mixture, whereas the sticky nonporous mixture prevents hatching, chiefly, no doubt, by depriving the eggs of oxygen. Where the soil is sandy and porous, rains dilute and mix feces with the soil and put the eggs in the most favorable condition in this regard for hatching. There would be far less mixing of feces with a sticky clay soil, and, if so mixed, hatching is prevented. This may explain the much greater prevalence of the disease is sandy regions.

Moisture is very necessary for hatching of hookworms, but no great amount is required. It is more essential for the maintenance of the life of the larvæ. They live well in water or moist earth, but drying soon kills them. Bentley found that gentle drying for six hours kills them. Rains are important in scattering the feces and mixing them with the soil, and also in keeping up the essential moisture. They are also important factors in producing skin infection by liquefying and helping to apply the infectious cultures to the skin, as we shall see later.

Shade is an important factor, both in the hatching of hookworm eggs and keeping the larvæ alive, by maintaining the essential moisture and preventing fatal drying. We exposed a culture of six-day old uncinaria larvæ to the direct April sunshine for two days, adding water as needed to prevent drying, and they were still alive and active at the end of the experiment.

If feces containing eggs are diluted with dirt, sand, or other material, and favorable conditions of moisture, warmth (temperature between 22° and 35° C. = 71.6° and 95° F.), and shade exist, the microscopic larvæ begin to hatch out and crawl about in the diluted feces in twenty-four hours. In two or three days they shed their skins. This is the first ecdysis. After about five days from the time they were hatched out the organism begins a second stage of development or ecdysis, but this time it remains inside of the skin it has cast or retracted from, and is spoken of as encysted. In this condition it is capable of infecting, but was not before. Before the larvæ become encysted they are easily killed by sunlight, changes of temperature, too much dilution of the feces with water (1 to 1,000 or above), drying, and often the chemical constituents of feces. It results, therefore, that actually very few larvæ that hatch out reach the encysted or infectious stage. Only in rainy seasons, or wet spells lasting six or more days, would sufficient moisture be continually supplied, except in some specially favorable spots, to bring them to this stage. Too much rain often results in sufficient dilution to kill them. Only in favorable places or favorable seasons do they escape the destructive sun's rays and drying. Only in warm seasons do they hatch out. From these facts result the very much greater prevalence and intensity of the infection in tropical countries.

In the encysted condition the microscopic larvæ may live many months under favorable conditions of moisture, shade, and temperature. They resist wonderfully well unfavorable conditions and such agents as chemicals, but are killed by strong solutions of salt, as pointed out in Chapter III. They live well in shallow water or moist earth, in which they come near the surface or go deeper with the rise and fall of moisture.

Drinking Water.

Drinking water may become a source of infection, but the probabilities of getting any considerable number of larvæ in this way seem pretty remote on account of the amount of contamination that would be required (less than one part feces to one thousand) to maintain the life of the larvæ until they reach the encysted stage, and especially in view of the fact that the larvæ soon sink in water. Water containing larvæ would have to be stirred up just before it is drunk to become a source of infection. Referring to this, Stiles remarks that, "granted that they do sink in water, a water bucket in a well also sinks, and the water from surface wells frequently contains sand particles that are heavier and larger than uncinaria larvæ; hence we can not altogether ignore drinking water as a source of infection." Leichtenstern showed that infection by mouth can occur by administering per os capsules containing the larvæ. In about six weeks ova of the parasites appeared in the feces of the patient. These experiments with ankylostoma have been repeated and confirmed with uncinaria Americana by Claude A. Smith and others in this country.

Food.

Food that has been contaminated with infected mud or water, or that has been handled with dirty, infected hands, may become a source of infection. Smith noted the habit the encysted larvæ have of crawling up along the sides and cover of a culture dish, which suggests another way in which certain food may become infected. Larvæ may crawl up on the leaves, stalk, or fruit of such vegetables as lettuce, celery, strawberries, water cress, etc., that are eaten raw, and they may be swallowed when these are eaten. No ordinary washing could be expected to remove all of the larvæ. The frequent practice of defecating in the barnyard, where the feces would be mixed with the barnyard manure and frequently used to fertilize the vegetable and other crops, may possibly be a source of infection. In the country the vegetable garden is usually located behind and near the house, and is one of the common places for the location of the privy, if one is provided. It serves also a frequent place for defecation of the women and children when no privy is used. This may not rarely be a source of the larvæ getting on vegetables, and thus infecting those who eat them raw.

Infection Through the Skin.

Looss, in 1898, while experimenting with cultures of ankylostoma larvæ, found that getting the culture on his hands produced a dermatitis. Later on, finding ova in his feces, he concluded that he had been infected through the skin. In 1903 he proved the correctness of his theory by experiments. Grassi, Pieri, and Noe dropped water con-

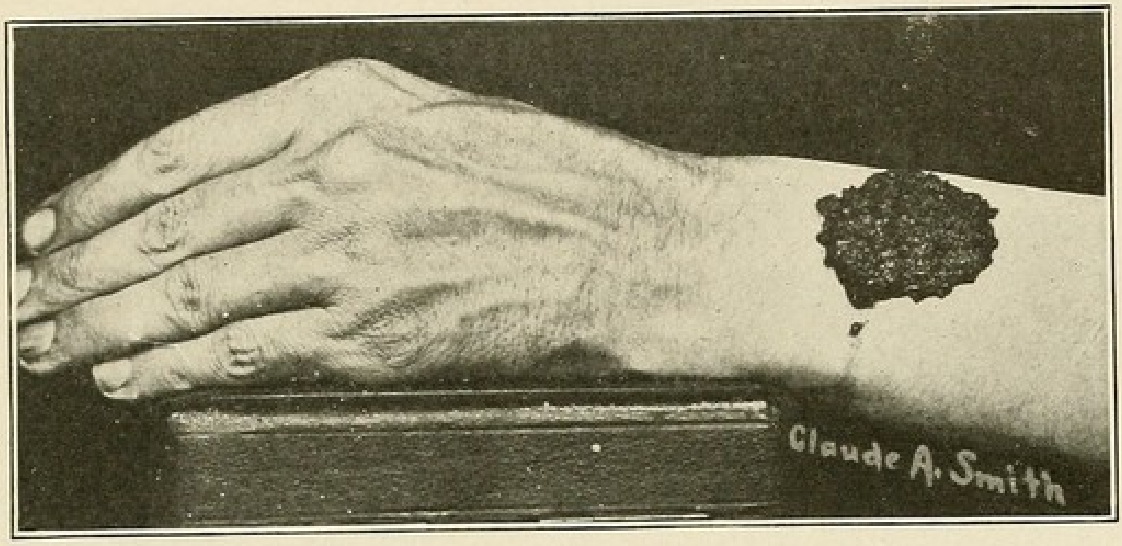

Fig. 14. Experimental hookworm infection. The soil containing the larvæ as it appeared on the wrist, the tendons and veins of the hand showing distinctly. (Photograph furnished by Dr. Claude A. Smith.)

taining ankylostoma larvæ on their own arms. In the feces of only one of them were ova found at the end of ten weeks. They, therefore, concluded that Looss' theory of

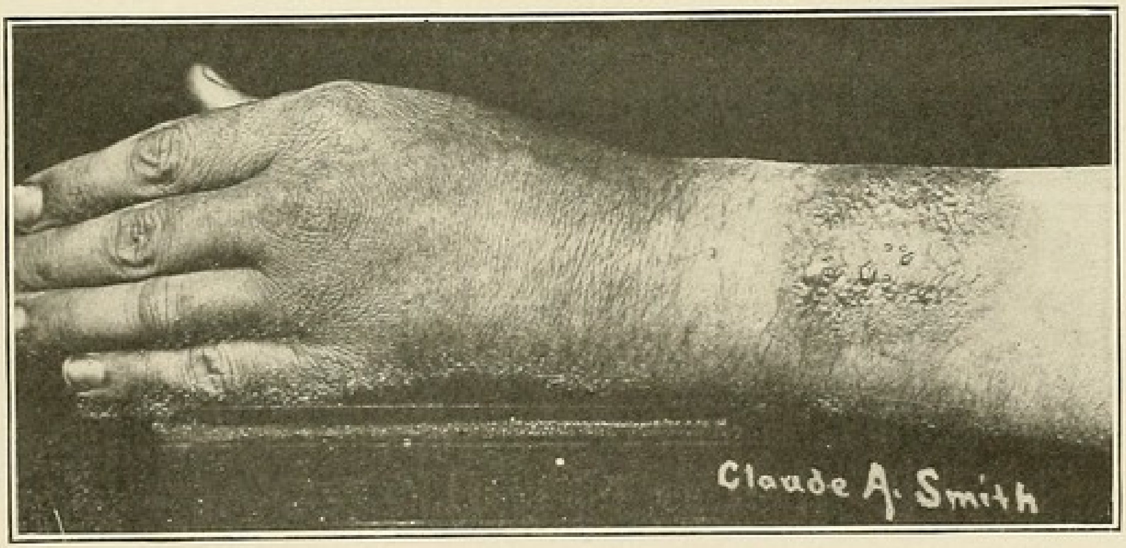

Fig. 15. Experimental hookworm infection. Shows swelling of wrist and tendons of hand, and vesicle formation. Second day. (Photograph furnished by Dr. Claude A. Smith.)

skin infection, deduced from his experiments, was not confirmed, and that their case and Looss' were instances of accidental mouth infection.

Looss then repeated his experiments, and established beyond all doubt that the larvæ enter the skin and finally reach the intestine, where they develop to adult life. He placed some drops of heavily infected water on the arm of a man whose feces showed that he was not infected up to that time. The characteristic dermatitis soon developed. The next day the arm was swollen, in a week the swelling subsided, and in seventy-one days ova were found in the patient's feces. He also shaved the back of a dog and

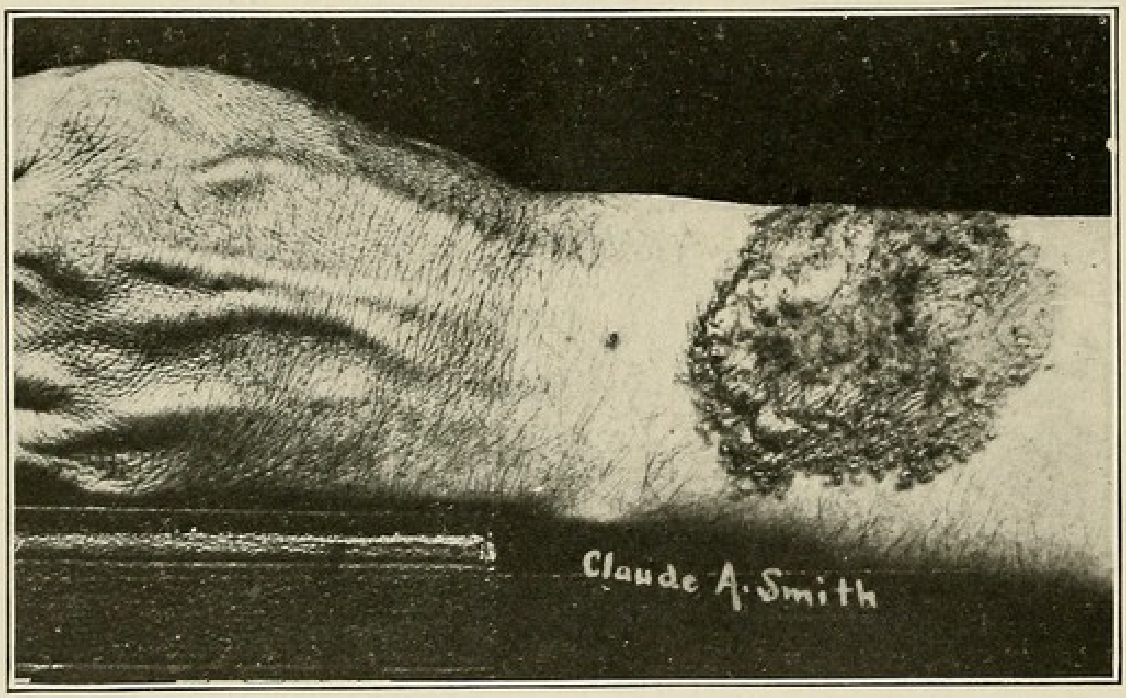

Fig. 16. Experimental hookworm infection. Shows the large crust forming over the area and the further decrease of the swelling. (Photograph furnished by Dr. Claude A. Smith.)

placed on it some mud heavily infected with uncinaria caninum. The animal was properly bandaged to prevent mouth infection, and after two hours the mud was removed and the area thoroughly scrubbed with absolute alcohol. The mud contained only one-sixth as many larvæ as it did when applied to the dog's skin. The dog died in ten days, and at autopsy an enormous number of larvæ were found on and in the walls of the small intestine. He infected two other puppies, one by feeding infected milk and the other by applying the infectious material to the skin. They both died in a few days, and their small intestines contained enormous numbers of young larvæ. These experiments were confirmed by Schaudinn, Lambinet, Hermann, Calmette, Tenholt, and Schüffner.

In 1902 Bentley found in a "water sore," called in this country "ground itch," "dew poison," or "toe itch," a young worm which he thought to be ankylostoma duodenale. He then made the following experiment: A culture of sterilized soil plus feces containing ova was made, and another one containing no ova; both were properly in-

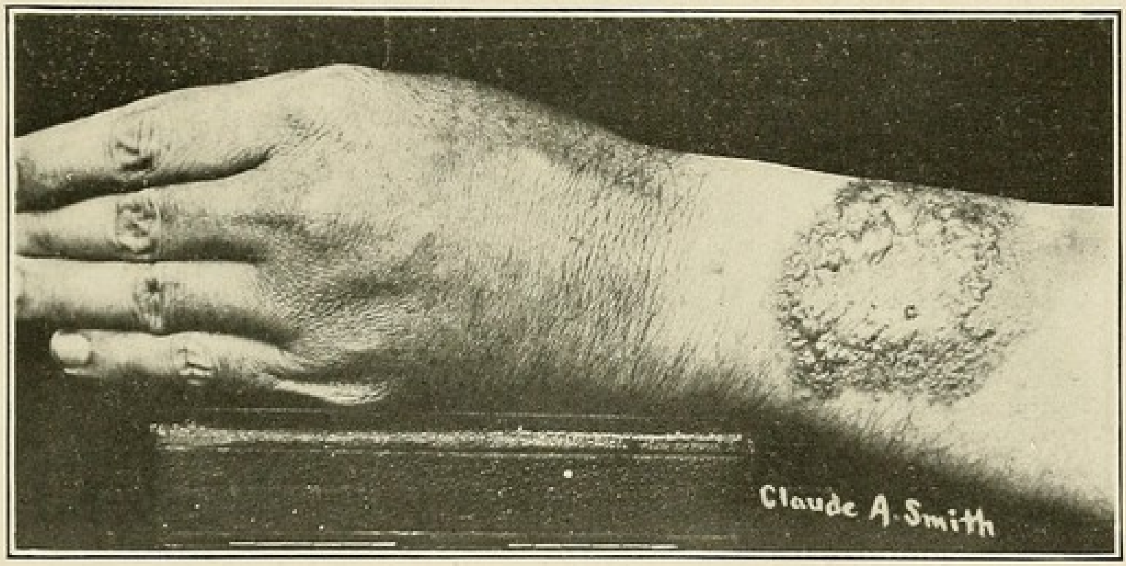

Fig. 17. Experimental hookworm infection. Shows confluent vesicle formation, with slight decrease of swelling. (Photograph furnished by Dr. Claude A. Smith.)

cubated at ordinary room temperature. A part of each was gently dried for eight hours. Six hours' drying had previously been found sufficient to kill the larvæ. After remoistening the specimens that had been dried, samples of the four specimens were applied to the wrists of the subjects of experiment for eight hours, and then they were removed. Within fifteen hours after the application, erythema and a papular eruption appeared over the spot where the living larvæ had been applied. Within twenty-four hours an itching, vesicular eruption had developed, followed by pustules exactly resembling those found in the lesions of ground itch.

In all the other cases no such lesions appeared. A re-examination of the mud showed that the live worms had disappeared, but that the dead ones were still present. The live worms had, therefore, apparently entered the skin, and their entry had been followed by lesions and symptoms similar to those of water sore or ground itch.

These experiments with ankylostoma have been paralleled by the brilliant work of Claude A. Smith, and the results found to hold good for uncinaria Americana. He placed mud containing encysted larvæ on the arm of a man

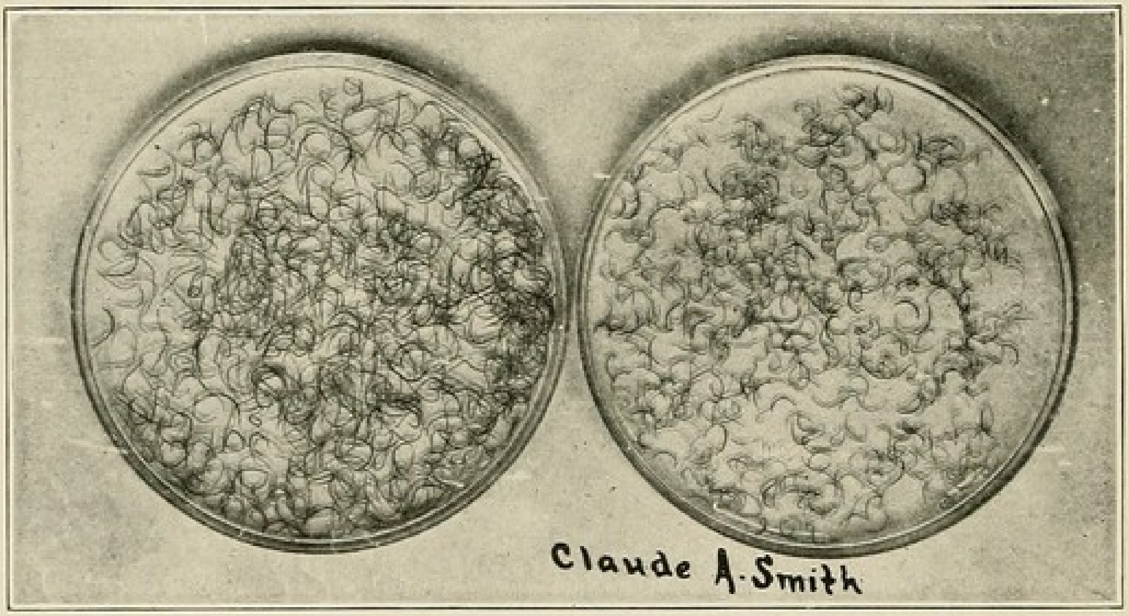

Fig. 18. Experimental hookworm infection. Shows 1,348 uncinariæ removed from the intestines twelve weeks after the eruption on the wrist. (Photograph furnished by Dr. Claude A. Smith.)

not previously infected and allowed it to remain one hour. In eight minutes itching was complained of, and on removing the soil a macular eruption was present. The next day the wrist was swollen. On the following day a vesicular eruption was present, and much itching was complained of. On the fifth day the vesicles had become confluent, the swelling increased, and the axillary glands enlarged and tender. The twelfth day no sign of the dermatitis remained. On the eighth day an attack of sore throat, with fever, developed. During the next three weeks an uneasy feeling about the stomach was complained of. Ova appeared in the stools at the middle of the seventh week. A small particle of mud was applied without the patient's knowledge to the prepuce of a man about to be circumcised. In four minutes he remarked that he felt as though a fly

Fig. 19. Section of skin as seen under the microscope, showing the hookworm larvæ crawling through the skin. (After Stiles.)

was crawling over the part, and in a minute longer said he felt as though his prepuce was being pricked with needles. In four minutes the larvæ had left the mud, as shown by subsequent examination, but under a low power lens the skin was seen covered with them.

Smith was also able to produce lesions resembling ground itch by applying an alcoholic extract of uncinaria larvæ, though aqueous and ethereal extracts gave negative results.

Sections of the skin, removed and hardened even in a few minutes after infectious larvæ have been applied, show numerous larvæ in the hair follicles, sweat ducts, and already actually in the tissues. In sections prepared after a longer time has elapsed many larvæ can be found deep in

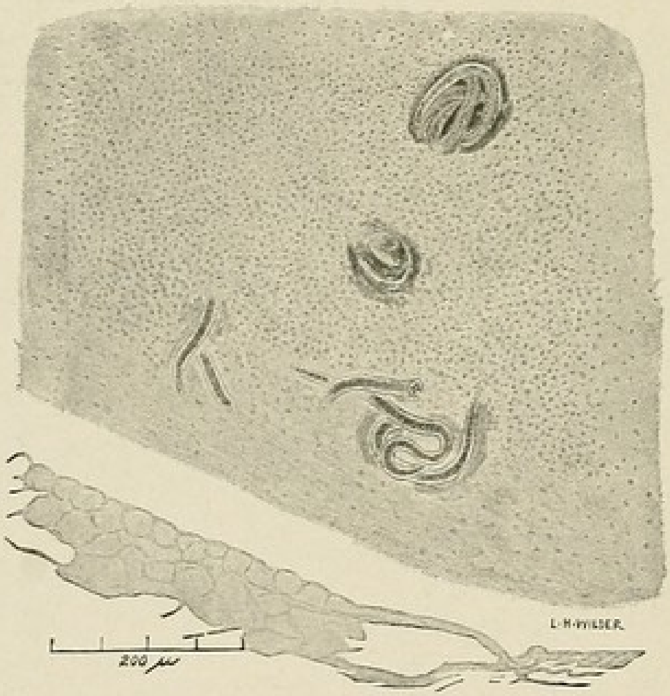

Fig. 20. Larvæ in axillary gland. (After Stiles.)

the skin and subcutaneous tissue, some of which may now be found in capillary blood vessels. They possess wonderful ability to plow through any kind of tissue in the encysted stage, but will not attempt to penetrate the skin before this stage is reached. Once in the blood stream, they are carried to the right heart. Sections have been made in which the larvæ were found in blood in the heart cavity. (Fig. 21.) From the heart they are carried by the blood stream to the lungs. Here they are caught in the capillaries, because they are so much larger than the smallest capillaries of the lungs and can not pass through. Meeting with obstruction, they again exercise their ability to penetrate tissue and soon get into the bronchial tubes.

Ashford and King infected the skin of a young guinea pig with a very heavily infected culture, and in three hours the animal died. Autopsy showed one lung solidified with blood and the other one contained many larger or smaller

Fig. 21. A hookworm larva in the blood in the heart. (After Stiles.)

hemorrhagic spots. Sections showed numerous uncinaria larvæ in these accumulations of blood.

After the larvæ reach the bronchi they are carried to the mouth, either as a result of the normal constant outward current of the bronchial and tracheal mucous membrane or by coughing. No doubt many of them are now spit out, but some are swallowed. More or less larvæ would be swallowed, according to whether the individual spits out what he coughs up. Habits vary much in this regard, as is well known. No doubt this is an important factor in determining the extent of infection in different individuals equally exposed, and, in view of this idea, it seems wise to advise patients who have ground itch not to swallow their sputum.

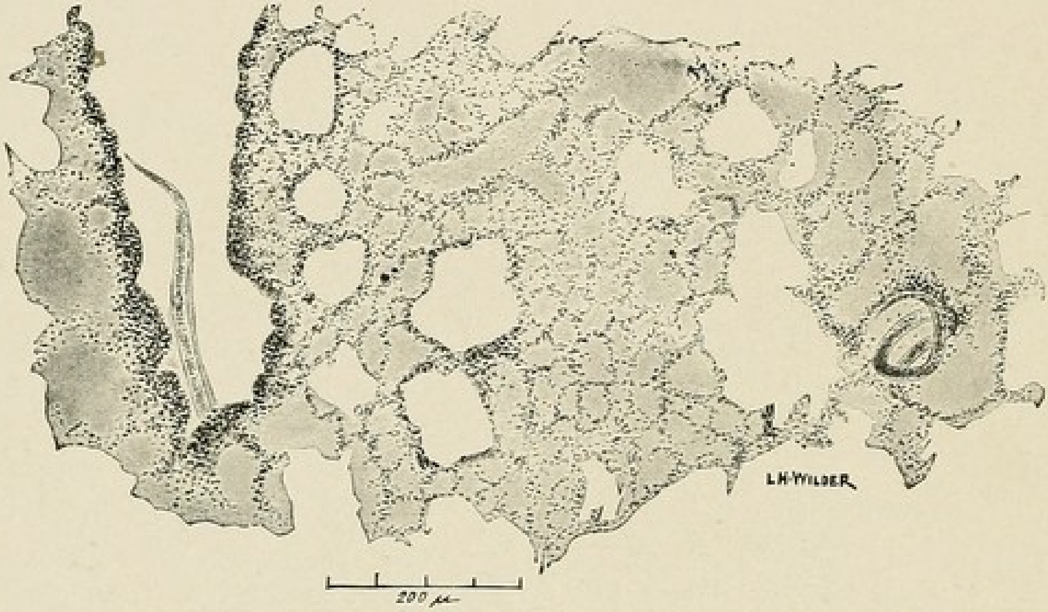

Fig. 22. Two hookworm larvæ in the lungs. The one on the left is entering the bronchus. (After Stiles.)

Larvæ that are swallowed pass through the stomach, resisting the gastric juice just as they resist other chemicals, sulphuric acid, bichloride of mercury, etc., and when they

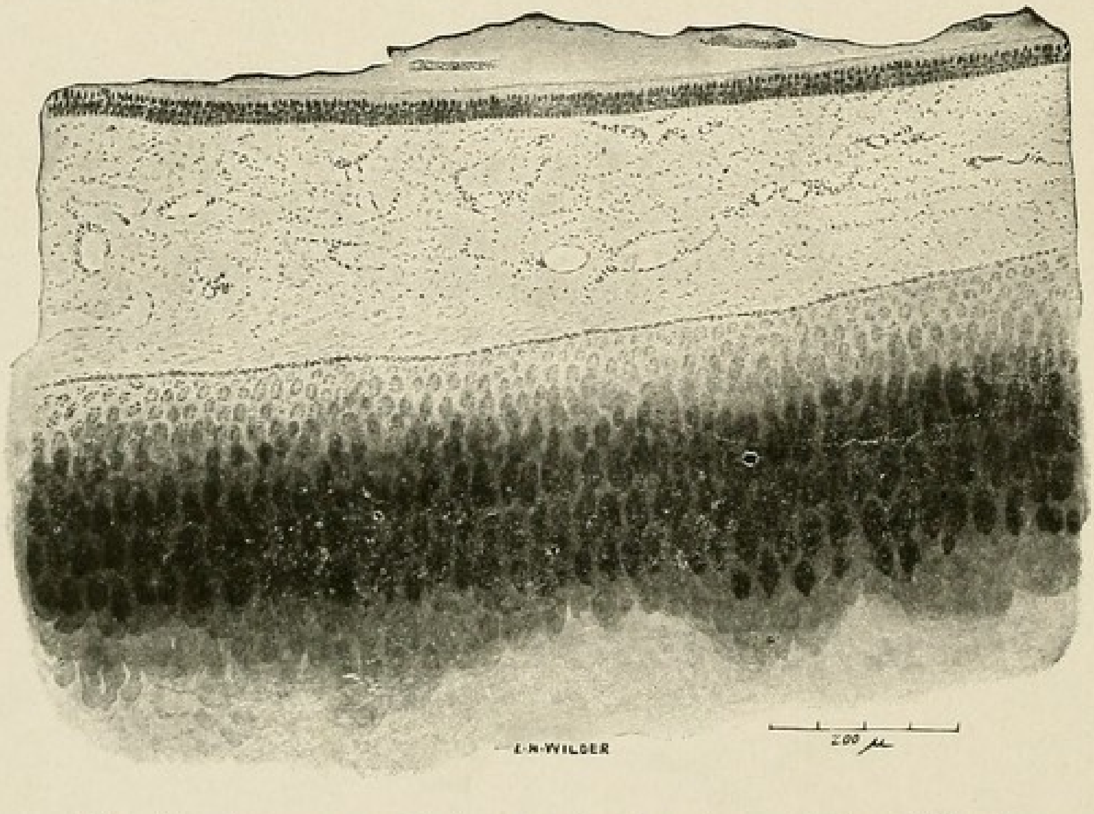

Fig. 23. Larvæ wandering up the trachea. (After Stiles.)

reach the small intestine, the natural home of the parasite, they undergo further development.

Four or five days after the larvæ reach the small intestine another ecdysis begins, in which they acquire a buccal capsule. With this capsule the worm fastens on to the mucous membrane by sucking in a plug of epithelium, which furnishes his nourishment. In another four or five days the last ecdysis begins and the last skin is shed. The worms, about one-fifth of an inch long, now grow rapidly, and in

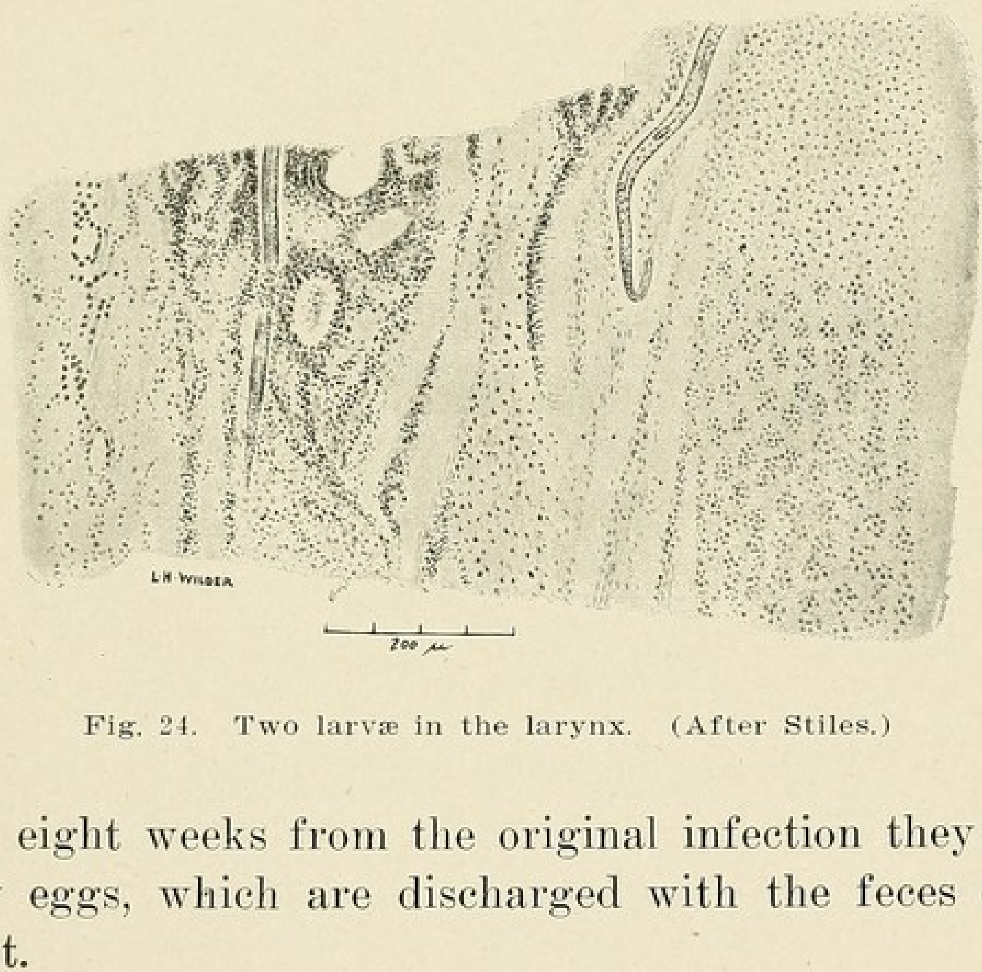

Fig. 24. Two larvæ in the larynx. (After Stiles.)

six to eight weeks from the original infection they begin to lay eggs, which are discharged with the feces of the patient.

That infection through the skin is possible from short contact with infected mud and water is proved. Every step and stage of this process has been demonstrated by several independent workers. Accepting this fact, it is only necessary to consider how much, in the lives of people who have hookworm disease, their skins are exposed to dirt and water containing appreciable amounts of material-containing feces to realize the much greater opportunity for skin than mouth infection.

Disposition of Feces.

How feces are disposed of and disseminated in localities in which hookworm disease is prevalent.—Hookworm disease is pre-eminently a rural disease, being limited in large cities to imported cases, those infected away from home, and a few cases infected in the suburbs. The disease is prevalent among inhabitants of small towns and those living on the outskirts of the town, especially in the poorer classes of people, where the same conditions conducive to infection exist as in the country, but to a less degree. The chief sources of infection for city people are visits to country towns, farms, and rural health resorts. Children, especially, often go to the country for their health, and return infected with blood-sucking parasites, which may continue to reduce their vitality and health for from seven to twelve years. City children, however, are less likely to become infected than the country children in the same place, because they are not so likely to go barefoot.

In the country there are few privies. With the better class of farm and other country families and in towns privies are more generally used. The objects in the construction of the privy, however, in general, in town and country are only shelter and convenience, and the sanitary disposal of the feces receives no consideration. We have indeed seen very few privies in country or town that were not open at the back, leaving the feces just as accessible to hogs, chickens, etc., as if no privy had been used. The animals root and scratch the feces, and thus scatter them about over the ground. Not only this, but they often eat feces, which pass through their digestive tract, a part being digested, but the undigested material is passed many hours later, often a distance from the privy. If the feces eaten by such animals contain hookworm ova, they pass through undigested and are thus widely distributed. We are not informed of any experiments to show whether ova will resist the digestive process of other animals, but we have recently

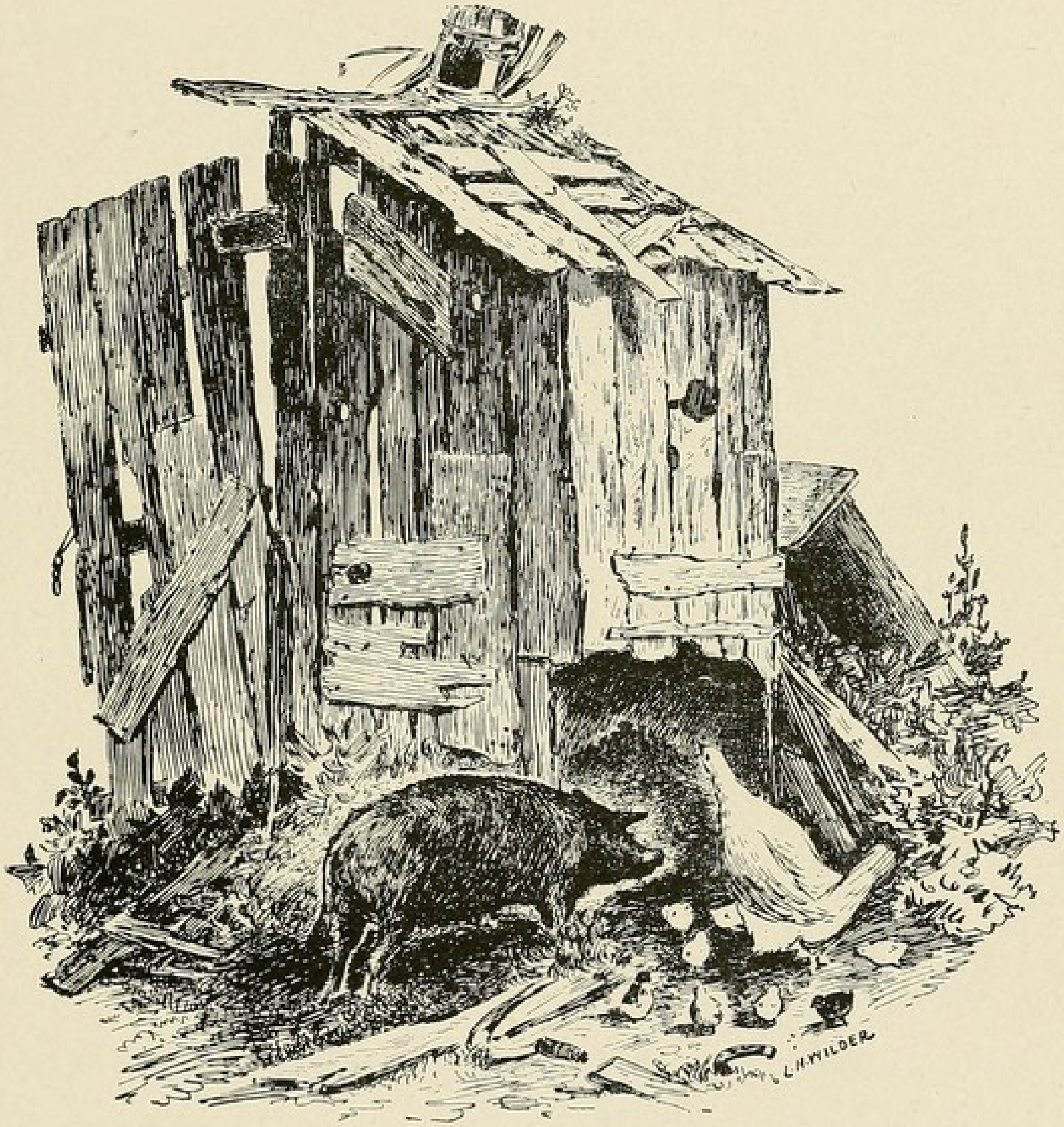

Fig. 25. A privy from which soil pollution is being spread by chickens and swine. (After Stiles.)

made the following experiment with the chicken: A chicken's feces were examined and found not to contain hookworm eggs. A quantity of feces containing many uncinaria Americana eggs were fed to the fowl through a tube. In thirty-six hours the chicken's feces were found to contain many uncinaria eggs, which appeared unchanged. Some of this material, mixed with charcoal and sand, was incubated, and in twenty-four hours larvæ began to hatch out. This proves that the chicken may scatter infected feces. Chickens will eat fresh human feces when they have

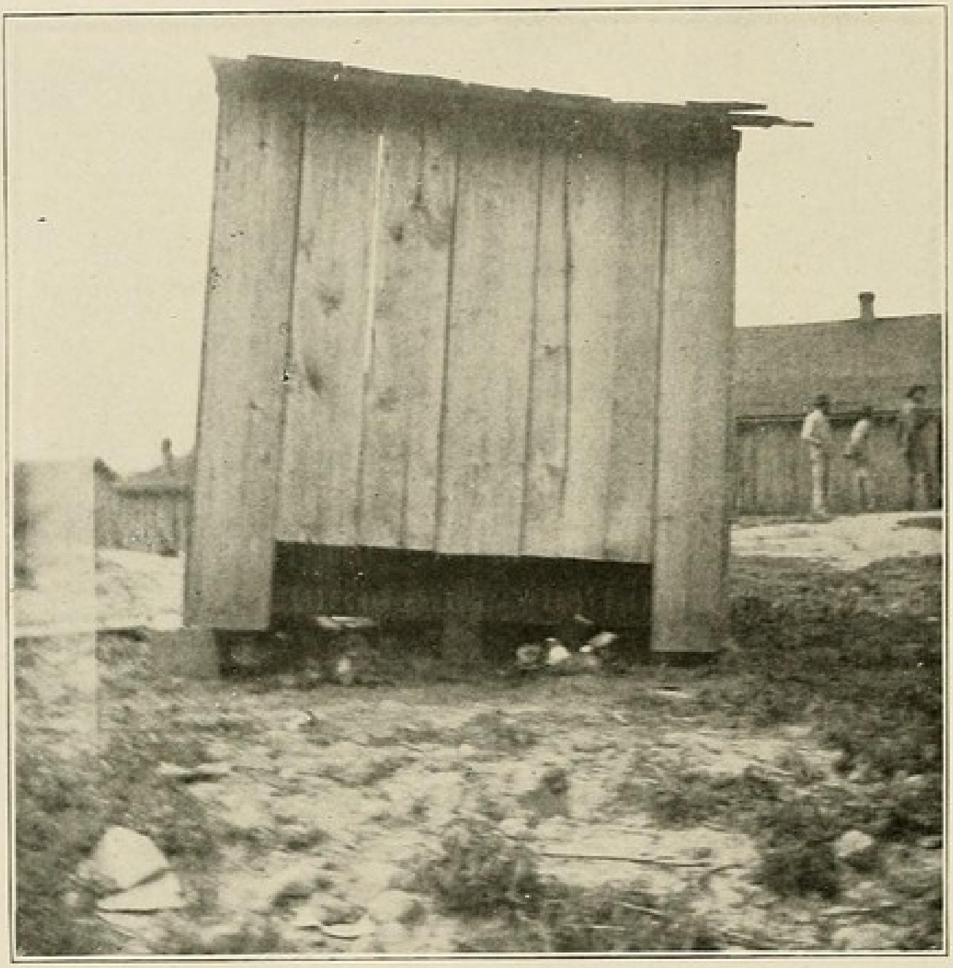

Fig. 26. A privy in the center of a town of about 2,000 population.

a chance, and, besides this, they scatter them about on their feet after scratching in them.

When the location of a privy is under consideration, if such a place is available, a hill side or sloping piece of ground is usually selected. It results that heavy rains wash the feces from under the privy, carrying them, and others scattered by domestic animals, into mudholes, ditches, etc. Later the barefoot boy comes along and wades or plays in the water or ditch. The result will be infection if the feces deposited contain ova. Only those who have had proper opportunity to observe the facts, chiefly by residence on the farm and in the country, will be able to realize fully the possibilities along this line.

Where do the 60 to 80 percent of rural population who have no privies deposit their feces, and what becomes of them? This varies very much with the people, the loca-

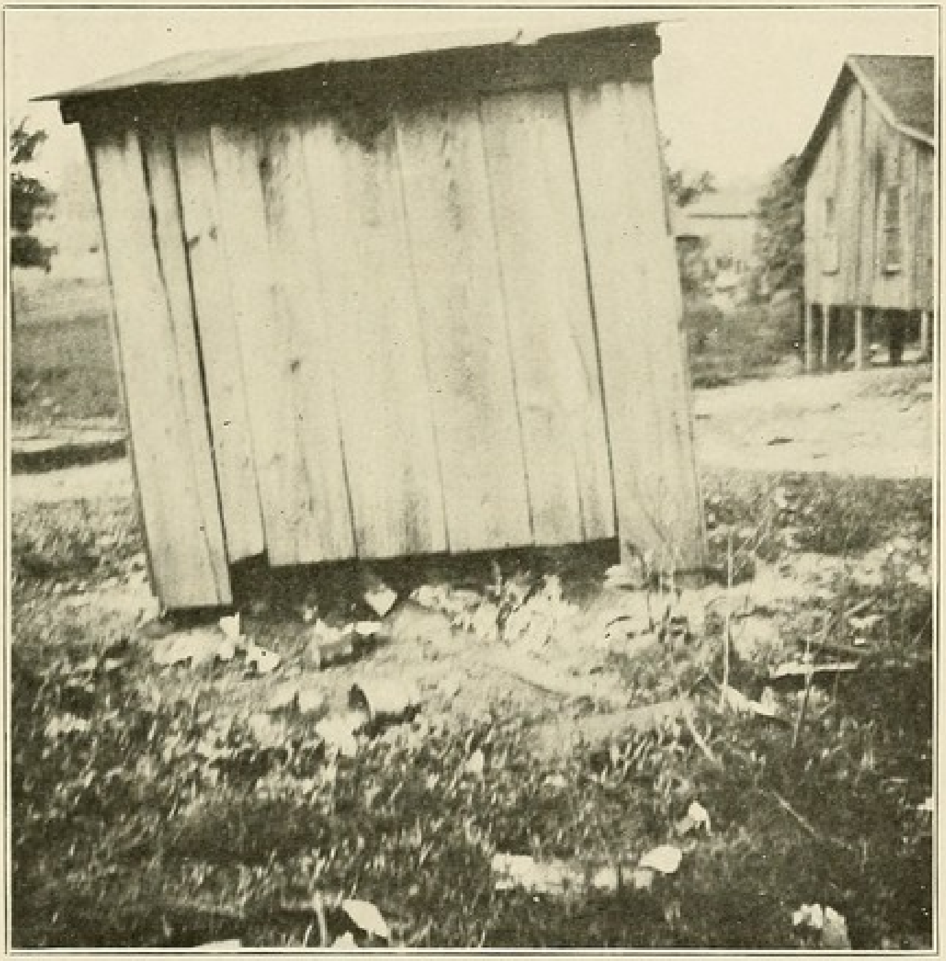

Fig. 27. The kind of privy in general use in small towns.

tion, their occupation, and local and family habits. Our own observations of these things were made during many years of residence in the country, where the class of people and habits and conditions are such as to induce infection of a large percentage of the population. The adults, and often the children, of these families usually go to the barn-yard or to the garden behind the house, or to "the bushes," or to "the thicket" if one is near by, or behind anything like stumps, trees, hills, or outhouses, that will hide them from the house. Often nobody else lives in sight, so it is only necessary to hide from members of their own family, regarding which they are usually not particular.

The children around a place not provided with a privy frequently do not get as far away from the house as the adults, especially the men. It is often possible to determine the number of children in a family by the number of piles of feces in the back yard. In the latter part of the day they are found partially or completely eaten up by chickens, ducks, and dogs, by which it is possible that eggs, if present, are again more widely distributed over the premises.

Many of the men in the country deposit their feces in almost any convenient hiding place near their work. The farm laborer drops his work whenever the desire seizes him, and goes to "the bushes," or the "fence jam," or "the gully" to relieve himself. The coal burner, belonging to the worst infected class of people in the timber sections of many of the southern states, defecates behind stumps near his coal kiln, around which he lies and attends for thirty or forty days, often barefoot. His children play around his working place much of the time, and assist him to pollute the soil and share the results with him. Around saw mills, public works, etc., the laborer usually repairs to some commonly used thicket or hiding place to deposit his feces on the ground. In small towns, where many country people come to market, etc., there is often some nearby thicket, or gully, or barnyard to which the country people go when they get "in a tight," in preference to privies, to which they are unaccustomed, even if they are available. The country people are more or less infected, and they thus convert these resorts into veritable hotbeds of hookworm larvæ. During a rainy spell the barefoot boy who runs around in this locality is sure to cry with ground itch the next few nights. We remember such a ''gully'' near a country town, and, with our present information of the disease and knowledge of the prevalence of it among the country people of that section, we now see ample explanation for the ground itch and anemia among many of the town boys who often went barefoot in warm weather. The most favored parts of the ''gully'' were so much used for this purpose that there often seemed to be no more room.

Many of the country schools are not provided with any sort of a privy, and, often when they are, the latter are not much used, because the children are not accustomed to them at home. Usually in such instances the girls go to one place and the boys to another, chosen by a kind of natural selection. A thick clump of bushes, a gully, or a hollow behind a hill are the places usually selected. A large percentage of the pupils in such schools are often infected. They pollute the soil, which becomes a source of infection and reinfection of all the barefoot children who visit it during a hot, wet spell. We recall many schools and churches in a country in which much hookworm disease exists, where the sanitary conditions were exactly as described. Ground itch was a common trouble, and every boy knew what it was—most of them from oft-repeated personal experiences. The coming of railroads, development of the country, and introduction of people accustomed to the use of privies, and to more general wearing of shoes, has reduced the anemia, once very prevalent, to an appreciably smaller degree.

Miners working sometimes deep underground often defecate in the mine, usually in some corner not being worked at the time. The temperature and moisture are favorable for hatching and development of the infectious larvæ. Mud and water of the mine become infected, and frequently get on the hands and feet of the laborer.

We have seen that, in the case of the class of people who are infected, their feces are pretty widely scattered about where they work and stay. It is only necessary to call attention to the very general practice of these people of going barefoot during the summer. This often is not realized by the city resident, who seldom sees barefoot people. The children go barefoot often until they are fourteen, fifteen or more years old, and often during the warmest weather the adults of the family enjoy this pleasure and saving also. They wear their shoes when they go away from home; so one must see them at home to see them as they really are. In these rural districts where shoes are not so generally worn we have often seen children, and even grown people, walking to church barefoot, carrying their shoes in their hands or on their shoulders. Their Sunday shoes often hurt their feet, which are unaccustomed to shoes. When they get near the church they sit down by the roadside and put on their shoes. These facts will be verified by anybody familiar with the habits and customs of the inhabitants of these remote rural districts where hookworm disease flourishes most.

It must be remembered that the conditions of shade, moisture, and favorable temperature required for the extensive development of the larvæ to the infectious stage occur only a few times a year—during long rainy spells. These wet spells also furnish the condition in which the barefoot individual has more or less mud and water on his feet all day. Those who wear shoes step in mud and water that may run in leaky shoes. If such mud and water contains larvæ, they will reach the foot in this way. The possibility of infection through wet shoes free from holes is suggested by a recent experiment made by Bass. He placed a culture of encysted uncinaria Americana larvæ, grown in a mixture of feces and charcoal, on one side of the arm part of a kid glove that had been soaked in water. On the opposite side he placed some mud made of sterile soil and water. After three hours the mud was removed, and on examination four living and two dead larvæ were found in it. Walking in infected mud would furnish similar conditions, and it is, we believe, possible that infection may occur in this way. It is possibly an explanation of the few cases of hookworm disease in people who do not know of having had ground itch.

It has been seen that experimental inoculation with uncinaria larvæ gives rise to symptoms identically like those of ground itch or dew poison. Ashford and King obtained a history of ground itch in 90 percent of their cases. This condition is not so clearly described technically for the diagnosis to carry with it any clear cut picture or idea of disease to the uninitiated, but every country boy, or man who was a country boy, knows what ground itch or toe itch is, and to him these terms mean a definite clinical condition, which he knows when he sees or feels it. We have not accurate tabulation of our cases with relation to this symptom, but we have made it a point to inquire about it in several hundred cases. We are certain over 75 percent gave a history of having had it. Only mild cases give a negative history, and probably had infections too mild for them to recognize as the ground itch.

We believe we are justified in concluding that the real source of hookworm infection is always the feces of infected persons, and, further, that the only practical mode of infection is by the skin. Walking barefoot in infected mud and water is the chief way in which infection gets to the skin. Probably next in importance is infection through leaky and wet shoes. Other modes of infection are possible, and no doubt do occasionally occur, but comparatively they are of little importance.

CHAPTER V.

PATHOLOGIC ANATOMY AND PATHOLOGY.

The anatomic changes caused by hookworm can be partly studied during life in the blood, and the changes in that fluid will be briefly described in this chapter on account of their close relation to the theories of the disease. The condition of the blood is also referred to in greater detail in Chapter VI, among the symptoms of the disease.

Post-Mortem Appearances.

Skin.—The skin of a hookworm subject is pale, sallow, or even lemon color, and waxy, so that the body may resemble a wax figure. (Ashford and King.)

The body shows varying states of development, as will be described more fully under symptoms. Emaciation is not always marked, as Wucherer noted. The subcutaneous fat is often well preserved, pale, and yellow. The mesentery, omentum, mediastinum, and pericardium are often unusually fat. The muscles are pale, sometimes brownish gray (Ashford and King), soft, friable, and bloodless. All the organs show great lack of blood. Serous effusions, on the other hand, are usually present. They are most frequent and most marked in the abdominal cavity and lower extremities, but general anasarca is also sometimes present. Straw-colored fluid may be found also in the pleural cavities, pericardium, and ventricles of the brain, and there is not infrequently edema of the lungs. Sandwith saw edema of the glottis.

The heart is sometimes small, but generally enlarged, dilated, and with more or less secondary hypertrophy, especially of the left ventricle. The subepicardial fat is often well preserved. Post-mortem coagula may be either soft and red, or pale and gelatinous, and the heart cavities and arteries may also contain pale liquid blood. Accidental valvular lesions are sometimes found; more frequently there are dilatations of the tricuspid and mitral valve from muscular weakness. Sandwith found the mitral markedly changed in 12 percent of cases.

The heart muscle is flabby, pale, sometimes showing small or even large bright yellow areas on transverse section of the papillary muscles.

There is often sclerosis of the arteries, even in young subjects. Similar changes may affect the cardiac valves, especially the mitral. Ashford and King have observed such changes with only slight anemia.

The lungs are bloodless and often edematous, as stated above, and sometimes the seat of hypostatic congestion.

The spleen is usually not enlarged, sometimes small, soft, and with wrinkled capsule. Sandwith found it enlarged in one-third of his cases in Egypt. It is sometimes tough, sometimes friable. In the pulp large numbers of eosinophile cells may be found. (Yates.)

The kidneys are pale and large; the capsule strips easily and shows a mottled anemic surface; the cut section is slightly fatty looking, and often shows traces of parenchymatous or interstitial inflammation and fatty degeneration. The kidneys are sometimes amyloid. Sandwith finds the changes so typical as to suggest the term "ankylostoma kidney." Granular contracted kidneys with cysts are often noted, but are accidental findings.

The liver is usually not greatly enlarged, but rarely smaller than normal, pale or bright yellow, or brownish or greenish yellow, and greasy looking. The tissue is brittle and fatty. Amyloid degeneration is rare. Daniels found an excess of iron-containing pigment, but Gutierrez could not confirm this. Yates, in a severe case, found necrosis about the central veins.

The pancreas shows no constant change. Some authors have thought it enlarged.

The stomach is often dilated, sometimes enormously so, especially in countries where bulky diet is the rule. Chronic gastritis in various degrees is commonly found. Hemorrhagic erosions have been described by Roth. Ashford and King occasionally found hookworms free in the cavity of the stomach, and Gutierrez found several adherent. Butterworth (Journ. Amer. Med. Assn., Aug. 21, 1909) has reported a case in which a large hair cast was found in the stomach of a girl 8 years old severely infected with hookworm.

Intestines.—Sometimes dark red or slate-colored areas can be seen through the serosa, and sometimes, but rarely on the whole, blood may make the intestine look dark. In severe cases of long standing, however, these may not be present, so that Ashford and King did not find even bloody mucus. Apparent contractions, such as Wucherer described, are for the most part accidental, but thinning of the walls is likely to occur in severe chronic cases, and Craig saw almost complete obliteration of the valvulæ conniventes.

In the examination of hookworm subjects for exact scientific purposes it is advisable to make the autopsy as early as possible, and the body should not be chilled, as the hookworms are more likely to remain alive in the warm body. The inspection of the intestines should be made first, after opening the body. The intestine may be ligated in small lengths, and each length opened in a vessel of warm water. The sections of intestine may at once be placed in preserving solutions, and the contents of the intestine, with the warm water in which the gut was opened, examined for free worms. In the majority of cases it is enough to open the intestine carefully on a flat surface and spread it out for inspection before washing it with water.

The contents of the duodenum, jejunum, and even the ileum are sometimes blood-stained. Besides the blood and the usual material, there is an excess of mucus, worms, and ova, and Charcot's crystals.

The mucosa is often covered with thick tenacious mucus, sometimes stained red to chocolate color by blood. The Peyer's patches and solitary nodules are often swollen. Ecchymoses and small erosions are frequent in the experience of most observers, varying from 3 to 4 millimeters in diameter or even larger. In some cases they are very numerous, giving a speckled appearance to the mucosa, as Whipple states. The lesions are usually the same level as the surrounding tissue, but may be swollen, as in the frontispiece. In the midst of the red area is a small pale elevation, at the summit of which the worm may be seen adhering, or the hole caused by its bite after the worm has fallen away. There may be considerable dark red or slate-colored pigmentation around the lesions, from old congestion and hemorrhage, and dense induration of the wall. Strong, and also Yates, found extensive eosinophile infiltration in the mucosa, submucosa, and even the muscular coats.

The hookworms are found in various parts of the small intestine, from the stomach to the lower ileum. Ashford and King found most in the upper and middle part of the jejunum; Allen J. Smith in the duodenum, jejunum, and upper part of the ileum; Tenholt in the lower part of the small intestine; Sandwith within 2 meters of the pylorus, as a rule—the lowest 6.30 meters. In one case he found 1,353 out of 1,524 worms in the first two meters of the gut.

They are found free or attached, varying much according to circumstances. Sandwith in one case found "217 out of 863 worms attached to the mucosa; 645 were free, 16 were alive, and one couple in copulation." Ashford and King and their colleagues in Porto Rico did not find many attached. In one case they found 83 in the stomach ("possibly dislodged in the manipulation"), 163 in the duodenum, and the rest in the jejunum. In some cases very few worms are found at autopsies; Sandwith, in a case with six bites in the jejunum and ileum, could find no worms. As regards position of the worms in the intestine, Sandwith suggests that in old cases the duodenum is riddled from former bites, so that the villi get "eaten away" and the worms prefer the jejunum. He found 6 cases out of 18 with less than 10 worms, no thymol having been given previously. O. Baker explains the small number of worms sometimes found post-mortem on the analogy of rats leaving the sinking ship—not without reason, as some other helminths seem to leave their quarters in case of severe illness of the host. Sandwith suggests that in severe cases the "half starved worms are dislodged by purges or repeated attacks of diarrhea."

The ecchymotic spots mentioned above are in some cases up to 1 centimeter in diameter, or even the size of a silver dollar. In the center of the hemorrhagic spots the worms are frequently found—the head and sometimes half the body buried in the mucosa. The males especially are frequently found almost buried in the mucosa, so that when removed, an operation often requiring considerable force, long narrow depressions mark their former positions. Sometimes there are minute holes, like pin-pricks, in the red areas. Many of the hemorrhagic areas are without worms, but show minute erosions or ulcers ½ millimeter in diameter. Though many observers have found numerous hemorrhages, it must be emphasized that they vary. Fearnside found congested areas in 60 percent of 78 cases. Whipple found hemorrhages often. Looss found the worms attached without hemorrhages more often than not, and he found hemorrhages especially in recent cases. Ashford

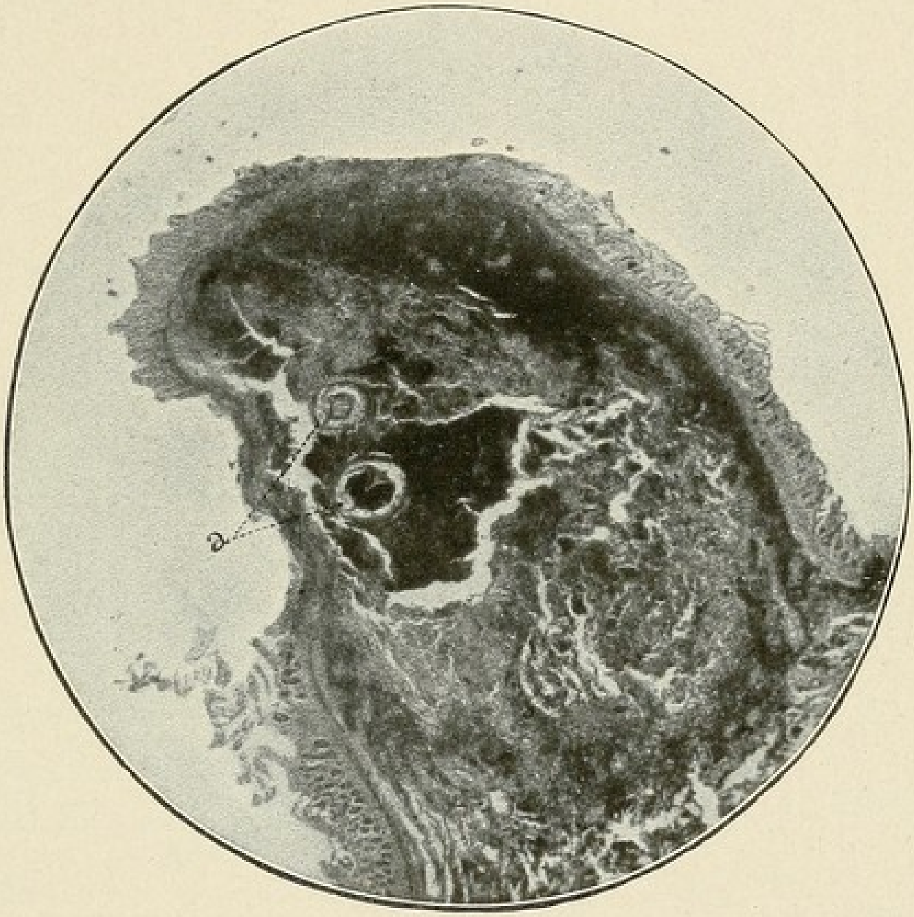

Fig. 28. Blood cyst below the mucosa of the jejunum, with cross section (a) of included hookworm. (After Whipple.)

and King say (1904): "In our autopsies the feeding ground of uncinaria Americana can easily be passed over without being noted."

Although one might expect the hemorrhages to be in proportion to the number of worms, there are reasons for anticipating variations from a simple ratio. Usually there are many more bites or lesions than worms. Sandwith found 250 worms and counted 575 bites in one case. Leichtenstern pointed out that young ankylostoma change their position more frequently than old ones. Like other helminths also, coitus is likely to be associated with change of location, and active ovulation with voracious feeding, possibly also with migration.

From the time of Bilharz, cysts in the submucosa, containing blood, have been described. Whipple found them not infrequently, measuring 5 to 10 millimeters in diameter, and gives photographs of sections. He also found hookworms in the cysts in 7 cases. The colon sometimes contains tarry feces.

Among rare findings in the intestine may be mentioned the perforating ulcer of the duodenum, described by Williams. Wucherer noted adhesive peritonitis; amyloid degeneration of the villi was seen by Bäumler.

Other parasitic worms are not rarely found in cases of hookworm infection, especially ascaris, oxyuris, trichiuris, and anguillula. Ameba and other protozoa are not rarely present in tropical and subtropical countries, including the southern United States.

The bone marrow is pale, sometimes lymphoid and grayish red; sometimes gelatinous or fatty. In the lymphoid marrow nucleated red cells and other evidences of increased blood formation are present.

The mesenteric glands are often hyperemic and enlarged, and reach a diameter of 2 or more centimeters.

The hemolymph glands were found by Gutierrez as large as hazelnuts, of the type of splenolymph glands.

Edema of the brain is not uncommon in severe cases. Meningitis has been observed sometimes, with extensive effusions into the ventricles, as in the child of 9 years, described by Ashford and King, dying with 8 percent hemoglobin and 720,000 red corpuscles per cubic millimeter.

The changes in the blood, in general, in cases that come to autopsy are as follows: pale color, watery consistency, so that the blood may resemble blood-streaked serum. It coagulates slowly and imperfectly. The specific gravity is reduced. The total bulk, according to Boycott and Haldane, is increased.

The hemoglobin varies from a point too low to read in the ordinary apparatus to about 50 percent.

The number of red cells is reduced, but less in proportion than the hemoglobin, so that the color index is low. There are rare exceptions to this. The red cells vary in size and shape. Polychromatophilia, normoblasts, microcytes, and macrocytes, but rarely megaloblasts, occur.

The leucocytes are usually increased, from twice to several times the normal, in cases of comparatively short duration. In older and very severe cases there is sometimes leucopenia of moderate degree. The leucocytes are chiefly remarkable for the increase of eosinophile cells, but the proportion of them varies very much—up to 72 percent, as in a case of Leichtenstern, and in severe cases, near the end, may be about normal or even lower.

The blood changes in hookworm disease, in brief, are those of secondary anemia plus eosinophilia. The statement so often made, that the blood resembles that in pernicious anemia, is based on imperfect knowledge of both conditions, and has come down from a time when the blood was examined much less minutely than at present.

Pathology.

The relation of the hookworm to the various anatomic and functional alterations in hookworm subjects is not yet thoroughly understood. The nearest and simplest explanation is that the worms cause great and sometimes protracted loss of blood, and that this interferes with nutrition in many ways directly and indirectly, including degeneration of the walls of the blood vessels. The fact that in some cases with severe symptoms only a few worms can be found, and the additional fact that even the worms found do not all or always contain blood, have led to a partial or complete rejection of this explanation, so that others have been advanced. It is therefore necessary to examine the facts and assign to them their probable relations. That the worms cause hemorrhage can not be doubted by any one who examines a number of worms, or who is able to make an autopsy on a case that has not had too protracted a course. Such a report as the following, from Ernst (1888), leaves no doubt as to the presence of blood in the intestine: "On the mucosa of the small intestine is an unusual amount of tenacious mucus, which even in the upper meter's length shows a reddish color in some places; the color becomes more intense lower down, so that at a distance of four meters the contents are a uniform dark chocolate brown tenacious mass, the color evidently due to blood. From two meters below the beginning the mucosa shows numerous petechial ecchymoses."

Such conditions are doubtless rare, though among reported cases they are not so rare as the cases of advanced anemia examined by the Porto Rico Commission without finding blood or ecchymoses in the intestine, or blood in the worms. Most observers, like ourselves, find many or most of the worms in any lot, especially the females, stained and sometimes stuffed with blood, so that they look deformed when fixed in preserving fluids that cause much contraction. In the dog hookworms practically all the worms contain blood. The absence of blood from the worms does not prove that the parasites did not suck blood, for the ejection of blood has long been known, having been graphically described by Ernst and Leichtenstern. These observers noted in living ankylostoma how "the gradually dying, but moving, worms threw out of their mouths at intervals clouds of red blood corpuscles, like a locomotive puffing out clouds of smoke." Leichtenstern saw this process especially in worms from acute cases, with severe anemia and rapidly ensuing death.

Whipple more recently writes that it is "unusual not to find a few worms containing blood when the autopsy has been performed within two or three hours after death." "When worms full of bright blood," he says, "were removed from the intestinal mucosa and placed in water or 0.8-percent saline solution, they soon discharged the blood. Under the microscope one could watch the red blood cells and blood-stained fluid being poured out from the mouth and anus. This explains the fact that worms found in the feces or at an autopsy performed several hours after death may contain very little or no fresh blood."[1]

The structure of the worms indicates that sucking is an important function, and it seems certain this must have the purpose of sucking fluid. If the worms fed mainly on epithelial cells, as will be discussed below, they would hardly bury themselves so deeply, nor suck into their alimentary canals such masses of tissue as have been described by Looss and others. The fluid, then, must be either blood or blood plasma, or such other body juices as can be obtained in the wall of the intestine. If the worms do not use blood as food, it seems strange that they do not exercise more selection and reject it at once. The process described by Whipple is not, of course, to be considered as a wholly natural one. Even if, as Looss points out, the blood cells in the worms' intestines are not digested, it may be questioned whether the observations on that point are final. The observation quoted from Ernst and Leichtenstern suggests that the blood corpuscles are not chiefly desired, but the plasma, the digestion of which is much more difficult

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[1] Whipple, G. H.: "Uncinariasis in Panama," American Journal of the Medical Sciences, July, 1909.

to observe than that of the cells. Whipple calls attention to the worms living in "worm cysts" in connection with the matter of blood-feeding. In these cysts the worms live for several days and remain vigorous. When the mucosa is fairly normal, as Whipple says, it is reasonable to suppose the worms feed chiefly on blood. When the mucosa is anemic, thickened, and infiltrated, the worms may live chiefly on the epithelium and mucosa.

Even if the worms live wholly on blood or blood plasma, the loss due to their feeding in a short time would not need to be very great. According to Lutz' estimates, 1,000 worms, a number often present in a single case, weigh 4 grams. If each worm took its weight of blood—not perhaps an inordinate amount—the loss at one time would be trifling, but, repeated day after day, might easily be of consequence to the host. It would not be so to a well-nourished individual, consuming much more than his need of blood-forming food, but to one living close to his margin of nourishment, or with gastro-intestinal disease that limited nutrition, or with insufficiency of the blood-forming organs, it would before long lead to a definite anemia.

But the loss of blood is greater than the greatest need for food on the part of the worms. As was stated above, the worms bite often and in various places. They cause a flow of blood that can sometimes be recognized in the stool by the naked eye, or by chemical tests, and that can often be found post mortem. There is evidence that worms themselves produce a substance that furthers the hemorrhage. Sabbatani had suggested that in many, perhaps all, blood-sucking animals such substances exist. A. J. Smith predicted their occurrence in necator. L. Loeb had shown that the intestinal mucous membrane and the mucus covering it have a strong effect in accelerating coagulation, so that ordinarily bites like those caused by hookworm should not bleed much. Loeb and Smith found that ankylostoma caninum produce a substance that delays coagulation; usually for many hours, sometimes for twenty-four hours or longer. The substance was found especially in the anterior half of the bodies of the worms, but it could not be determined where it was produced—in the glands of the head, neck, or esophagus, but probably the esophageal glands, as suggested by Smith, or the head glands. The large size of these glands suggests an important function. Control experiments with round worms and a tenia were negative—in fact the coagulation was accelerated by the products of the worms in question. Liefmann investigated with reference to the presence of a substance inhibiting coagulation in ankylostoma caninum, but found none in two out of three observations. He thought the inhibition was brought about by the co-operation of peptone and pancreatic secretion. Loeb and Smith (1906) deny this latter, for various reasons not necessary to state. They admit that there may be variations in the amount of the coagulation-inhibiting substance in different worms and in different lands. Loeb and Smith also found the substance was weakened by boiling.

From the biting and sucking, and the accidental hemorrhages, there is a loss of blood in hookworm disease that varies with the number of worms and their age and activity. The loss will affect the host partly in proportion to its extent, but partly in proportion to his resistance to the flow of blood from the bites, and partly to his power to make new blood. The larger the number of worms, and the less active the host's nutrition and blood-formation, the more rapidly and more severely will anemia follow.

The process is not unlike that seen in some cases of bleeding hemorrhoids or gastric ulcer, or other local diseases with oft-repeated hemorrhages. In these we got blood changes much like those of hookworm disease—practically identical in fact, with the exception of eosinophilia—low hemoglobin, low color index, increased water, or so-called chlorotic blood changes, poikilocytosis (with variations in the size of the red cells), and sometimes normoblasts, but rarely megaloblasts. Puffiness of the subcutaneous tissue, or even dropsy and anasarca, follow as the result of the hydremia. Nutrition suffers in many respects—partly due to the anemia and partly to the consequent malnutrition of the blood vessels.

Even the more severe changes can be explained on the ground of prolonged loss of blood. Compensation is maintained as long as possible, but, when the loss of blood continues too long, the blood-forming organs may react as they do in pernicious anemia or in so-called aplastic anemia, from perversion or paralysis of their functions.

The existence of hemolytic toxins has been assumed very often in hookworm disease on account of the discoveries in bothriocephalus anemia. But the blood changes in the case of infection with the broad tape worm are very different from those in hookworm disease—so the analogy is not a good one.

Gabbi and Vadala (1903), Goldmann, Preti (1908), and others have asserted the production of hemolytic poisons by hookworms. Allesandrini thought glands in the anterior part of the body produced hemolytic poisons that caused hyperemia. Romani, who has done much experimental work, found the serum of ankylostoma subjects hemolytic to chickens and rabbits, but not to normal or anemic human subjects. He even found the red blood cells of ankylostoma anemia more resistant to rabbit serum than those of healthy men, but, on the other hand, the blood serum of ankylostoma subjects injected into the veins of rabbits produced toxic symptoms and hemoglobinuria in smaller doses than the serum of healthy men.

Loeb and Smith (1904) found no evidence of hemolysis in extracts of dog hookworms (ankylostoma caninum).

Whipple points out some of the difficulties in the way of accepting the idea of hemolysis from the conditions in the blood cysts already mentioned, and shows the need of wholly new experiments in order to prove the hemolytic theory. As he points out, the worms often "remain in

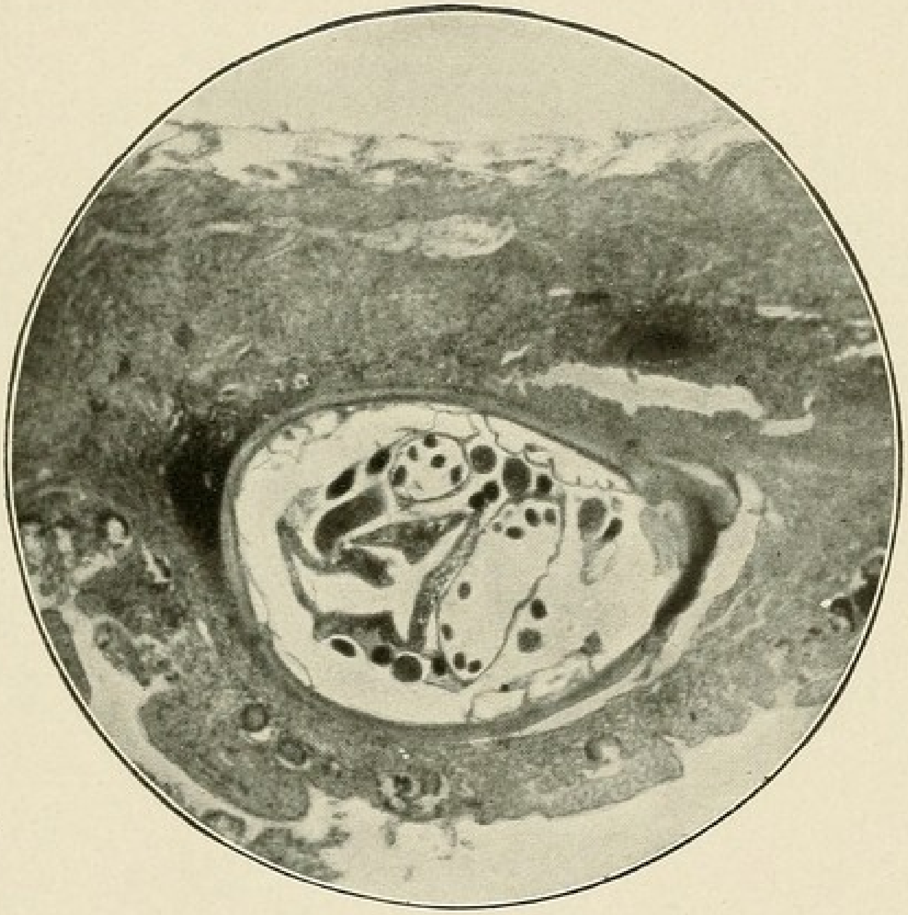

Fig. 29. Hookworm in the submucosa, with very little extravasation of blood. Cross section of the body of a female worm. (After Whipple.)

these submucus blood clots for a few days at least. The worms are not injured by their stay, yet there are well-preserved red blood cells in all parts of the cysts." The worm, therefore, "causes the loss of more blood through damage to the mucosa than it can hemolyze under favorable conditions. It does not seem likely, therefore, that this same worm could secrete a hemolytic substance which, taken up by the human intestine, could act on the circulating blood, where conditions would be less favorable for hemolysis than in the blood cysts.'' Whipple has also shown that the worms contain a very weak hemolytic principle which is active in vitro, but is demonstrable only in concentrated extracts of the hookworm. Hemolysis takes place very slowly, very little being observed in six hours. The hemolysin is present in all parts of the worm, and probably is related to its alimentary canal and its digestion of the host's blood. Whipple's observations on hookworm were controlled by experiments on various other worms, dog hookworm, whip worms, and round worms. His negative findings confirm those of Loeb and Smith.

Preti claims to have discovered a hemolysin in the old world hookworm, not soluble in saline, but freed and made soluble in water by trypsin. He believes the substance is similar to that of bothriocephalus latus, but, as we have said before, the blood changes in the two conditions are so dissimilar that further proof and control observations are much needed.

The pigmentation of the liver and spleen have been looked upon as evidences of a hemolysin secreted by worms and absorbed by the host, but, as similar changes occur in many secondary anemias—tuberculosis, for example—the pigmentation can not be looked upon as proof of a hemolytic poison.

It is necessary to discuss the other effects of the hookworms upon the intestinal wall. Besides blood, the worms are supposed to eat mucus—in fact, Sangalli believed that to be their normal food.

Looss has shown a much more important source of food—the intestinal mucosa itself. He points out that the worms do not merely bore into the intestinal wall, as if for the purpose of applying suction, but that they cause an actual defect in the tissue. The mass of tissue, then, drawn into the esophagus, as shown by the beautiful photographs of Looss and the Porto Rico Commission, is not mucosa alone, but largely submucosa, a plug of which reaches far down the esophagus or even into the intestine, in which it can be seen to break down into its histological elements. "The latter form the exclusive contents of the intestine in the ma-

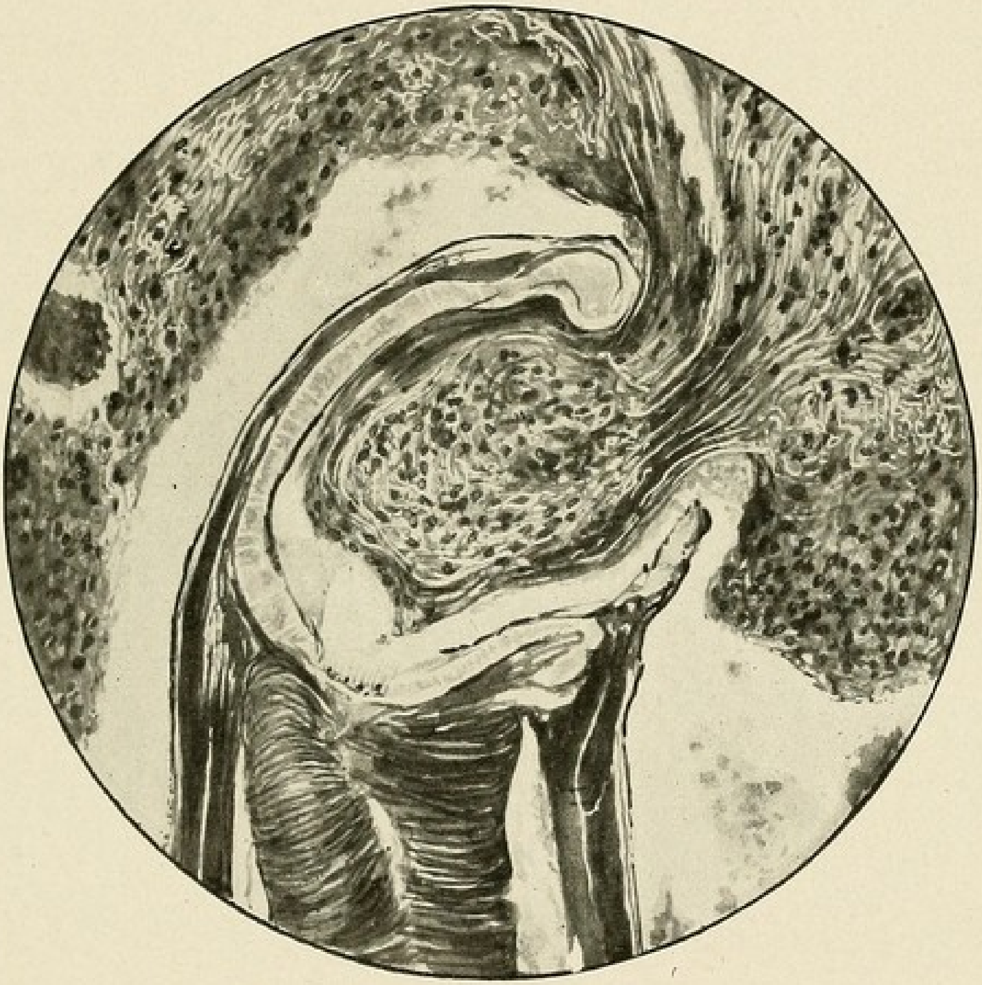

Fig. 30. Photomicrograph of uncinaria Americana sucking mucosa. By the late Dr. W. M. Gray, Washington, D. C., from the report of the Porto Rico Commission, 1906-1907.

jority of cases; in others there is an admixture of blood, which varies from a few blood cells to pure blood. A perfect digestion of these corpuscles does not take place; the nuclei retain their tinctorial qualities unchanged, and only the plasma becomes more or less cloudy. Accordingly, the intestinal mucosa itself is the food of the ankylostoma; the worms eat into it, and, if thereby they accidentally meet a blood vessel, the wall of the latter becomes eroded. The blood that flows out is partly swallowed, the rest escapes beside the worms, forming the well-known hemorrhages." (Looss.)

It is important to realize the difference between epithelial cells only and the mucosa, including the submucosa, which

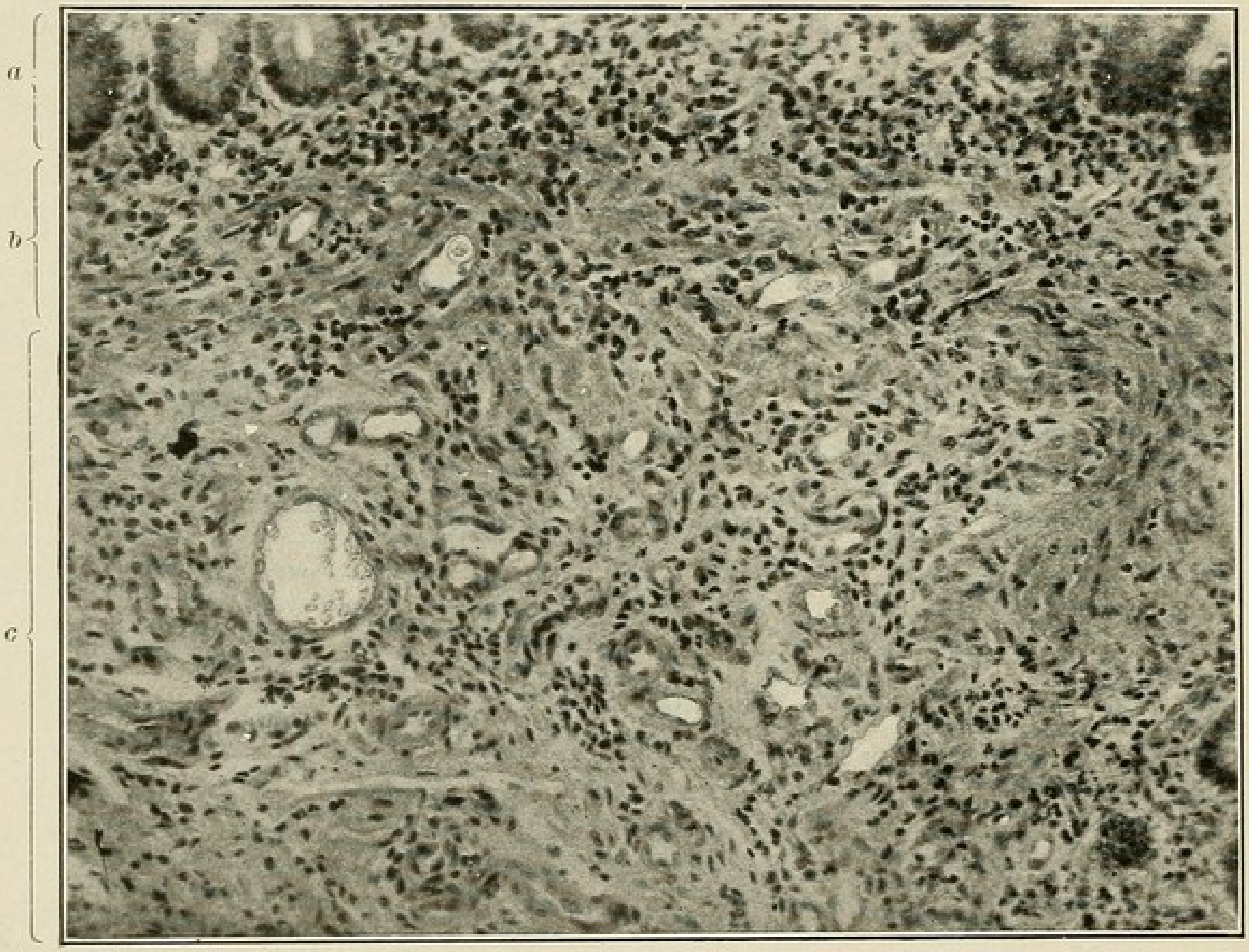

Fig. 31. Jejunum in a fatal case of uncinariasis, showing extensive scarring and inflammation of the intestine. *a*, Bases of crypts of Lieberkühn; many polynuclear leucocytes in the interglandular tissue; *b*, muscularis mucosæ distorted and scarred, invaded by many wandering cells, many of them eosinophiles; *c*, submucosa, which is much thickened and full of every type of cell—eosinophiles, polynuclears, and "polyblasts." There is much scar tissue; new-formed blood vessels are seen. (After Whipple.)

Looss thinks forms the food of the worms, and we doubt if the process as described takes place as often as mere blood-sucking. If it did, one would expect to see much more serious defects of the intestinal walls in cases with, say, 1,000 or 1,500 worms, and we should expect to see the worms destroying or undermining the mucosa, like ameba, but on a larger scale.

An event that must be of greater importance than the consumption of mucosa by the worms is the infection of the bites. This was first emphasized by Allen J. Smith, who wrote in 1904:[1] "It is possible too . . . that these lesions may fail to heal, and from infection by pyogenic organisms become ulcerated, small follicular ulcers, with a marked zone of hyperemia, thus being produced. These sometimes run together to form irregular linear ulcerations in the mucous membrane." The possibility of toxic absorption from such ulcerative lesions can not be ignored, and Smith went on to say that the type of anemia and the failure to find hemolytic poisons "by no means set aside the idea of a toxin having widespread and important interferences with the integrity of the general tissues and of the nutritive functions of the host."

Whipple believes that the "anemia may be due to the poisonous products absorbed from these foci of inflammation in the intestine," and that this explains the fact that some cases with relatively few uncinariæ may show a profound or even fatal anemia. The case he cites in this connection is most instructive, and we quote it in full, with Whipple's deductions:[2]

"A male Jamaican negro, aged 60 years, shortly before his death had 15 percent of hemoglobin. There was nothing unusual about the gross pathology of the viscera. The tissues were all very pale. The heart was greatly dilated, with watery, pale clots—hydremia. The lungs were pale and cushiony. The liver and kidneys showed a definite yellowish brown pigmentation and anemia. The bone marrow was very firm, pink, and cellular. The jejunum con-

[1] "Uncinariasis," International Clinics, vol. 2, 14th series, 1904, p. 82.
[2] Whipple: "Uncinariasis in Panama."

tained between 100 and 200 hookworms, but the types were not identified. The mucosa was very pale and smooth. There were no notes concerning the presence of fresh blood in the worms, and no notes regarding ecchymoses. We can not assume that the worms were discouraged by the anemia, abandoned the mucosa, and were carried out in the feces, for we find cases with even greater anemia and many hundreds of worms in the intestines. Microscopic sections of this jejunum are most interesting. (Fig. 31.) The mucosa shows rather short villi and crypts, with a little distortion of the architecture of the glands, due to an increase in connective tissue. The interglandular tissue in the villi and at the base of the gland tubules shows a marked infiltration with polymorphonuclear leucocytes and eosinophiles, which in some fields are more numerous than the mononuclears. The muscularis mucosæ is thickened, scarred, and infiltrated with wandering cells of all types. The submucosa is thickened and scarred. It is not sharply separated from the muscularis mucosæ, and many polymorphonuclear leucocytes and eosinophiles are present. Accumulations of large mononuclear wandering cells are found about the vessels in the submucosa. The outer muscle coats are normal. This is a very definite pathological change, a picture of diffuse inflammation, evidently of some duration, due to the hookworm, as evidenced by the eosinophiles.

"When one considers the amount of tissue which was involved in this change—several feet of the jejunal mucosa—it is not difficult to account for an advanced anemia. Perhaps the same explanation may hold for the liver necroses which were present in this case, and similar to those described by Yates in a fatal case of infection with the new world hookworm. Many of the liver lobules show a necrosis of the central half or third, where the liver cells are quite hyaline, and wandering cells are invading such areas. The other liver cells show some fatty infiltration and a deposit of a finely granular, yellow pigment."[1]

Many efforts have been made to isolate the poison of hookworms, but hitherto without results of value.

Lussana first thought he demonstrated a toxic action by experiments with the urine of ankylostoma patients in animals. Rabbits so treated developed anemia. Arslan got similar results. But such experiments are very crude, and do not permit definite conclusions, so that it is not surprising to learn that Crisafuli and Aporto got similar results from the urine of healthy men or from those with intestinal disease. Vannini found the urotoxic coefficient higher at the height of the disease—0.88—than after treatment, and a gradual fall to 0.422, but this is equally inconclusive.

Besides poisons that may be produced in the lesions in the intestine, it is possible that the decomposing blood excreted by the worms or flowing from the bites may play some part in the chain of events.

To summarize this part of the subject, we suggest:

1. That hookworms cause loss of blood by sucking and subsequent hemorrhage; that this alone produces the anemia in many cases.

2. That infection of the bites is an important part of the pathology of hookworm disease, and may be the most important, either from the number of the lesions or the severity of the subsequent bacterial infection.

3. That other toxic processes may play a part, but at present they have not yet been proved to exist.

Secondary anemia and toxemia are the only conditions that could cause the symptoms in all but advanced and complicated cases, and nevertheless permit the rapid recovery that follows in such cases on removal of the worms. In

[1] In some cases an actual mixed infection takes place. Sabrazès has reported a striking example of this. (Arch. de Méd. expér., 1907, p. 85.)

these it is obvious that the lesions in the intestine are not such as could account for the anemia, for in that event, though compensation could occur, it would hardly be so closely related to causal treatment and so rapid as the improvement that follows thymol.

Anemia, with its important effects on all nutritive and metabolic processes, including oxygen metabolism, explains most of the striking features of hookworm disease, such as the physical and mental weakness; it predisposes to other diseases, and renders the patient more likely to succumb to those that affect the circulation when they occur as complications. It may explain the lack of development occurring in early life, though this is probably due even more to the local lesions in the intestine. A specific influence on development can not be either asserted or denied, but it is very desirable that investigations along the lines suggested by Dr. I. I. Lemann in a case to be reported be carried out in proper cases.

The cause of the eosinophilia is almost certainly to be ascribed to a toxic action by the worms, but whether it has any relation to the other suspected toxins must be left to future observations.

CHAPTER VI.

SYMPTOMATOLOGY.

There is probably no disease in which the symptoms are so variable in degree as in hookworm disease. This is to be expected when the mode of infection, which is fully discussed in another chapter, is understood. It is certain that every worm that enters the body of an individual comes from without, and that a patient can not directly infect himself, because the eggs can not hatch in the intestinal canal. The number of worms that may get into an individual depends on several very variable factors and conditions, and, in fact, frequently on accident. It follows, therefore, that the number of worms present may vary from one up to the lethal dose for the individual patient, which frequently runs up into the thousands. Immunity, both racial and individual, also contributes to this variability of symptoms. Fatal cases, in which only ten or twelve worms were found at autopsy, have been reported, and other cases have been reported that expelled over 4,000 worms, followed by complete recovery. A frequent source of variability of symptoms is the presence of associated diseases that produce more or less anemia themselves.

The symptoms of hookworm disease are due to loss of blood and the effect of a toxin which may also be capable of destroying blood. This blood destruction results in anemia of variable degrees, and this, in turn, gives rise to other symptoms, the direct result of long continued loss of blood. In fact, we question whether the symptoms of hookworm infection may not all be attributable to this, except possibly the eosinophilia so frequently seen. Certainly all the most prominent symptoms are attributable to this cause.

Before taking up the description of symptoms in detail, we want to impress on the reader as forcibly as we can that a great many cases of hookworm infection present no symptoms that can be recognized as variations beyond the

Fig. 32. Mother and three children, subjects of hookworm disease. Prematurely old mother; youngest child also infected. (Photograph furnished by Dr. C. C. Thompson, Columbia, Miss.)

normal. If, however, these patients with no recognizable symptoms are cured of their worms, though often very few are present, they frequently gain five or ten pounds, feel better generally, and even show improvement of blood count and hemoglobin. Recently we carefully measured and weighed fifty-six grown men with hookworm infection so mild that they could not have been diagnosed or even suspected without a fecal examination. Many of them had so few ova in their feces that none could be found until the specimens were centrifuged. We also weighed and measured one hundred and twenty-nine men of the same class who had no infection. The infected averaged eight and one

Fig. 33. Family with hookworm disease of moderate intensity. (Photograph furnished by Dr. W. A. Dearman, Purvis, Miss.)

quarter pounds lighter and two and one-third inches shorter than the uninfected. It is not improbable that many of the infected had had greater infection in earlier life, and therefore we can not conclude that the average of weight and height below that of the uninfected was due to mild infections altogether. A medical student, 25 years old, under our observation expelled twenty-two worms from one

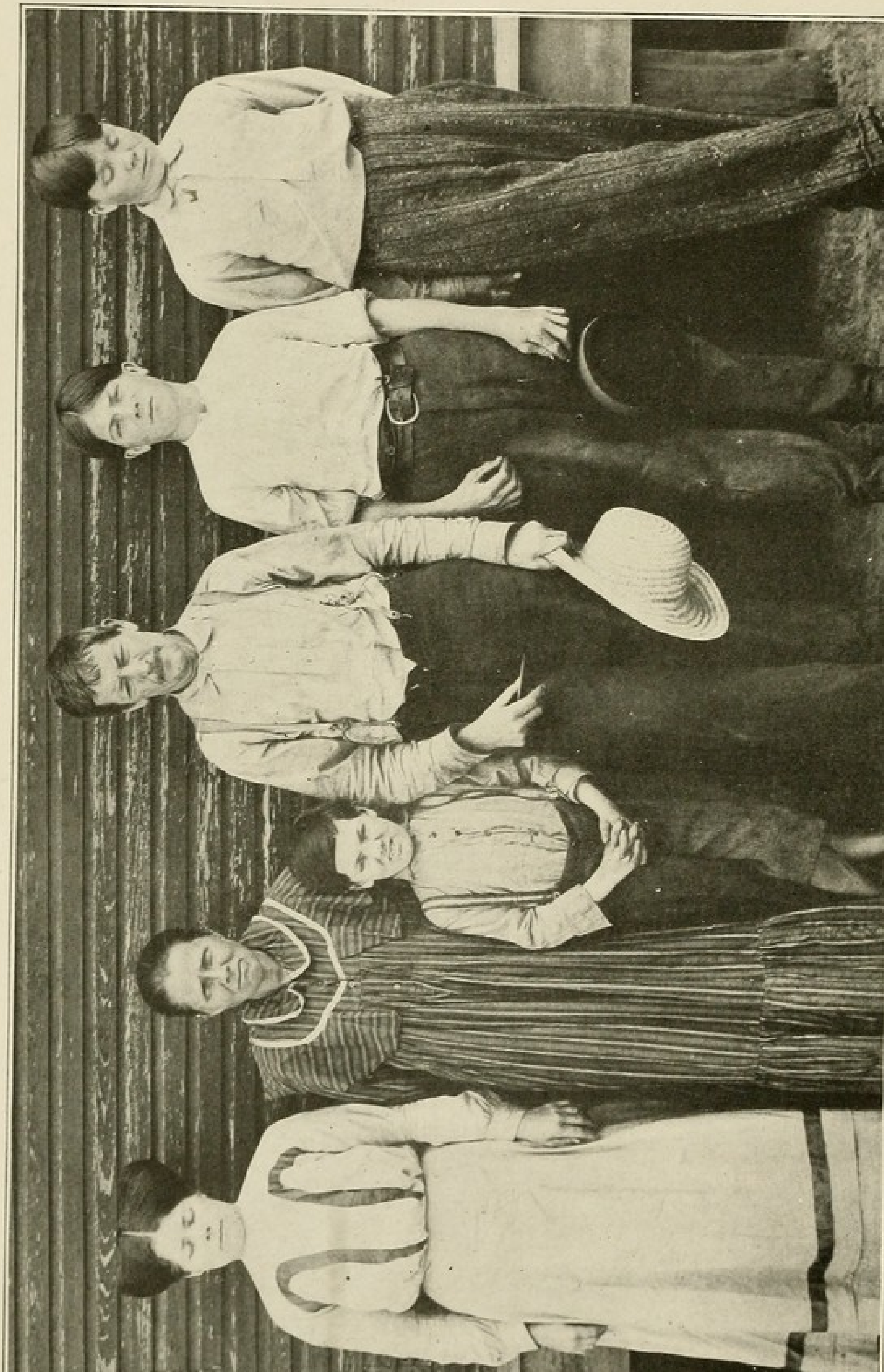

Fig. 34. Family affected with hookworm. Parents dwarfed; father almost beardless; children less severely affected by reason of settling up of the country. (Photograph furnished by Dr. C. C. Thompson, Columbia, Miss.)

course of thymol, after which no more ova could be found. He was then as heavy as he had ever been in his life—one hundred and thirty-seven pounds. In thirty-seven days he gained nine pounds, and felt more vigorous and more like studying than he had in his recollection, though he had never been sick. In fact, he said the present treatment was the first dose of medicine he had ever taken. Such a patient can not be said not to have had symptoms, but they were not recognizable. The slight diminution of weight and vigor, though certainly present and caused by the infection, was within the normal variation.

Another student had a hemoglobin percentage of 100 and was as red-faced, healthy looking, muscular a man as was in the class, and played on the football team as a star. He had so few ova in his feces that it was necessary to use the centrifuge to make the diagnosis. Two months after treatment he weighed five pounds more than he did before, but saw no difference in himself otherwise. Many of the mild cases have slight reduction of hemoglobin, but so many other things may cause the hemoglobin to fluctuate within normal limits, and the practical methods of estimating hemoglobin are so crude, as to prevent recognition of this symptom in the mild cases. A reduction of hemoglobin 1 or 2 percent could not be recognized, though actually present and caused by the infection. Ten or 15 percent would be considered within the normal limits. In fact, the clinical methods of estimating hemoglobin permit a variation of at least 10 percent from technical inaccuracy.

With our present methods of recognizing the symptoms, we would have to say that many of these mild cases have no recognizable symptoms and can not be said to have hookworm *disease*. They are classed as hookworm carriers, but, as we have repeatedly seen, many of them improve in weight, feeling, appearance, and hemoglobin after getting rid of what would be considered an insignificant infection. We must, therefore, conclude that such cases have symptoms, but that they are so mild as to be unrecognizable. The insidious and chronic nature of the disease prevents the

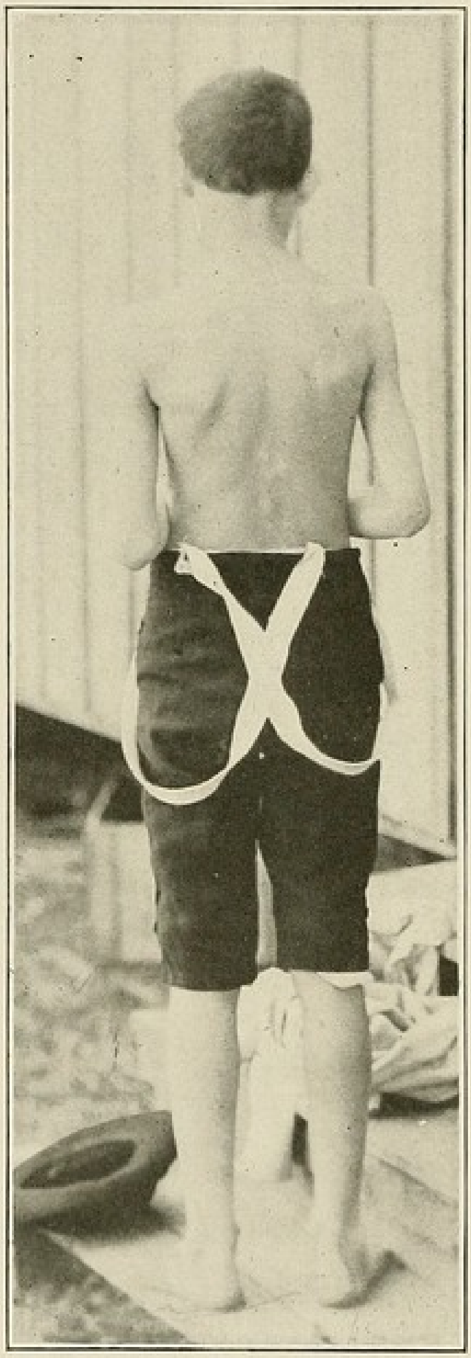

Fig. 35. Hookworm case of average severity; subject 13 years old. (Photograph furnished by Dr. H. H. Ramsey, Darbun, Miss.)

patient from recognizing that his health is impaired. He often is healthier in every way than others who are well, so far as can be determined. One of the symptoms frequently seen in very mild infections in adults is mild digestive disturbance, such as slight reduction of digestive ability, tenderness, and pain and discomfort in the epigastrium. These come on so slowly, and often have lasted so long, that the patient does not recognize them as symptoms

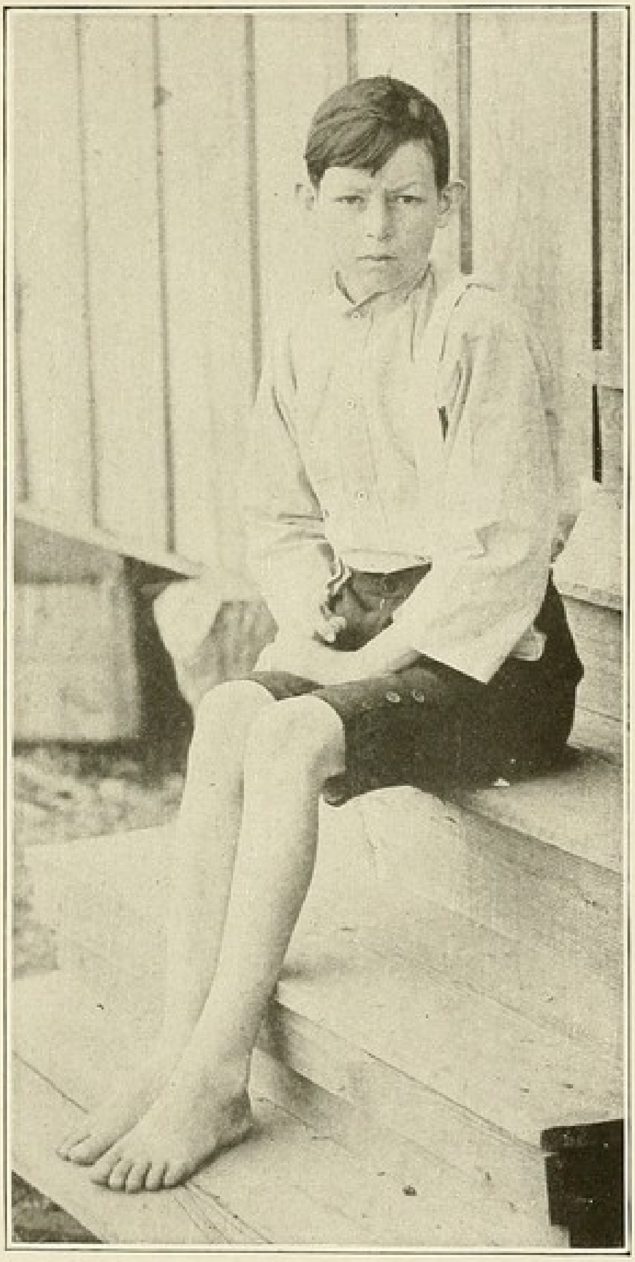

Fig. 36. Same subject as Fig. 35. Shows slight edema of face and expression of illness. (Photograph furnished by Dr. H. H. Ramsey, Darbun, Miss.)

of disease, but considers them natural. Let such a patient be cured of his worms, and he notices at once the change. This type of the disease in which the symptoms are too mild to be recognized when looked for is usually caused by a small number of worms, but occasionally as high as two or three hundred worms may not produce recognizable symptoms. Adults who have ceased growing have seemed to us more susceptible to the effects of a few worms than vigorous, rapidly growing children. We are unable to say whether negroes may present this type, but it is quite cer-

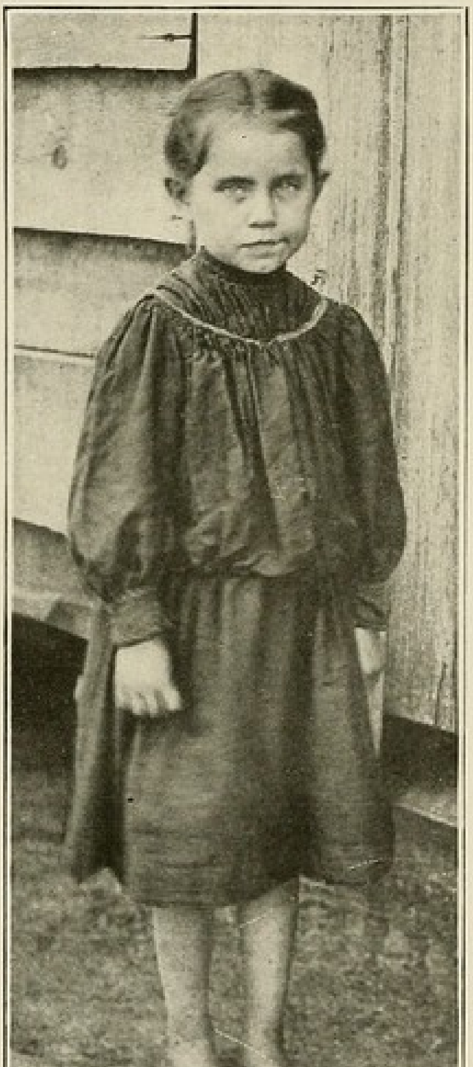

Fig. 37. Seven-year old girl with hookworm disease. Small for age; edema of face. (Photograph furnished by Dr. H. H. Ramsey, Darbun, Miss.)

tain that the small reduction of hemoglobin could not be recognized on account of color. Their reputed relative immunity makes it probable that it would require a greater number of worms to produce the same amount of anemia and other very mild symptoms. This very mild type of the disease is, we believe, the most common in this country, except in the heavily infected regions. Even in the latter there are many of this type among the adults and the better class, who are less exposed.

A mild type of the disease is next most common in this country. In badly infected sections there are many who

Fig. 38. Hookworm case of average severity. Low stature, sloping shoulders, no mammary development, large abdomen; cachectic face and prematurely old expression. (Photograph furnished by Dr. H. H. Ramsey, Darbun, Miss.)

show only moderate pallor, lowered vitality and energy, and, though they are not considered sick, their hemoglobin reading may be as low as 60 or 70 percent. Children with this type of the disease grow a little less rapidly than their fellows. A comparison of the weights and measurements of several of this type of a given age with a corresponding number of uninfected children of the same age always shows the former are under weight and under size. They are a little later in reaching puberty. Even this type seldom consults the physician for symptoms due to the disease, and the diagnosis is often missed when they do come under observation, unless hookworm disease is suspected and an examination of feces made. Physicians practicing in hookworm districts who are fully aware of the presence of the disease in their practice, and who have diagnosed and treated severe cases of the disease, usually have no correct idea of the prevalence of the disease of this and the very mild types. They often discuss with pride their having discovered so many cases of hookworm disease, usually relatively very few, in their practice, when, as a matter of fact, more than half of all of their patients have the disease, either alone or associated with other conditions. In one instance we know of, a cotton mill physician had treated several cases of severe hookworm disease in the past two years, and thought himself quite expert when he diagnosed two cases in mill employees. About that time the manager read in a newspaper that hookworm disease was the cause of laziness, and, believing that all of his employees presented this one of the symptoms, he summoned the physician to examine the sixty-two boys and girls for hookworm disease. He decided, after looking at them all, that the two cases already diagnosed were all there were in the mill, and thought it unnecessary to examine the feces of any more of them. They decided, however, to send specimens from all of them for examination, regardless of the doctor's negative diagnosis, and of the sixty-two there were found fifty-six infected. Many of them were, of course, very mild cases, but that not a few were more pronounced is indicated by a letter from the manager four months after treatment of the fifty-six cases, in which he says: "The time keeper had been absent nearly three months on account of sickness in his family, and on his return he found that many of the children had changed so much he often had to ask the

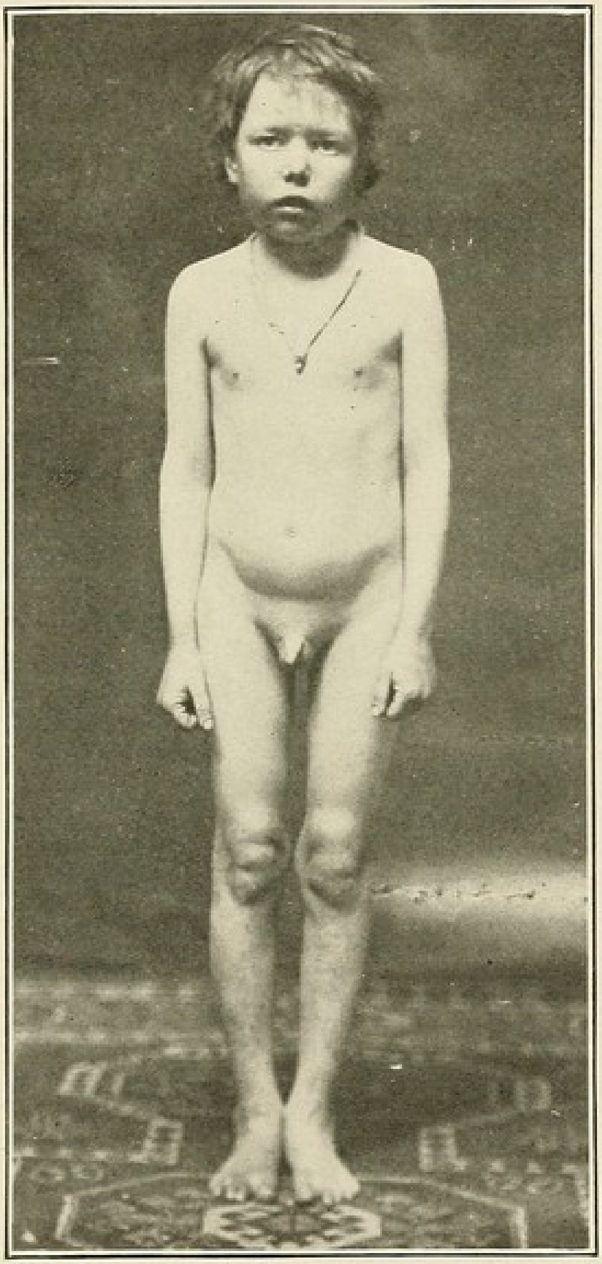

Fig. 39. Severe hookworm case; subject 14 years old, but appears to be about 7. (Photograph furnished by Dr. C. W. Stiles.)

names of some whom he had previously known well. The working capacity of the hands has been increased at least 25 percent, and I feel that the small fee I paid you is insignificant in comparison with our gain."

We may, for convenience, recognize another type—the severe type, in which the hemoglobin ranges from 60 down to 30 percent, and the patient is too weak and dyspneic on exertion to be overlooked. He is pale, anemic, and, if not an adult, his growth is interfered with. He often grows very little for years, and, if the infection is kept up, the patient may be no larger than a 12 or 13-year old child when he is actually 20. He will continue to grow until he is 26 or 28 years old if the infection lasts a long time, but the size attained is never what it would have been if the infection had never occurred. The pubic and axillary hair appears one, two, or even four or five years late, and the beard does not start until the patient is 24 or 25 years old. We know of an instance in which there were two deaths in a family from what we now know to have been the very severe dropsical form of hookworm disease, and several other boys had this severe type. They were often crippled with ground itch, and were typical anemic dirt eaters. One of the boys at 14 went to live with an uncle in a small town, and was thus removed from the continued reinfection to which the other four were exposed. When he left home he looked no better than his brothers, but at the age of 20 he weighed about one hundred and fifty pounds and had a pretty heavy beard. He sometimes went home and thence to church with his brothers, two of them older than himself, and it was comical to see them together, knowing their ages and relation. One of them made a small man at the age of about 27, but had little or no beard at about 30. When about 35 he had grown a fairly heavy beard. If the severe infection occurs, however, after the patient is fully grown and the beard has come out, the latter often feels and looks dry and dead, but does not disappear. In this type in women menstruation is delayed, irregular, scanty, or absent. In certain hookworm sections in this country this type is common.

Fig. 41 is from an interesting case of this kind, reported from Dr. Dock's clinic in the Charity Hospital, New Orleans, by Dr. I. I. Lemann. The subject, 22 years old, was usually taken to be 13 or 14. The bony development corresponded to that of 11½ years. The careful analysis of Dr. Lemann shows that the dwarfing process was general. "There is no disproportion between the lengths of the limbs and the trunk; no undue size of the ex-

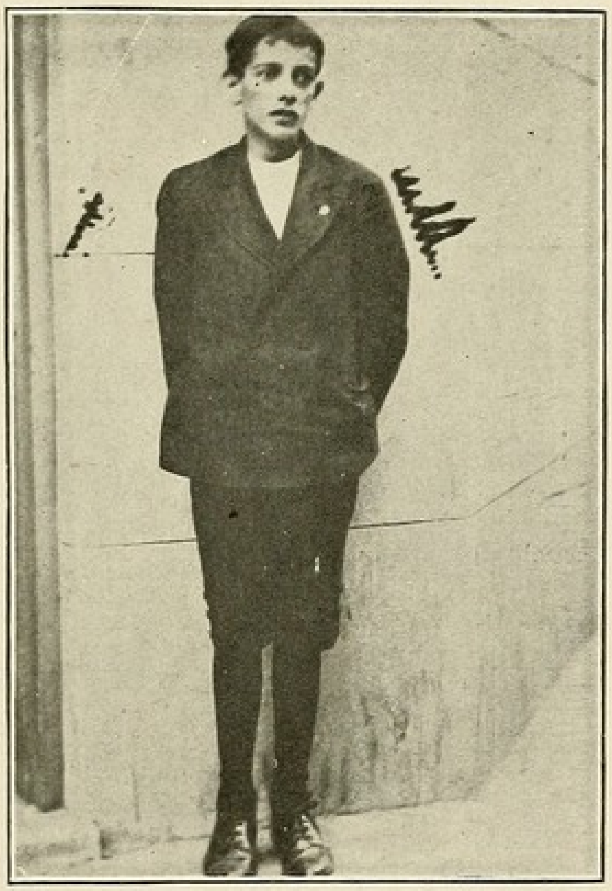

Fig. 40. Severe hookworm case; subject 16 years old. Emaciation; no edema.

tremities or the head." The height at the time was 139.5 centimeters, or about four feet eight inches.

We may recognize a severe type of the disease in which the hemoglobin ranges from 30 down to 8 or 10 percent, and is frequently accompanied by albuminuria and dropsy. The anemia, pallor, and weakness usually incapacitate patients for any kind of work, and when dropsy is present they often have to remain in bed. In this type death may occur from the hookworm disease alone, whereas in the previous types death does not occur, except as a result of some intercurrent

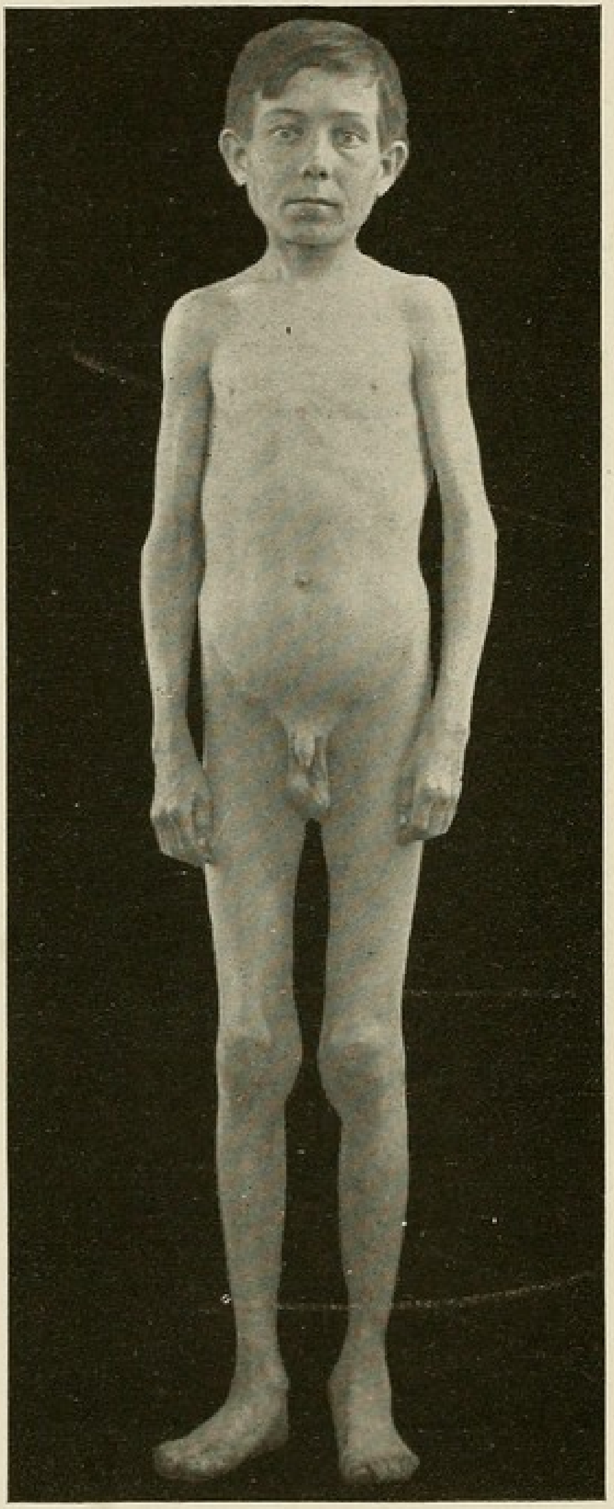

Fig. 41. Hookworm subject 22 years old. Three hundred hookworms expelled two years ago; numerous ova now (1909). (Case to be reported by Dr. I. I. Lemann, 1910.)

disease. This type of hookworm disease is, however, a fruitful source of death by lowering the patient's vitality and resistance against other diseases to which he now succumbs, though normally he would have recovered from them. There are relatively very few cases of this type in

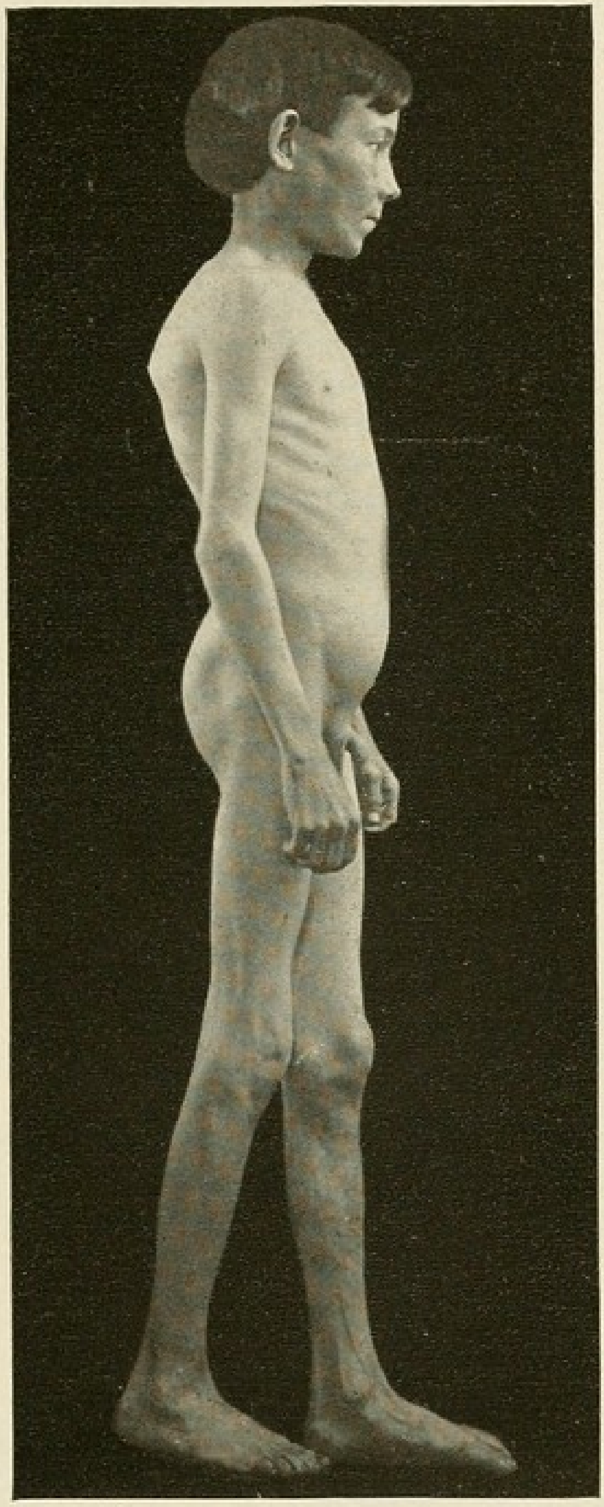

Fig. 42. Side view of Fig. 41.

the United States. According to the opinion of the Porto Rico Anemia Commission, about 30 percent of all the deaths in the island are due to this type of the disease.

This arbitrary division of the disease into several different types is useful mainly to enable us to convey in our de-

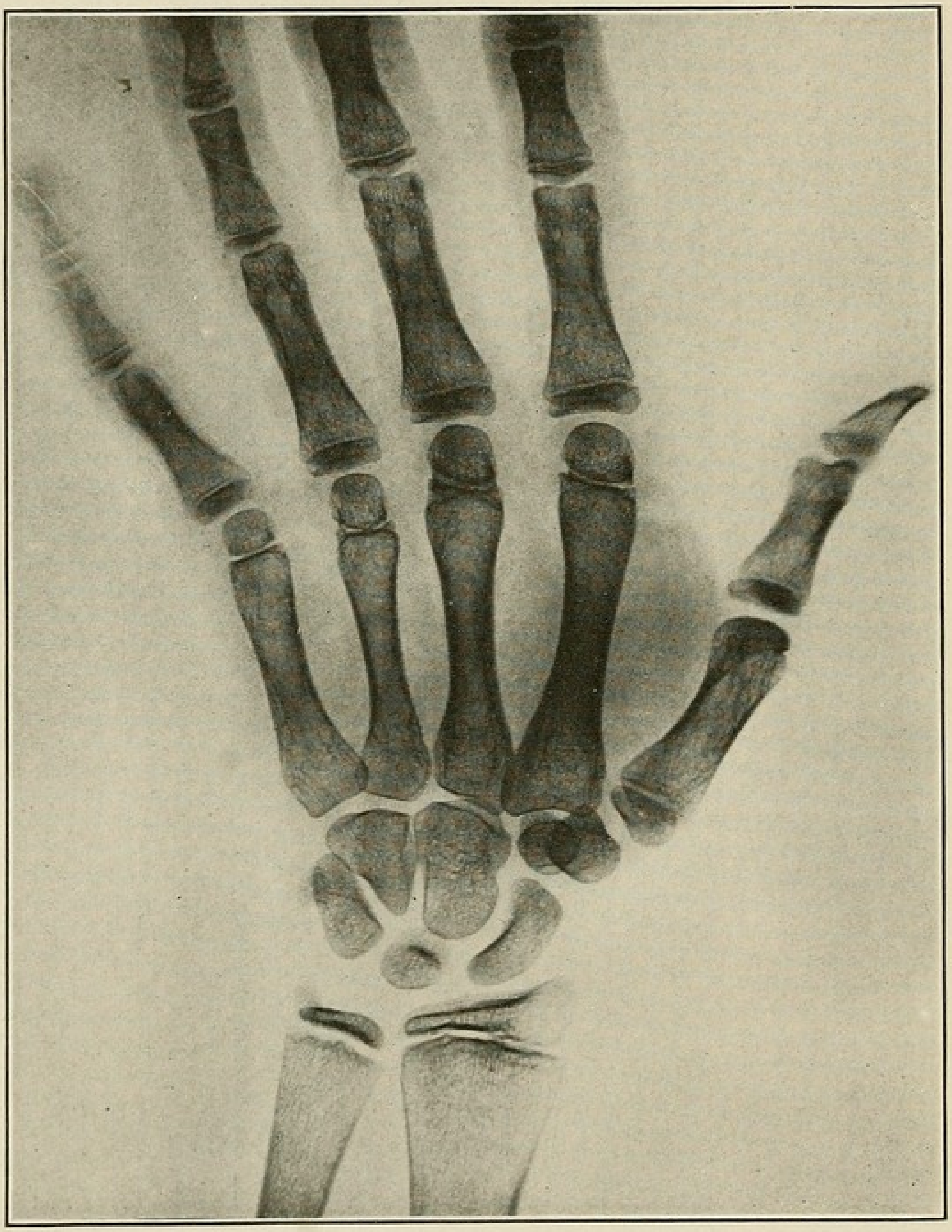

Fig. 43. Röntgenogram of hand of hookworm subject shown in Fig. 41. (Negative furnished by Dr. A. Granger, New Orleans.)

scription of the disease a more definite idea or meaning for such terms as very mild, mild, severe, and very severe cases. Each type must merge imperceptibly into the other. In-

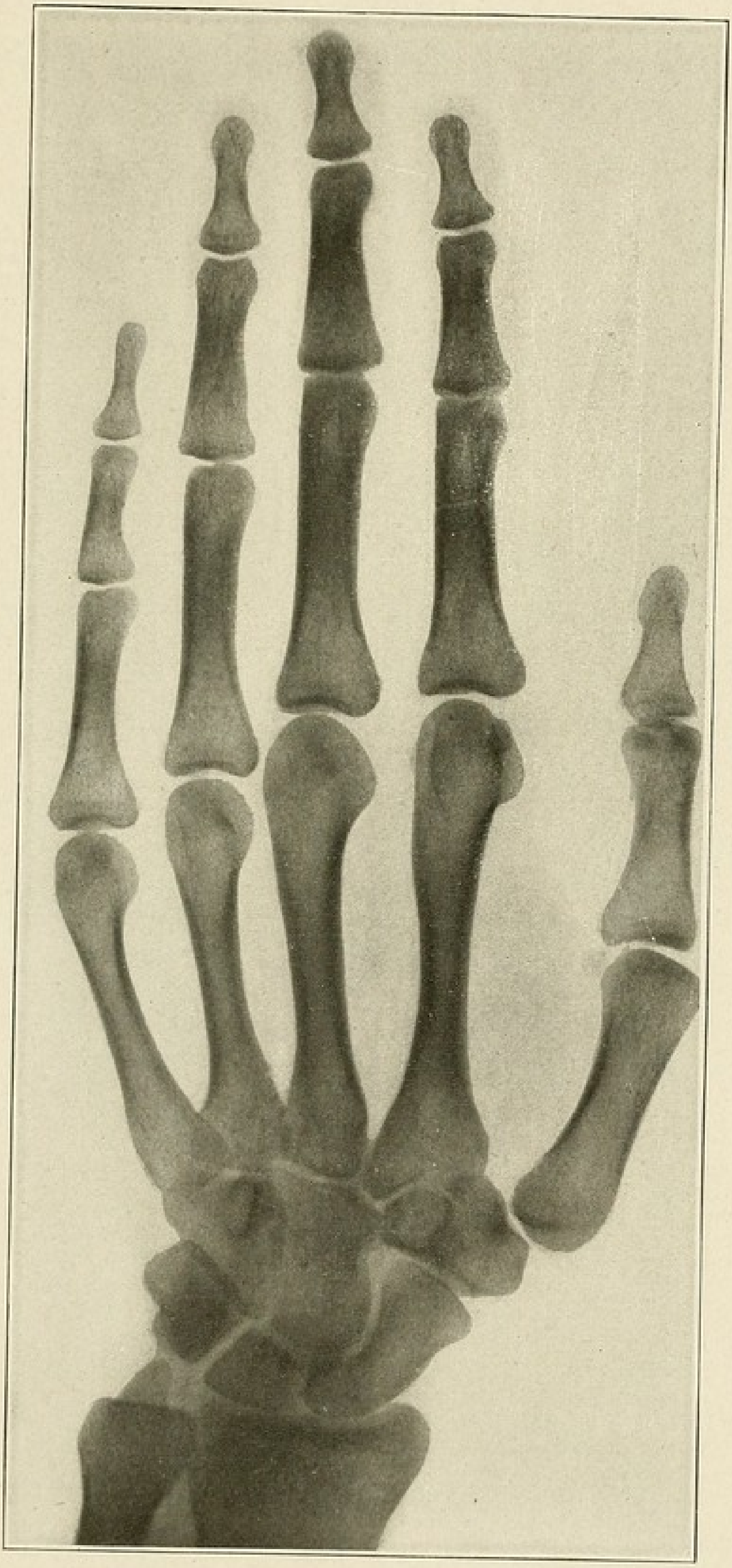

Fig. 44. Röntgenogram of hand of normal man 19 years old. (Photograph furnished by Dr. Thomas Morgan Rotch.)

asmuch as the symptoms and results of the disease are due chiefly, if not wholly, to anemia, we believe whatever classification is necessary should be based on the amount of hemoglobin a patient has. We would classify cases with over 80 percent hemoglobin as very mild; those with 80 percent to 60 percent, mild; those with 60 percent to 30 percent, severe; and those with less than 30 percent, very severe. Ashford and King distinguish three grades of the disease—slight, moderate, and marked. Their "slight" cases correspond about to our mild cases, their "moderate" to our severe, and their "marked" cases to our very severe ones. Their summary of the symptoms under each head is so complete, and yet brief, that we quote it below in full. Up to this writing (1910), theirs is the only very large series of observations and statistics on hookworm disease due to uncinaria Americana.

"**Slight cases.**—Such as those who possess little or no pallor, or, at best, show but an indefinable, dirty yellow tinge of the skin in whites and a slight pastiness in mulattoes. There is a reduction in the normal amount of perspiration. The appetite is apt to be capricious. Attacks of gastralgia are felt at odd times, or at least a little uneasiness in the epigastrium, a tendency to meteorism, slight breathlessness on exertion, occasional palpitation of the heart, dizziness, headache, lack of attention to details, and a little dulling of the mental faculties. The muscles are flabby, and weakness and indisposition to labor exist. The hemoglobin of such persons generally lies between 60 percent and normal, the former sometimes in spite of a good color.

"**Moderate cases.**—These form the usual type seen in Porto Rico, although, naturally, marked cases predominated among those applying for treatment. Here all symptoms noted under slight cases are more prominent. The pallor is definite, the mucous membranes are paler than normal, the skin is quite dry, and sweating is rare. Appetite may be exaggerated to the point of bulimia, or even perverted to geophagy. Nausea is frequent, and vomiting may occur at times. The tongue is coated, and often flabby and enlarged. There may be some tenderness of the epigastrium and abdomen, with spontaneous pain and heaviness. Breathlessness is much more easily elicited. Palpitation of the heart is frequent and severe, and not always relative to exertion. The pulse is more rapid, and is liable to be weak and compressible. There is often a hemic murmur of the heart and a little hypertrophy. The pulsation of the vessels of the neck is noticeable. There is much pain in the sternum and chest, with a feeling of weakness of knees and legs. The patient feels sick. There is much dizziness, especially on sudden changes of position, noise in the ears, and frequent headache. The mental condition is decidedly depressed, and the patient is quite passive to his surroundings and appears stupid. Sometimes the patellar reflex is exaggerated, but more often it is diminished. There is susceptibility to cold, and tingling of the feet, which frequently 'go to sleep.' The muscles are flabby and a little painful. Joint pains are so common that a diagnosis of rheumatism is often made. Work is undertaken with great effort. The hemoglobin is apt to be between 30 and 60 percent.

"**Marked cases.**—Here the patient has arrived at that stage where fatal termination may occur at any time. The pallor is very extreme. Edema of the feet and ankles alone, or sometimes extreme anasarca, is seen. The digestive disturbances have changed in character, and appetite is often nil—often enormous. Some of the worst forms of geophagy are here seen. Nausea and vomiting are frequent. Ascites is liable to appear and become alarming. Diarrhea may alternate with constipation. There is distressing dyspnea on the slightest movement, and sometimes when the patient is perfectly quiet; severe palpitation of the heart; precordial pain; rapid, weak, compressible pulse, and often dilatation of the heart. Marked pulsation of the vessels of the neck and of the base of the neck may be noticed at some distance. There is often pulsation of the great veins, with bruit-de-diable of the jugulars. Dizziness and tinnitus aurium are extreme. There is much headache and insomnia. The patellar reflex is abolished. In men, impotence is an almost invariable symptom, and amenorrhea in women. The intellect is much dulled; mental processes are slow, and the patient seems confused and stupid. The facial expression is melancholic and anxious. Paresthesias become very marked. There is a tendency to dilatation of the pupil, and blurred vision exists. The urine has a low specific gravity, is abundant in quantity, and usually contains no albumin. The muscles are flabby, sore, and painful. Extreme weakness, even to the simulation of paralysis, is observed and the patient is incapacitated for labor. There may be irregular fever, with intervals of subnormal temperature."

Acute hookworm disease may occur without previous infection, or an acute attack may supervene on a chronic infection. These acute attacks occur in the spring and summer, and their symptoms will vary with the intensity of the infection. If sufficient infection occurs, there will be digestive disturbances, epigastric pains, rapid anemia, and generally elevations of temperature as high as 101° or 101 1/2° F. One difference to be noted between acute and chronic cases is that in the acute the patient looks waxy white, with severe anemia, whereas in chronic cases, with the same amount of anemia, there is a more yellow tinge ("tallow faced") to the skin, due to more or less pigmentation. Children with acute hookworm disease have not the "pot belly" present in so many of the chronic severe cases.

Symptoms on the Part of Certain Tissues and Organs.

Blood.—Anemia is the most constant symptom of hookworm disease, and determines the severity in a given case. It may vary from the slightest degree below normal to a sufficient degree to label the patient. The type is almost always that of a secondary anemia or chlorosis. The hemoglobin ranges from 8 percent up, according to the severity of the case. Most of the cases in this country range from normal down to 40 or 50 percent. We have records of the hemoglobin estimation in four hundred and thirty-two cases occurring chiefly in Mississippi and Louisiana. The lowest is 15 percent, and several records of very mild hookworm carriers are 95 and even 100 percent. The average for all the cases is 67 2/3 percent. It must be understood, however, that the number includes a great many very mild cases. Ashford and King found in five hundred and seventy-nine cases on entrance a hemoglobin percentage of 9 to 101 percent—average, 43.09 percent. Soon after infection the hemoglobin falls much faster than the number of red cells. In fact, it may even reach a pretty low figure before they begin to decline.

The number of red cells is reduced slowly as the anemia develops, but most severe cases have 3,000,000 to 5,000,000 cells. The average count in sixty cases reported by Ashford and King was 2,406,416. We have made a blood count in forty-two cases and obtained an average of 3,459,246. Forty university students found to be hookworm carriers gave an average of 5,246,322. The cells are pale, and stippling is generally present, but to no great extent. Normoblasts are generally present, but megaloblasts are rare. Poikilocytosis and polychromatophilia occur as the anemia increases, but are never as pronounced as in pernicious anemia. Anisocytosis is present, as in all the severe anemias.

Though this secondary type of anemia, with relatively low hemoglobin percentage, giving rise to low color indices, is what is generally seen, there occur a few cases in which the number of red cells is reduced as much as or more than the hemoglobin percentage, giving rise to color indices sometimes above 1.0. We have seen an index of 1.35, counting 5,000,000 red cells normal and estimating hemoglobin with the von Fleischl apparatus. Patients with this type of anemia are the most resistant to treatment, and often remain anemic as long as even very small numbers of worms remain. In fact, they sometimes have only small numbers before any treatment is instituted. They recover very slowly, but usually finally get entirely well after expulsion of all their worms.

The leucocytes are not generally increased. Counts of 13,000 or 14,000 occasionally occur. We saw a case with a history of recent severe ground itch in whom the leucocyte count went as high as 19,400. The patient had fever sometimes as high as 101°, and no cause could be found, except the hookworm disease. We have records of the leucocyte count in sixty-eight cases of hookworm disease of various degrees, the average of which is 8,746.

The differential leucocyte count usually shows nothing abnormal, except as regards the eosinophiles. These cells vary in number considerably, but without following any known fixed law. Generally, their percentage is increased. Leichtenstern saw a remarkable case with 72 percent. The highest we have seen was 34 percent. Fifteen to 25 percent are ordinary counts for our severe cases. Though most cases have counts above normal, a few have a normal number. The eosinophile percentage often is not in proportion to the severity of the disease. In very severe cases the count is low—maybe within normal limits—and rises after treatment for some time, and then again comes down slowly. Very few patients have eosinophilia when they die. The eosinophilia seems to depend on other factors than the number of worms. While expulsion of all worms is followed in certain instances by a normal eosinophile count even before the hemoglobin has reached normal, in many it is several months before normal counts are obtained. The eosinophile counts in five hundred and thirty-two cases of all grades seen by us give an average of 5.7 percent, but nearly half of them were of the very mild type, nearly all of which had only slight increase or none at all. It is to be remembered that eosinophilia occurs in a variety of other diseases besides hookworm disease, which detracts from its diagnostic value. It is, however, present sufficiently frequently in this disease to indicate an examination of the feces whenever it is found. When, however, no increase is found, hookworm disease can not be ruled out. An increasing eosinophilia after treatment would be of favorable prognostic value.

Joint pains.—The observation of Leichtenstern that joint pains and pains in the bones occur is confirmed by Ashford and King, who say that pain, especially in the sternum, is an almost universal symptom.

Skin—Ground itch.—Synonyms: Water itch, water blister, water pox, toe itch, dew poison, dew crack, mud itch, "new sump bunches" of Cornish miners, sore feet of coolies, "pani-ghao," "mazomorro" (Porto Rico).

Ground itch varies very much in its symptoms with the intensity of the infection, the location, and the secondary infection. It is now certain that it is caused by the hookworm larvæ, which penetrate the skin. Claude A. Smith produced symptoms resembling ground itch by the application of an alcoholic extract of the larvæ to the arm of a patient. This experimental ground itch resembled that caused by applying the larvæ to the skin. The amount of infection may vary, of course, from one microscopic larva to several thousand, and would give rise to quite variable symptoms.

Ground itch is a collective term, and, although in hookworm countries it is usually due to the larvæ of those worms, conditions clinically similar, at least to inexperienced persons, may be due to other causes. Van Durme and Looss have shown that strongyloides larvæ can penetrate the skin just as hookworm larvæ do, and our associate, Dr. J. C. Gage, has confirmed this. From the experiments with various species of hookworm larvæ in different animals it is probable that various nematode larvæ can penetrate the skin and set up local lesions, but not develop in the body. So the larvæ of the hookworms of dogs and other animals may possibly cause ground itch. Similar lesions may be caused by ticks, harvest bugs, sand fleas, fly larvæ, and other insects.

The disease is most likely to be located on the feet, but the hands may be affected, as in gardeners, miners, and others whose occupation leads them to handle infected earth and mud, or in children from playing in infected sand and mud.

In rural districts, where hookworm disease is most prevalent, little children often wear only one dress or shirt, or an apron. Sometimes children in their "shirt tail" sit down on infected mud and sand, and thus get infected on the buttocks. By far the most common location is the feet, and between and beneath the toes. This is because infected mud is squeezed in between them, and is more likely to remain until the larvæ have time to penetrate the skin. The lesion is also often located around the edge of the soles at the juncture of the thick and thin skin. It is not so common on the dorsum of the feet, except just above the toes. The soles are not so much affected as other parts. The inner side of the sole, where there is little pressure, is a favorite location. All of these places, it will be noted, are those most likely to get mud on them and have it remain if the child steps in it. We have seen the eruption involve the legs from wading in infected water on the farm, and it sometimes comes around the ankles when muddy water gets over the shoetops. A few minutes after infected mud is applied, stinging of the skin occurs. This occurs so promptly that little boys often learn what kind of places they get ground itch from and avoid them. Within a few hours redness, stinging, and itching put the victim to rubbing and scratching. Many a country boy has cried and spent restless nights with his ground itch. The cry then increases, there occurs more or less swelling, and the itching is more intense. The desire to scratch is irresistible and the satisfaction of scratching partially repays for the unpleasantness of the disease. In twenty-four to thirty-six hours small pinhead sized vesicles appear, which, according to the amount of infection, may not be numerous, or they soon become confluent. The vesicles are common on the inner surfaces of the toes, where they are in contact. The macules which precede the vesicles where the infection is very slight are larger and more painful, and itch worse on the soles and thick skin. The vesicles are more likely to become confluent between and in the folds beneath the toes, which results in loosening considerable skin. It is tougher here, and usually comes off in a thick, heavy layer after a week or two, leaving the tender skin beneath. Scratching and rubbing often break the small vesicles, and scabbing occurs, but usually slowly on account of the fact that the itching continues so intense for several days that scratching can hardly be avoided. In twenty-four to forty-eight hours the eruption becomes pustular, due, no doubt, to secondary infection. This occurs much more in certain individuals and at certain times than others, doubtless due to the conditions governing pyogenic infection in general. Examination of the pus usually shows staphylococci. Bentley found an ankylostoma larva in a vesicle. The pustules are frequently ruptured, as are the vesicles, and leave a raw surface, with rather profuse sticky exudation. This exudate sticks the socks or bandages to the foot, and a part of the undressing performance every night with little boys so affected is the necessary soaking of the feet to loosen the adherent dressing. Deep ulcers do not occur, except in the folds beneath and between the toes, where they may be deep and last several weeks. Beneath the toes the deep ulcers or cracks are kept up by the bending of the toes, and often remain after all other traces of the disease have disappeared. The toes are often glued tightly together by the sticky exudate, and where it remains moist the skin is white and often loosened. In cases where the vesicles are not ruptured, or where they are rubbed off, they dry up in about five days, and in about eight or ten days exfoliation and healing are complete. Little evidence of the lesion now remains, except between and beneath the toes, where the skin is so thick that it is not shed so rapidly. Patients often trim this off, and, unless the ulceration is especially deep, or deep fissures occur, the healing is not delayed much beyond that of other parts.

In very intense infections, as in Claude A. Smith's experimental case, great swelling occurs on the second and third days. The lymphatic glands draining the part are often swollen and tender. Looss has noted red lines running up the limb—probably lymphangitis. There is local fever during the height of the inflammation, but no systemic elevation of temperature, except in very severe cases. When the disease is located on the feet, the diagnosis is usually easy. In fact, nearly any country boy, or mother, or father in a hookworm country knows what ground itch is usually from experience, and recognizes it on sight. When located on other parts of the body, the differential diagnosis often can not be made from other diseases causing very similar lesions. The history of exposure and the course of the disease help to settle the diagnosis. The prompt occurrence of eosinophilia in most cases helps to strengthen the diagnosis. This is present in four to five days after infection.

The color of the skin in chronic hookworm disease is usually pale, with a yellow tinge. This gives rise to the frequent description, "tallow faced." In acute cases, where the anemia rapidly develops, the patient is paler and whiter. Exposure to the sun finally hides more or less of the anemia. The pallor is generally in proportion to the anemia, but this is not always a true guide. Patients with 60 percent hemoglobin may look better than others with 90 percent. In negroes the skin becomes gray or ashen from severe anemia.

The skin of severe hookworm disease is often wrinkled, so as to give the patient the appearance of being much older than he is. This usually fills out again after proper treatment.

Liver.—No change in this organ or its functions can be made out clinically.

Spleen.—The spleen is unchanged, except in cases complicated with such diseases as alter it, as malaria, leukemia, splenic anemia, etc.

Respiratory system.—During the few days (first ten) after an attack of ground itch, if the infection is very considerable, there may be cough, bronchitis, and sore throat. Experimentally there occur hemorrhages into the lung tissue, and it is not impossible that there may be secondary bacterial infection and a condition resembling pneumonia develop. The possibilities are illustrated by an experiment done by Ashford and King. They applied a culture of uncinaria Americana larvæ to the back of a four-day old guinea pig. In three days the animal died. Autopsy showed one lung solid with blood and the other containing several hemorrhagic spots or blood cysts, many of which contained uncinaria larvæ. Such instances would, of course, not be diagnosed as hookworm disease, but we believe the possibilities are sufficiently great to warrant consideration in cases of ground itch. Examinations of the sputum might reveal larvæ. If the blood were examined at such times by the method of Stäubli—dissolving in 3-percent acetic acid and centrifugating—the larvæ might be recovered from it, as have trichinæ by Herrick and Janeway. It is not clear from Stäubli's (1908) article that he really found hookworm larvæ.

Dyspnea.—On exertion, dyspnea is one of the most prominent symptoms in cases with hemoglobin below 50 or 60 percent. It often has existed so long that the patient looks on it as normal for him and as a necessary part of his life. This is one of the symptoms that reduces the patients' working capacity, and contributes to the reputation they often have of being lazy. Edema of the lungs and hydrothorax are likely to be present in the severe cases, with general edema. Ashford and King mention a "dry cough" in severe cases. This may be due to edema of the lungs or hydrothorax.

Circulatory system.—Pulsation of the neck veins, much increased by exertion, is frequently present in all severe cases of hookworm disease. The heart, on inspection in severe cases, shows a wide area of cardiac impulse, such as is seen in dilatation from any other cause. Pulsation in the epigastrium is a prominent symptom, and often this and the extensive cardiac impulse attract the attention of the patient. These symptoms are very much increased by exertion, as are also the pulsations in the neck. On palpation the heaving, easily seen impulses are found to be weak. On percussion the area of cardiac dullness is increased to the left, but not much downward. There often is right-sided enlargement. Relative cardiac dullness in many cases extends to the left of the nipple line and far to the right of the sternum.

Auscultation generally reveals, in cases with hemoglobin below 50 or 60 percent, a hemic murmur, best heard in the left third interspace, but frequently heard all over and sometimes beyond the cardiac area.

The pulse in mild cases is little changed, but in the severer ones is weak and dicrotic, irregular, and compressible in the severest cases, and in the latter it is rapid, thready, and intermittent. The frequency increases with the severity of the disease, but often is marked in mild cases. The following is the pulse rate of twenty selected uncomplicated representative cases from Mississippi and Louisiana, between the ages of 15 and 25, and we believe represents the average in hookworm patients in this country who are sick enough to consult a physician: 84, 84, 89, 96, 98, 99, 110, 113, 114, 114, 124, 128, 128, 129, 132, 133, 141, 142, 146, and 148. The average of the twenty cases is 117.6. The blood pressure averages below normal, and usually goes lower as the severity of the disease increases. In two of our cases albuminuria and nephritis were present, and the blood pressure by the Riva Roci instrument, with two-and-one-half-inch band, was 145 and 163. Twelve cases of average uncomplicated hookworm disease over 15 years old seen by us had an average blood pressure by this instrument and in the sitting posture of 110. They were in detail, 89, 93, 94, 99, 104, 106, 109, 117, 124, 126, 127, and 132.

Digestive system.—The symptoms relative to the digestive system will necessarily vary much on account of the very great variation of the amount of the infection. In severe cases the tongue is pale, coated, and often indented, and occasionally shows purple lines on either side of the median line, probably due to dilation of the veins. Pigmented spots on the tongue have been noted in dark-skinned races. It is possible that these may be caused by larvæ penetrating the mucous membrane after they have come up from the lungs. The shedding of the first teeth and eruption of the permanent set is delayed sometimes one, two, and three years, according to the severity and duration of the disease. The teeth keep up, however, pretty well with the development of other parts of the anatomy.

Following a severe attack of ground itch, sore throat usually occurs in a few days. Claude A. Smith noticed this in one of his experimental cases in eight days. After this the patient begins to complain of pain, uneasiness and discomfort in the epigastrium, due, no doubt, to the traumatism and irritation of the gastric and intestinal mucosa. The young larvæ penetrate the mucous membrane and produce considerable blood-cyst formation. If any difference, the right upper quadrant of the abdomen is the seat of most of the trouble. There may be tenderness, especially in this region and in the epigastrium. Lutz believed this was definitely connected with hookworm infection of the intestine. We have been impressed with the relation between epigastric uneasiness and pain and hookworm disease. Dr. J. B. Elliott, Sr., formerly professor of theory and practice of medicine in Tulane University, was one of the first in this country to recognize the influence of mild hookworm infection in producing epigastric pain and discomfort, usually of a vague and indefinite description. Several years ago he learned that a few such cases in which he could find no explanation for the symptoms were hookworm carriers. Often they had very few worms. He was in the habit of having them examined, and the accuracy with which he recognized these cases was in keeping with the characteristic keenness of which he was known to be possessed by all who had the good fortune to know him.

The following cases, reported by one of us (Bass, 1909), illustrate this point:

Case 1.—J. B., aged 39, male, white, merchant, was well developed and looked fairly well; had never had ground itch; lived in town. He had had vague pains in the right side of abdomen as long as he could remember; said he was nervous and had "indigestion." Pains were not related to the time of eating. Physical examination failed to reveal anything abnormal. There were a few eggs in the stools; fourteen worms were recovered. The patient recovered entirely and gained nine pounds in nine weeks.

Case 2.—L., aged 61, white, farmer's wife, had had no ground itch. The negroes on the plantation had it. The patient had had pains in the right side and uneasiness in the abdomen for the past six years, not related to meals; tenderness was not present. Physical examination showed nothing abnormal. There were a few eggs in the stools; no anemia. The patient recovered on treatment with thymol. Eight months later she was still well.

Case 3.—Paul H., aged 42, male, white, lawyer, complained of indigestion and frequent headaches. He had tenderness in the right side of the abdomen. There were a few eggs in the stools. The patient was relieved of indigestion and headaches after the first course of thymol.

Ashford and King say that epigastric pain and tenderness are the most constant, most suggestive, and most clearly marked of all the symptoms of the digestive tract. We do not believe that this is true of the type of the disease most prevalent in this country, but we have noted it in many of our cases. We are also quite confident that it is a more common symptom in adults than in children, and, further, that a small number of worms may produce it. If such discomfort and mild epigastric pain were not so often observed in other conditions, it would be a more serviceable diagnostic symptom.

The appetite is increased in most mild and medium severe cases, but anorexia is frequent in the severest cases. Perversions of appetite are common, even in mild cases. All sorts of unnatural things are eaten, such as earth, paper, slate pencils, lead pencils, coffee "grounds," ashes, feathers, hair, charcoal, unripe fruit, etc. We know of a woman with hookworms and a history of ground itch who developed such a craving for laundry starch that she ate a pound and a half a day. After keeping that up for some months she showed symptoms of pellagra. (Case to be reported by Dr. Bass.) Many have an abnormal appetite for pickles, lemons, salt, etc., and resin chewing is common among those living in the "piney woods" section. Many chew hickory or other bitter bark. Butterworth's case of hairball in the stomach, already referred to, illustrates the extremes to which this unnatural appetite may go. Dirt or clay eating is common, and the worst cases in an infected locality are called by the natives "dirt eaters" or "clay eaters." The anemia is supposed to be due to dirt or "trash" eating, and parents often accuse their children, and often whip them in spite of their denial. They think the anemia is sufficient evidence of their guilt.

With the laity in hookworm sections and others the belief is pretty common that eating dirt and "trash," including various kinds of candy and sweets, and unripe or spoiled fruit, is a source of worms, and hookworm families are generally believed to be "wormy," usually meaning they have ascaris infection.

We recall an instance of an anemic family, due, as we now know, to hookworm disease, in which many different remedies were tried to break the children from eating dirt from the clay of the stick-and-dirt chimney. One of the remedies tried was to sprinkle urine on the chimney, but the final successful one, so far as that chimney was concerned, was rubbing over the chimney in the presence of the children a large rattlesnake that had been killed on the place. The fear of snakes was sufficient to cure them. These children were among the most inordinate resin chewers, and finally all took to chewing tobacco. Chewing tobacco is encouraged by this unnatural appetite, and we believe this partly explains the very extensive use of the weed among hookworm people. Boys who do not grow well are often advised by their physician or some one else to begin chewing tobacco. They do often begin to grow at this time, and we have heard many a man or boy say he never took a start to grow until he began to chew tobacco. There is no constant beneficial result, for we have seen many of these tobacco chewers who had practiced the habit for many years and still had not "taken a start to grow." The reason many of them begin to grow after they begin chewing tobacco is, no doubt, that many of them at about the same time begin to wear shoes or otherwise reduce reinfection. It may, however, be possible that the tobacco juice swallowed kills or injures the worms. It has been our observation that when dirt is eaten in a country having red clay soil, this is generally selected, and children often get the habit of picking and eating from the stick-and-dirt chimneys used by the poorer class. They seem to prefer the very dry clay, and we knew one negro woman who would bake her clay in the stove. She often made it up like bread and baked several days' supply at a time. Half an ounce or an ounce at a time was often used. She liked to put a small piece in her mouth and suck on it for several minutes at a time. When asked why she ate it she said, "I just craves it." Others pick up little soft pebbles and suck on them. In one instance a 16-year old anemic-looking boy, whom we would now recognize as a hookworm patient, became very ill, and was given a glycerine enema. He expelled in a few minutes several ounces, consisting chiefly of pebbles, which he then admitted he had been eating for over two years. If earth were the only substance eaten, the opinion that this symptom is due to an instinctive effort to supply iron and manganese with which to build up hemoglobin might be admitted to have some basis. Other substances are selected often when clay is just as available. We saw a severe case in a girl whose father had tried in vain in every way possible to break her from eating coffee grounds thrown out the window. She would often steal the "grounds" from the pot if it was not put out of her reach after the coffee was drained off, though she did not drink coffee. The habit was cured in a short time by thymol administration, which resulted in the expulsion of several hundred hookworms. While many patients with hookworm disease have the capricious appetite and the habit of geophagy, there are many even severe cases that never take up such habits. It is seldom that a child or adult guilty of the habit will acknowledge it, due, no doubt, to fear of chastisement or to shame.

A good deal of work has been done on the gastric secretions by Japanese investigators. Yoshida (1908) gives results in 101 Formosans and Chinese, comparing them with those in people on similar diet, and finds that in ankylostomiasis the total acidity is most often normal, hyperacidity rare, and subacidity still rarer. Free HCl is usually normal, and subacidity more frequent than hyperacidity. No exact relations between anemia and HCl could be made out, but, with some exceptions, the more intense the anemia the lower the free HCl. In the cases examined there was a relation between appetite and free HCl in the stomach contents.

Diarrhea occurs in the first few weeks of an acute infection in many instances, but is not a symptom of chronic hookworm disease, except in very severe cases, in which it is not uncommon. Constipation is often present, but we doubt if it is more than an accidental symptom. Children under the age of puberty are often ''pot bellied'' when they have the chronic severe type. This is due to dilatation of the stomach and intestines chiefly, and partly to excessive mesenteric fat. Only children with chronic infections have this symptom.

McGehee has reported a case in which hookworms, but no ova, were found in an appendix vermiformis, the seat of a catarrhal inflammation.

The feces contain the ova, which have been more fully described in the chapter on Diagnosis. They also contain minute traces of blood, which, however, can not be made out macroscopically or microscopically, except in the severest cases. Even the mild cases will usually give a positive reaction for occult blood in the feces, provided a very delicate test for blood is made, such as Adler's benzidin test. A convenient way of performing this test is to add to a few (5 to 10) cubic centimeters of liquefied feces 1 or 2 cubic centimeters of glacial acute acid and 5 to 10 cubic centimeters of sulphuric ether. Mix without shaking, then pour off the supernatant ether and test it by adding a few drops of strong hot alcoholic solution of benzidin and 1 or 2 cubic centimeters of peroxide of hydrogen. In the presence of blood, even in minute quantities, a blue color will promptly follow.

Genito-urinary system.—The genito-urinary organs are delayed in their development in proportion to the general developmental impairment. Boys develop later, accordingly to the severity of the disease, and girls begin to menstruate later than normal—often in severe cases this function is not established until they are 16 to 18 years old. Amenorrhea and scanty and irregular menstruation are common. There are instances in which pregnancy occurred before menstruation was established. In girls the breasts share the general retardation in development.

The quantity of urine is uninfluenced until the very severe degree of the disease is reached, when the reduction is often great and general anasarca supervenes. Albumin is often present in small amounts in patients with hemoglobin below 50 or 60 percent, and often in the very severe cases is present in very large amounts. We have seen several times from 40 to 50 and 60 percent of moist albumin by the Purdy ferrocyanide test. Casts are strikingly absent, but sometimes may be seen in the very severe cases. We have seen a case with 60 percent of albumin and extreme dropsy in which no casts were found on repeated examinations. General dropsy is common in very severe and almost all fatal cases, and often is extreme. There is more or less puffiness of the loose tissue of the face, feet, and legs in most cases with hemoglobin below 50 percent. When hookworm patients get pregnant, the tendency to dropsy is very much increased by the disease, and in severe cases the swelling is often great. Swelling of the labia is especially troublesome as the pregnancy approaches term.

Lactation is impaired according to the degree of anemia. Mothers are often unable to properly nourish their children.

The promptness with which this function improves after treatment is striking—often actually faster than improvement of the anemia.

Eyes.—The eye grounds showed changes in 7 to 8 percent of cases examined by Lutz. Menche found that the temporal half of the visual field showed obscurity. Neuroretinitis has been reported. Nieden, of Bochum, Westphalia, has shown that patients with hookworm often have retinal hemorrhages, such as occur in pernicious anemia. They occur especially and early in the peripheral parts rather than near the papilla and the macula, are punctate, often in groups, without any tendency to confluence. Sometimes they accompany the vessels close up to the papilla. In long standing and severe cases there are larger plaques of extravasation, with radiating edges. Along with the hemorrhages are the usual changes of anemia, such as pallor of the retina, porcelain-like papilla, tortuous vessels, often strongly pulsating. The disturbances of vision are due rather to the general alterations than to those in the retina. Asthenopia, paresis of the internal or external recti, diplopia, vertigo, nystagmus, and hemeralopia (or night blindness) may occur. Concentric contraction of the visual fields has been noted. Nieden and others look on the retinal hemorrhages as evidence of toxic processes. Stiles has called attention to the appearance of the pupil. He says: "If the patient is directed to stare intently into the observer's eyes, there will be noticed a symptom which it is difficult to describe, but which I have found more constant than almost any other noticed—namely, after a moment, the length of time apparently varying slightly according to the degree of the disease, the pupils dilate and the patient's eyes assume a dull, blank, almost fish-like or cadaveric stare, very similar to that noticed in cases of extreme alcoholic intoxication." Ashford and King found dilatability of the pupil noticeable in their Porto Rico cases. We have often noticed that the pupil dilates readily, and usually remains wide, even in the presence of considerable light, but this is a common symptom of all severe anemias.

Nervous system.—Nervous and mental symptoms of various kinds are not infrequently present in hookworm patients, and sometimes cause great diagnostic difficulty. There are few, if any, nervous symptoms, however, that can not be ascribed to the anemia. There is a general benumbing of the mental faculties in acute cases, but the chronic hookworm child is generally well up in mentality with others of his size and vigor, but usually not equal to those of his age. In the acute and very severe form the disease produces often melancholia, hypochondriasis, and a careless expression. Insomnia and night terrors are very common, due, no doubt, to feeding and moving about by the worms, which the nervous system feels more when the patient is perfectly quiet, as in sleep, than when active. Somnolence, on the other hand, often occurs, and the patient keeps awake in day time with difficulty. Lack of ambition is noticeable, and has given rise to the idea that the patient is lazy. Hookworm patients do not work as much or as well as those not infected, but it is because they are sick and not because they are lazy. In the last few years a great deal has been said in the newspapers jokingly about the ''lazy disease,'' and, if the same amount of publication had been devoted to dissemination of knowledge of the sources and the prevention of the disease, there is no doubt that it would be less prevalent today.

Signorelli (1909) reports some interesting cases. In one, a boy of 10, with mild anemia, had a meningeal syndrome, with headache, vomiting, neuromuscular hyperesthesia, cervical rigidity, Kernig's sign, etc., cured by thymol. A girl of 17, with neuralgia, especially crural, anesthesia, and paresthesia, was quickly cured by thymol after the blood count showed 30 percent of eosinophiles and the anamnesis revealed previous residence in Brazil. In another case, a woman of 23, vasomotor disturbances and epileptiform convulsions were equally amenable to specific treatment with thymol. Signorelli emphasizes the tendency of hookworm, like the malarial parasite, to cause vasomotor abnormalities.

Austregesilo and Gotuzzo (Rio de Janeiro, 1909) call attention to the possibility of severe psychic alterations in ankylostomiasis. They report the case of a man of 26, free from history of alcohol or syphilis, who became apathetic and melancholic, later complained of severe and continued pain in head and abdomen, and of dyspnea and fatigue on exertion, and finally had delusions of poisoning. Severe anemia with eosinophilia led to thymol treatment and to complete recovery. In another case there were many evidences of psychic degeneration, with loss of memory, religious hallucinations, and delirium of grandeur. Anemia and 18 percent of eosinophiles suggested thymol treatment, and complete recovery followed. In another, with hemoglobin 35 percent, red blood corpuscles 3,100,000, and eosinophiles 16, there was complete loss of sense of time and place. Later, the condition described by Oppenheim as "Witzelsucht" developed. The patient was ironic and sarcastic, ridiculed everything and everybody. Improvement of the ankylostomiasis coincided with that of the mental condition, and finally both were cured.

MacDonald, in Australia (1908), has seen various perversions besides dirt eating among hookworm patients, especially children, mentioning disobedience, profanity, lying, stealing, drinking, forging, and sexual perversions. These, of course, are not rare manifestations without hookworm, but the important thing is that in the cases reported recovery followed cure of the hookworms. The youngest patient was only 8 months old. Allan has called attention to the frequent association of neurasthenia and hookworm, as might be expected. It would be interesting to make observations on the psychic reactions of such cases of various degrees of severity. Perhaps some of the exuberant lawlessness of hookworm regions may be due to the lack of control caused by the infection.

Sodré, and also Austregesilo and Gotuzzo, suggest that the parorexia of hookworm infection is an evidence of the altered mental condition, rather than the direct result of the disease in the intestinal tract.

Finally, we want to emphasize the fact that hookworm disease is likely to have associated with it other diseases, and the symptoms of each be altered by the other. All symptoms presented by a hookworm patient must not necessarily be attributed to this disease. On the other hand, a part of the symptoms in cases having other diseases may be due to hookworm disease.

CHAPTER VII.

DIAGNOSIS.

"The secret of the diagnosis of ankylostomiasis, like that of many other diseases, is to suspect its presence." (Manson.)

An absolutely certain diagnosis of hookworm infection can not be made without finding the eggs or worms in the feces. It is possible, however, to diagnose it symptomatically with reasonable certainty in most cases showing well-marked symptoms, provided this disease is kept in mind. The combination of the characteristic anemia associated with underdevelopment, weakness, dilated heart, and a history of ground itch is not likely to be confounded with anything else. We can not emphasize too forcibly the importance of this history of ground itch, or "toe itch," within the preceding years. In all patients from warm climates presenting anemia and impaired development without obvious cause this should be inquired for. Whenever a history of toe itch is obtained, nothing short of thorough examination of the feces for eggs permits elimination of hookworm from the diagnosis.

A history of ground itch, or hookworm disease, affecting other members of an individual's family, or those living on the same plantation or in the same surroundings, usually indicates that the patient is also infected, though he never had ground itch himself.

The history of going barefoot during the summer in a locality known to be infected usually means that the patient is infected, though he has not had a definite attack of ground itch. So few larvæ may enter the skin at a time as not to produce recognizable or characteristic lesions.

In infected localities, as Tenholt found among miners in infected mines, and Stiles in his journeys through the southern United States, the diagnosis of hookworm disease can often be made by inspection, and will turn out to be correct in the majority of cases. In such places, where time for examination is short, treatment may be carried out on the ground of the symptomatic diagnosis and the accurate diagnosis made by examining the stools for worms afterward. The diagnosis of cases can be made almost as accurately from the great improvement after thymol treatment. This sort of diagnosis, however, can not be looked on as satisfactory or scientific, nor will it discover the important class of hookworm carriers.

Though the diagnosis may be indicated by the history and symptoms present in all well-marked cases of hookworm disease, these fail in a large number of cases that have not obvious symptoms, either because of small number of worms, or because of more or less immunity to the effects of the worms. The most practical and satisfactory way of arriving at a certain diagnosis is by examining the feces for ova of the parasite. These are characteristic, easily recognized, and, when worms are present in sufficient numbers and under such conditions as to cause symptoms, are so easily found that the diagnosis becomes one of the most simple procedures in the practice of medicine, provided one is equipped with a microscope and proper knowledge and experience, which can be easily acquired. The microscopic examination of feces is of so much importance in diagnosis that we believe a complete description of every detail is warranted, including descriptions of the many things likely to be mistaken for or confused with hookworm eggs.

Obtaining Specimens for Examination.

The quantity of feces needed for a microscopic examination, even when the most comprehensive examination described on pages 171 to 177 is to be made, need not exceed two or three drams at most. Unless instructed on this point, the patient will often bring or send large quantities or the whole stool in fruit jars, large pickle jars, etc. Large vessels of feces are much more exposed to accidents—such as breaking or spilling, especially when the feces are liquid—than smaller ones. More malodorous gases are given off from a large amount of feces than from, say, one-twentieth of this quantity. The opening up and handling of a small quantity of feces in the laboratory or office is not nearly so unpleasant as handling a much larger quantity. It is not sufficient to tell the patient to bring only a small quantity. This point must be impressed on him when requesting him to bring the specimen. He should be told to bring only a small quantity of the actual feces, and the physician should make this more certain by furnishing him with a suitable receptacle in which to bring or send the specimen, and when it is given him to explain that he wants only a small quantity in it and not to fill it full. Vaseline bottles, two-dram quinine bottles, or other low form wide-mouth bottles serve the purpose well. One who expects to have many specimens of feces brought to him by his patients should provide himself with a proper supply of two-ounce wide-mouth bottles with corks. They are also appropriate for sputum bottles. These should never be used a second time. Wide-mouth bottles also have a great advantage in permitting feces to be put in and taken out of them. Moreover, when feces are put in a narrow-mouth bottle, they usually lodge partly in the neck, and, after the stopper is put in, gases form which often blow out the cork and feces, soiling anything or anybody near by. When bottles are entirely filled with feces, especially if liquid, the stopper is very likely to be blown out when the package is unwrapped, if not before. If only partly filled, this is not so likely to occur.

Kind of Feces to be Examined.

Any kind of a stool will do for examination, but there are reasons for preferring the formed feces instead of liquid material. These reasons are that the preparation on the microscope slide can be more satisfactorily made with formed feces; that liquid feces are more odorous and more likely to get out of the bottle accidentally; and that eggs sometimes tend to settle to the bottom of a liquid, and greater care is therefore necessary in making the preparation on the slide; and that, if the specimen is very liquid, eggs are likely to precipitate and stick to the bottom and sides of the bottle, and be missed when only a few eggs are present, in spite of considerable agitation. Pepper has called attention to the peculiarity possessed by hookworm eggs of sticking to the slide after they have once settled in a slide preparation. One who wishes to thoroughly familiarize himself with examination of stools for hookworm eggs should try this for himself. Place on a slide some sediment from centrifuging, described on page 173, containing hookworm eggs. Dip or invert the slide in a beaker of water after allowing the material to settle a few minutes. Now examine the slide under the microscope, and the eggs will be found to have stuck to the slide even after considerable agitation, though everything else came off.

Making the Preparation for Microscopic Examination.

For the examination of feces the ordinary 3-inch slides are too small for the most satisfactory manipulation. We prefer 2x3-inch slides, or even larger. Photographic negative glasses 3¼x3¼, 3¼x4¼, or 4x5 are all very convenient, and usually easy to get. The ordinary 1x3 slides, however, serve the purpose well, especially if a mechanical stage is used.

Put in the center of a slide one to three drops of water,

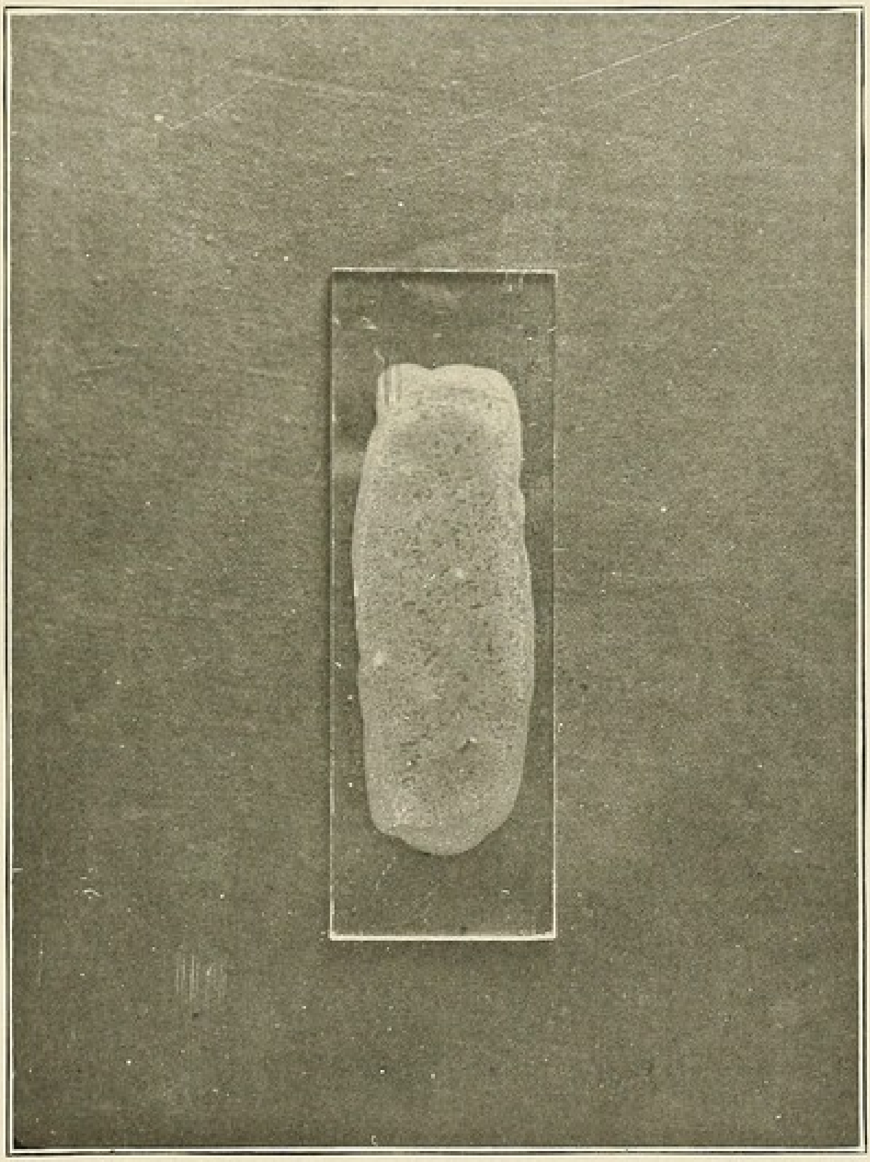

Fig. 45. Diluted feces on slide, ready for microscopic examination.

and with a toothpick take up a quantity of feces about the size of a match head. Stir this into the water until it is about as cloudy as can be examined well with the microscope, spreading out the diluted feces properly over the slide at the same time. The diluted feces should not come quite to the edge or ends of the slide at any point, as they would then easily run off on the hands, microscope, etc. The preparation should cover at least one-half the area of the slide if the ordinary 1x3 slide is used. (Fig. 45.) The thickness of the mixture must be learned by experience, but it is desirable to have it dilute enough to allow a good light to be had and a clear outline of the material on the slide. A preparation that allows ordinary print to be read through with the unaided eye is usually not too thick. It is not necessary to continue stirring the feces off the pick after the mixture becomes of the proper consistency. If properly manipulated so as to rub off the feces gradually, it is easy to stop at any point desired and to throw away any excess of feces with the pick. Ordinary toothpicks are the best things we have ever seen for making such preparations. They have been used for a long time for this and similar purposes by many laboratory workers. They should be of good quality and have one thin flat end. The same pick should never be used for examining another specimen on account of the possibility of carrying eggs from one to the other. Matches or other such pieces of wood serve the purpose also, but not so well. A convenient way to dispose of the soiled picks is to burn the used end over a flame, or they may be dropped into the bottle, which is then stoppered so as to avoid contamination and infection.

Use of Cover Glasses Unnecessary.

It is unnecessary to use cover glasses in examining feces for hookworm or most other parasite eggs. With the magnification generally used they are absolutely unnecessary. It is usually necessary to examine preparations larger than the regular cover glasses and sometimes several of them. If it is desired to study a specimen with high powers for some special purpose, it is easy to place a cover glass over the part to be examined, and press it down gently to thin it out. Cover glasses are also necessary if a great deal of time is to be spent in examining a given slide, to prevent the preparation drying out so rapidly.

Examine Only Wet Preparations.

The preparation is to be examined wet. As soon as it dries it is useless, and, if this happens before an examination is completed, more water is to be added, or another preparation should be made. A properly made preparation can be entirely gone over with the low power lens before it dries out appreciably. If spread out too thin, it will dry much more rapidly. Most of the solid particles, including eggs, if present, settle on the surface of the slide soon after it is prepared, and are then found about in the same level or focus, so that the thicker the layer, provided it does not prevent seeing through it, the more concentrated will be the objects on the surface.

Magnification.

The low power of any of the commonly used microscopes is to be employed. The 2/3 objective and 1-inch eyepiece, or the 16-millimeter objective and corresponding eyepiece, give the proper magnification of about 100 diameters. Higher magnification is undesirable for general work because the field is correspondingly reduced, and therefore it takes much longer to look over a preparation.

Time Required and Number of Slides to be Examined.

The time required to examine for eggs varies with the experience and speed of the examiner, the number of eggs present, the thickness and size of the preparation, and whether there are many particles resembling eggs, requiring close observation to differentiate them. If many eggs are present, the diagnosis may often be made on the first field examined, but to stop after finding a few hookworm eggs is not good practice. The examination should be continued to find, if present, eggs of other parasites which are likely to be present in small numbers, and to get some idea of the number. When less than ten female worms are present, there may be an average of less than one egg to a slide. It is estimated that one actively laying female produces two thousand to three thousand eggs in twenty-four hours, but many of the worms lay much fewer eggs and a few old ones lay none.

We recently had each man of several groups of five medical students examine five or more slides of one hundred different specimens of feces, twenty-nine of which finally showed mild hookworm infection. The remainder, seventy-one, were negative. Several instances occurred in which only one or two men of the group found one or two eggs in a particular specimen. These men had been thoroughly instructed and practiced in the recognition of hookworm eggs, and it is believed were not likely to overlook them. Eggs were found in only twenty-three specimens from this examination of twenty-five slides of each. The negative specimens were now examined after being carefully washed and centrifuged, and six found to contain eggs. In this instance examination of twenty-five slides failed to demonstrate eggs in 20 percent of the cases in which they were present. These were the ordinary 1x3 microscope slides, and the specimens were from adults who had very few worms—not enough to produce any recognizable symptoms, except in one or two instances. Most of them had not been reinfected in many years, and their worms certainly were not laying as prolifically as younger worms do.

Another group of ten men were first well drilled on the diagnosis of worm eggs and then set to work to examine one hundred and thirty-six specimens of feces that showed on final examination fifty-eight infected, as follows: six hookworm, thirty-two trichocephalus, eight tenia nana, twelve oxyuris. One to five slides were examined—an average of two or three. Thirty-one, or 53 percent, of the specimens containing eggs were diagnosed negative by this examination. They were mild infections, and all these worms other than hookworms lay comparatively few eggs, as is well known. These figures show that examining two or three, or even twenty-five, ordinary slide preparations is not sufficient to discover eggs every time when very few are present. It is necessary to examine at least six to ten slides before a practical negative diagnosis can be made, but, if one hundred or more worms are present, eggs can be found in every slide, except under rare conditions. The number of worms in many well-marked or severe cases is from one thousand to four thousand, and eggs, often several, can be found in almost every microscope field. We can look over thoroughly an ordinary slide in two to four minutes. We have seen comparative beginners become able, with a few days of practice, to examine well one slide in six to ten minutes.

Light.

The amount of light used should be that giving the best detail to the small particles in the preparation. On an ordinarily bright day, or with artificial light, the maximum light available when using any standard microscope will be entirely too strong, and must be reduced by partly closing the iris diaphragm under the Abbe condenser. The light is increased or decreased with this diaphragm after the reflector has been adjusted so as to reflect directly all the light falling upon it. The light should be such as permits eggs, when present, to be seen well in detail. The outline of the yolk and shell should be distinct, and the clear albumen space should be well shown. With too bright a light the whole egg is blurred and indistinct.

Method of Going Over the Slide.

If a mechanical stage is used, it is a good plan to begin at one side of a preparation and to move the slide systematically from end to end, moving back or forth the width of a field every time the end is reached until the entire slide has been gone over. With a large slide, or if no mechanical stage is used, the slide should be moved in the same manner with the fingers. With practice and with low power, this can be readily done.

Description of Eggs.

The ova of uncinaria Americana are ellipsoid, fifty-four to seventy-two microns long by thirty-six to forty microns broad, in some cases partially segmented in utero. The ova of ankylostoma duodenale are ellipsoid, fifty-six to sixty-one microns by thirty-four to thirty-eight microns, laid in segmentation. The two varieties have practically the same general appearance, and can not be differentiated except by careful measurement. Uncinaria Americana eggs are said to be more pointed at the poles. (Looss.) Eggs may be seen lying flat, or they may be on end, in which case they appear round. There are all variations between these extremes, in which they appear shorter than normal, due to their being seen in an oblique position on the slide. With experience a mental picture of the size is formed, which is all the guide to size necessary. Different individuals see the size of things under the microscope differently. To our eye, with a 1-inch eyepiece and a 2/3-inch objective, hookworm eggs seem to be three-eighths to one-half inch long by about one-fourth less than this in diameter. The outline of the chitinous shell is smooth and regular, and shows as a narrow band. The regularity in outline of the shell often serves to differentiate them from the capsular membrane enveloping the chlorophyl of many different varieties of vegetable cells. The yolk is made up of fine granular dark gray material and contains a central lighter area. When seen sufficiently early, the yolk is of the same shape as the egg shell, and usually situated about the same distance from it on all sides. There is a distinct clear albumen space between the shell and yolk from one-eighth to one-fifteenth as wide as the diameter of the egg. Most of the eggs begin to segment before the feces are discharged, and therefore those found in fresh material contain two, four, or eight, or more segments. (Figs. 11, 13.) In older stools embryos may be seen inside of the egg shell, nearly ready to come out and moving around slowly in their shell, which they nearly fill. (Fig. 11.) For a complete description of the embryos and larvæ see the chapter on zoology.

Number of Worms Indicated by Number of Eggs.

Leichtenstern has proposed to estimate the number of worms present by the number of eggs found in the feces. He divides the number of ova contained in one gram of feces by the factor forty-seven. Grassi and Parona estimate the number of eggs in one centigram of feces and calculate the number of worms, assuming that one hundred and fifty to one hundred and eighty eggs per centigram represent one thousand worms.

Ashford and King have called attention to the fact that certain things may prevent the correct estimation of worms by the eggs present. They well say that the worms cause an increase of mucus at the site of their feeding ground, and, as this mucus often comes off *en masse* and contains most of the eggs, the actual feces would contain relatively few. They say eggs are more difficult to find in diarrheal stools for some reason or other, and in this connection we mention the fact that the quantity of feces passed by different individuals varies greatly with the size and age, the kind and amount of food eaten, the digestive ability of the patient, and also with the water intake and elimination, intestinal bacterial flora, etc. Ashford and King saw cases of heavy infection that at times had no ova in their feces, especially soon after thymol had been given, but they also had patients with many ova two days after full thymol treatment. With us it has been a common experience to have a patient's feces reported negative within a few days after a course of thymol and on subsequent examination eggs be found in large numbers. This is more likely to occur, of course, when the examination is not thorough. In one instance after a course of thymol the most exhaustive examination revealed no eggs one and two weeks afterward. The patient remained in the city, and therefore was not exposed to reinfection. It was winter, during which infection does not usually occur. Six weeks after the thymol ova were again found, and one hundred and nineteen male and female worms were expelled as the result of another course of thymol. Dieminger found that the number of eggs was very much diminished when patients were drinking hard. He examined twenty-one men on Monday and found only four infected; on the following Friday he found many ova in eleven who had shown none on Monday. In another instance he found a man heavily infected on Saturday, but on the following Monday he could find no ova after repeated search. The reason he assigns is that these men had been drinking to excess on Sunday. It is not improbable that the activity of egg production by hookworms is influenced by season of the year. Salt herring or other very salty food also has some effect. One of us (Bass) has recently reported the examination of two hundred and forty-seven female uncinaria Americana, 7 percent of which contained no ova, and suggested the possibility of old age being the cause. Dr. Stiles, in discussing this question at the recent Hookworm Conference in Atlanta, 1910, said he was not prepared to say whether the worms live long after old age induces cessation of ovulation, but, reasoning from analogy, he did not think this probable. Though animals highest in the scale cease to ovulate at the end of about two-thirds of their usual life, it is not probable that any lower forms do this, at least to the same extent. We have recently examined three hundred and ninety-seven female uncinaria Americana from patients whose ages and histories indicate that they have not been reinfected for several years, and these showed 9 1/4 percent of barren worms, whereas three hundred and twenty dog uncinaria from young dogs showed only 1/3 percent without eggs. It is very doubtful, however, whether a patient may be infected with any considerable number of worms without a few eggs being present in the feces and always demonstrable by thorough examination. However, we believe the possibility of only a very few old worms being present is to be thought of in cases with a history indicating previous existence of the disease and persistence of symptoms. This may explain some of the cases of persistence of eosinophilia and other symptoms, though no eggs are present. If such cases occur, the only way to clear up the diagnosis positively would be to give a course of treatment and examine the feces thoroughly for worms.

Differentiation of Uncinaria Eggs from Other Ova, Etc.

The eggs of uncinaria are easily differentiated from those of other parasites, except possibly strongyloides. Strongyloides eggs have the shape and appearance of hookworm eggs, and measure about seventy microns long by thirty-five microns thick. The shell is clear, but yellow. They are seldom seen, because they almost always hatch while in the intestine and sometimes before they are expelled from the uterus, and when an egg is found there are also to be found in the feces thousands of strongyloides larvæ. These can not be easily differentiated from uncinaria larvæ, but, if it is remembered that uncinaria larvæ are not found in fresh feces, little difficulty is experienced. If the stool is sufficiently old (twenty-four hours or longer) for uncinaria larvæ to have hatched out, there will still be present in any specimen of undiluted feces far more eggs than larvæ—a thing never seen with strongyloides. Strongyloides larvæ are differentiated from uncinaria larvæ by the presence of a larger double dilatation of the esophagus and by the development of the filariform stage when the material is kept for six or eight hours or longer. The primordium, which later develops into the sexual organs, is seen at about the middle of the body of each, but in strongyloides it is large and oval, whereas in uncinaria it is small and round. They develop long (four-tenths to seven-tenths of an inch), narrow, very active worms, with an esophagus almost one-half their length. Hookworm larvæ, on the other hand, become encapsuled in four to five days. Double infection may occur. Ascaris lumbricoides eggs are larger, fifty to seventy microns long by forty to fifty microns thick, have a thick, rough, albuminous, bile-stained coating of the shell, are more oval, and have less albumen space. Trichocephalus eggs are smaller, about fifty by twenty-three microns, more oblong, and have a cap on each end, "lemon shaped." Oxyuris eggs are smaller, fifty by twenty microns, more oblong, and have a relatively smaller nucleus. One side is straight and the other curved, and one end is smaller than the other. They are more refractile, giving them a shining appearance, and slightly yellow. Most of the eggs seen are empty shells from which the embryo has already escaped. Tenia eggs are smaller, have a thick shell consisting of an inner and an outer membrane, between which there is a thick layer of albuminous material. In tenia saginata, tenia solium, and tenia diplogonoporus grandis this is distinctly striated, while the tenia nana has only a few longitudinal bands running through this part of the egg, starting from the poles. All have hooklets or the resemblance of hooklets in their nuclei. Bothriocephalus latus eggs measure about forty-five by sixty-eight to seventy-one microns, and the nucleus entirely fills the shell. They are brown, and a cap or lid can be seen at one end.

The beginner often has difficulty in differentiating from eggs various vegetable cells and sometimes other food material, balls of bacteria, etc. After fixing a correct mental picture of the size and shape of hookworm eggs by studying known specimens, including the appearance of the nucleus, and observing the rule that nothing is to be called an egg that does not consist of a definite shell, yolk, and clear space, little trouble is experienced. The beginner often diagnoses vegetable cells as uncinaria eggs. Those foods that are ''mealy'' when cooked—like beans, peas, potatoes, etc.—or when raw—like apples, etc.—furnish the greatest quantity of deceptive vegetable cells. Many a time we have known cells diagnosed as hookworm eggs by those who had seen eggs several times before, notwithstanding the fact that there were often in the same fluid many other similar cells not at all egg-shaped and several times larger or smaller than the cells diagnosed. Vegetable cells are irregular in outline, shape, and size, while hookworm eggs are regular in these particulars. While vegetable cells may be found strongly resembling hookworm eggs, there will be found in the same specimen, and usually in the same field, many cells, otherwise like the one in question, which vary much in appearance from uncinaria eggs. The segments of the yolk of hookworm eggs are made up of very fine granular matter, whereas the chlorophyl granules of vegetable cells are much coarser. Finally, the space between the yolk and shell of eggs varies much at different points, whereas the outer membrane of vegetable cells dips in over depressions in the nuclear material, and in fact makes a covering of the same thickness over the irregular nuclear mass. If in doubt as to the diagnosis of the eggs, they may be hatched out in twenty-four to forty-eight hours and the characteristic larvæ looked for. To this end some feces may be placed in a Petri dish, or other suitable container, and a few folds of filter paper stuck down in it, with one end extending above the material. This serves to dry it out sufficiently, and, if the culture is kept in a warm, shady place, hatching soon occurs; or the feces may be mixed with one or more parts of charcoal or sterile sand, in which the eggs hatch well. This should be moist, but not covered with water, which interferes with hatching. The larvæ may be found in material from around the edges of the paper or dish, but after a few days will crawl up on the sides and cover of the dish, as shown by Claude A. Smith in his excellent experimental work on this subject. He noted little grayish smears, consisting of numerous larvæ, on the sides and cover of the culture dish. Larvæ of uncinaria in stools are not found, except in rare instances, until twenty-four hours or longer after evacuation. We have often found them in feces, always associated with large numbers of eggs, sent by mail—usually specimens that had partly dried out. It must be remembered that there is a large number of nematodes, to which uncinaria belong, the rhabditiform larvæ of which can not be easily differentiated from each other.

Special Methods for Greater Certainty in Finding the Eggs.

Pepper's method.—Pepper, as mentioned above, has called attention to a peculiarity of hookworm eggs which makes it possible to concentrate them considerably, or at least to get rid of much of the fecal matter and thereby render them more easily found. He notes that when material containing eggs is allowed to settle on a slide, the slide may be immersed in water and considerably agitated without the eggs coming away, though the slide is inverted and all the feces rinsed off. We have often confirmed his findings. The best results are obtained if a part of the fecal material is removed by use of the centrifuge before the slide preparation is made. Otherwise the method is often disappointing.

Külz recommends Telemann's method of examining feces. In this, equal parts of ether and pure hydrochloric acid are shaken up with a bit of feces, filtered through gauze and centrifugated. The fat rises to the top; in the middle layer are the solution and detritus, and at the bottom insoluble remains and eggs. We have found the method admirable with some stools, but in others not enough solution occurs to permit a concentrated layer of eggs to be thrown down.

Sedimenting the feces by diluting with ten or more times the amount of water, and allowing the mixture to settle for fifteen minutes or longer in a beaker, test tube, or conical glass, assures greater success than examining the untreated feces. The eggs, being larger and heavier than many of the particles making up the fecal mass, settle faster and are more numerous in the bottom of the container. Material may now be taken from the lower layers and a slide preparation made in the usual manner. By repeating the sedimentation several times, still better results may be obtained. Concentration of the eggs with the centrifuge has been referred to by Looss, Claude A. Smith, Ashford, King, and others. Simply centrifuging the diluted feces does not, however, give the best results. They are obtained only when the most careful attention is paid to details which we believe are of sufficient importance to warrant thorough consideration here. One-third or more of the fecal mass consists of bacteria which are relatively very small compared with the size of eggs. They have, therefore, a much greater surface per given weight than eggs. Most of them have a lower specific gravity also. Much of the feces consists of food particles ranging in size from that of bacteria up to coarse macroscopic particles. Most of these food particles are irregular in outline and shape, making their surface per given weight greater than that of the round, oval eggs. The specific gravity of much of this material is less than that of eggs, and some of it even heavier. Feces also contain variable amounts of concretions—"fecal sand," vegetable cells, crystals, etc.—which are usually heavier than eggs.

Centrifuges.—These are of three kinds—hand, water, and electric. The speed of a hand centrifuge varies according to the rapidity of the operator, but fairly high speeds can be obtained. They can be started and stopped quickly. Water centrifuges do not, as a rule, get up high speed, and they start and stop slowly. Good electric centrifuges run at high speed, and start and stop quickly. The Purdy centrifuge, made by Williams, Browne, and Earle, is the best we know for this purpose, though some others are good. Satisfactory work for practical purposes can be done with a good hand machine that costs only about $8.00.

The feces should be diluted and well mixed with ten or more times their bulk of water. This should be strained through two or three layers of gauze in a funnel to remove the coarse particles. The exact length of time necessary to centrifuge, in order to throw most of the eggs suspended in water to the bottom of the tube, should be determined by experimenting with a known specimen that has already been washed once or twice and contains many eggs. This must be determined with the particular centrifuge used. The Purdy centrifuge used by us, running at full speed, throws eggs to the bottom in four seconds. With a hand centrifuge it takes considerably longer, depending on the speed obtained. As the first diluted feces are much thicker than the washed feces and eggs on which the working time of the centrifuge has been determined, the eggs will go down somewhat slower the first time. It is, therefore, a good plan to centrifuge double time at first. If, for instance, the working time of the centrifuge is four seconds, the first centrifuging should be eight seconds. This throws to the bottom most things heavier and larger than eggs—like crystals, sand, large vegetable cells, etc.—and all eggs present. There remain suspended in the supernatant fluid nearly all bacteria and fine particles, and many coarse particles lighter and more irregularly shaped than eggs. If the centrifuge is run longer, many of these go down, which is, of course, undesirable. Pour off this fluid, and two-thirds, and often much more, of the feces are removed by this washing. Refill the tube to about three-fourths its capacity, shake up thoroughly, and centrifuge again, running now only the working time of the centrifuge. It is important not to centrifuge longer than the working time of the centrifuge, as many fine and light particles would otherwise be thrown down. Considerable material remains suspended, and may be removed by pouring off the supernatant fluid. Again the tube is filled, shaken, and centrifuged a proper length of time, and generally this will be sufficient for practical purposes. A part or all the sediment is removed with a pipette, spread out on a slide, and examined for eggs. It consists of crystals, sand, and heavy, coarse food particles, and eggs if present. It is important to remove the sediment properly. A clean pipette, with the finger held over the end of it, is carried to the bottom of the tube. Before removing the finger and allowing the sediment to run in, it should be well broken loose from the bottom of the tube by means of the pipette. Then the finger is partially removed, and a part or all the sediment allowed to run up into the pipette. Part or all this is spread on a slide and examined as usual. A worker accustomed to this procedure is able to wash, centrifuge several times, and get the sediment of a specimen on a slide ready for examination within four or five minutes. The examination takes about the same time as is required to examine an ordinary preparation of feces of the same size, but usually all the sediment may be placed on one slide, and one slide is, therefore, all that it is necessary to examine. A mechanical stage enables one more thoroughly to go over the slide. A large amount of the sediment can be examined if Pepper's technic is now used. After allowing the thick smear to settle well, the slide is immersed in a beaker or glass of water. Uncinaria eggs remain, but most other things wash off. One serious objection to following this technic is that, while looking for hookworm eggs, we also want to find any other eggs present. No other eggs we know of stick to the slide like hookworm eggs. This procedure cannot, therefore, be recommended for general work. Great care must be exercised to clean the centrifuge tubes before using them after they have had eggs in them. A proper centrifuge tube brush is serviceable.

The method of centrifuging described above is all that is necessary for ordinary practical purposes, and, if properly done, permits the finding of eggs when less than half a dozen laying females are present, and often when only one is present. It is of additional service because it permits at the same time diagnosis of infections with many other worms by which much fewer eggs are laid, such as the tenias, oxyuris, bothriocephalus, etc. Bass found that he could still further concentrate the eggs by washing with calcium chloride solution after washing with water. The

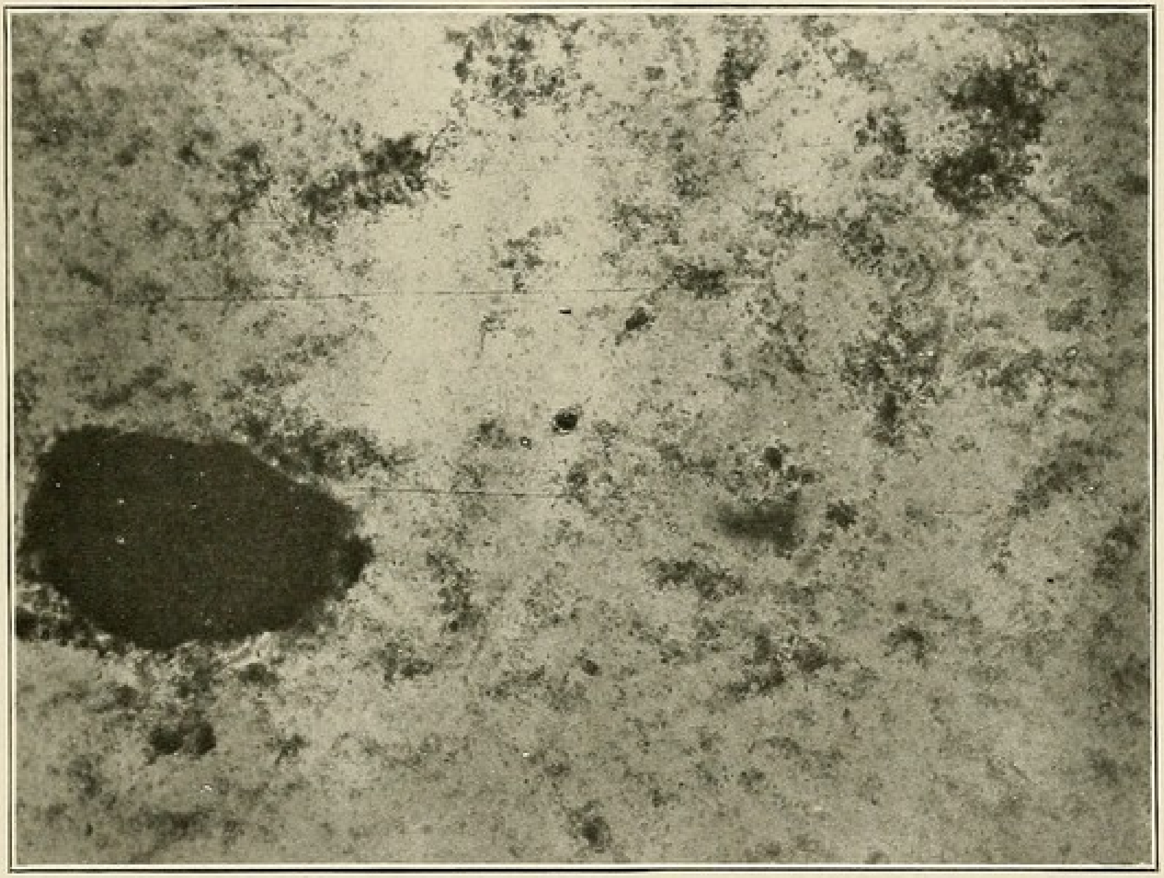

Fig. 46. Microscopic appearance of feces, showing poorly one egg in center.

specific gravity of fresh hookworm eggs is near 1,100. This usually increases as the specimen gets old. A solution of calcium chloride having a specific gravity of 1,050 will suspend considerable of the sediment, though the eggs still readily go to the bottom. By washing with this solution two or three times after washing with water, much material not removed with the water can be removed. If still better results are desired, the crystals and very heavy things can be removed by washing with a solution of calcium chloride of 1,250 specific gravity, in which most of them go down, but hookworm eggs float. After centrifuging, the supernatant fluid containing the eggs is poured off and appropriately diluted with water, and the eggs again thrown to the bottom, from where they are easily taken up. This calcium chloride washing is necessary only when very great accuracy

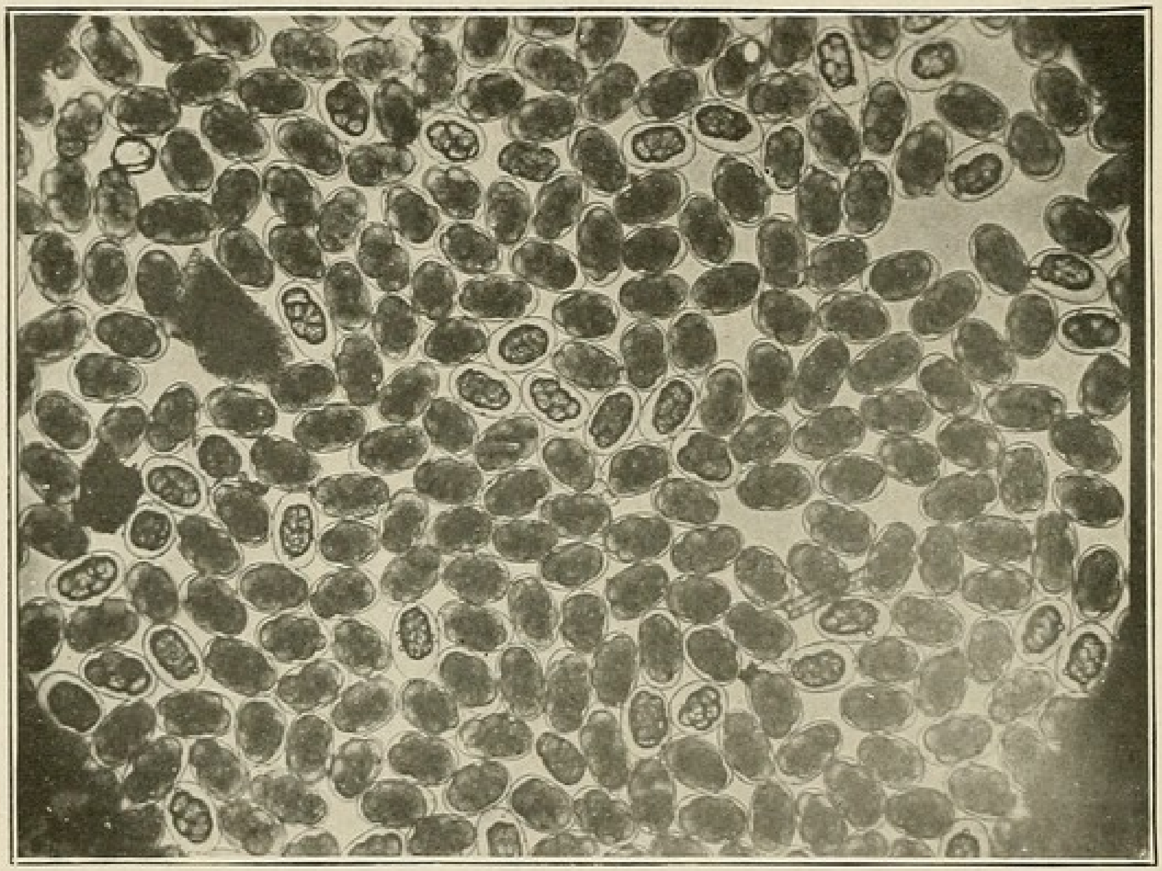

Fig. 47. Preparation made by Bass' method from feces shown in Fig. 46. Appear about as large as they do with 1/6 objective and 2-inch eyepiece.

is desired, or when it is desired to collect eggs absolutely free from fecal material for scientific purposes. Solutions of calcium chloride of several different strengths should be employed for this purpose, and much is also gained by keeping the patient on a wholly digestible diet. Bass found that with this technic he was able to recover 96 percent of one thousand eggs placed in one ounce of feces, 94 percent of one hundred eggs in the same amount, and 60 percent of ten eggs in one ounce. The value of the centrifuge is shown by the work of Gage and Bass. They examined the feces of 315 university students. One to 25 slides were examined in the ordinary way, and 104 cases were found infected with some intestinal parasite, 79 of them being hookworms. The specimens found negative by the ordinary technic were centrifuged, either using water only or water and calcium chloride solution, as described. By this method 38 additional hookworm cases were found. Of the entire 104 cases of intestinal parasite infection 47 percent were found by the usual technic, and 53 percent were missed until the centrifuge technic was employed. It is to be emphasized that most of this series of cases were mild cases of uncinariasis, or infection with other worms that lay fewer eggs than uncinaria. Gage and Bass conclude after this extensive experience that, for all practical purposes, washing with water alone is all that is necessary, and that the washing with calcium chloride solution is unnecessary, except for special purposes.

As to whether it is necessary to use the centrifuge in every case, we would say that it is not in the ordinary diagnosis and treatment of hookworm disease, but that it is necessary for the recognition of many cases of mild worm infection. The time consumed, ten to fifteen minutes, is not as great as that required to make a much less reliable examination by the ordinary technic, and the satisfaction derived from being certain that no eggs are present is worth the effort.

Diagnosis by Examining Stools for Worms after Treatment.

Either thymol or beta-naphtol may be given for this purpose, and, though usually recommended in smaller doses for diagnosis than for treatment, we believe that, unless special contraindications exist, the full regulation dose should be given, preceded and followed by the same purgation and starvation as if a well-marked case was being treated. All feces passed during the first twelve to twenty-four hours after the last purge should be examined by washing, as described by Dr. Stiles. They are stirred in a bucket or other suitable vessel with water, after which the mixture is allowed to settle a minute or two. The supernatant fluid is poured off and the sediment rewashed several times. After washing thoroughly, the residue is placed in a flat dish or vessel with water in it, and the worms searched for. A glass dish placed over a black surface, or one painted black, makes the identification of the worms easier. The worms may be collected with a pair of tweezers. They are about the thickness of a common brass pin, from three-eighths of an inch (shortest males) to five-eighths of an inch (longest females) in length, and are white or gray in color, according to the amount of food and eggs they contain. A complete description of the worms is given in the chapter on zoology.

It should be said here that the worms are not likely to be found in the stools, except after treatment. The history often related by people that they saw hookworms in their stools usually means that they have mistaken some other worm or food particles for hookworms. In fact, the worms are often not found even when many are present, unless they are properly looked for and with great care.

Blotting Paper Test.

Stiles has found that in a large proportion of medium or severe cases of uncinariasis this test is positive. It is made by placing on a piece of white blotting paper, or other soft white paper, some fresh feces. In about fifteen minutes these are removed, and when the test is positive the paper will show a red or reddish brown blot where the feces had been. Though of service in some cases, the test can not be recommended for general use, because of the many other sources of positive tests besides hookworm disease, such as other hemorrhages, vegetable coloring matter, etc. We have found it positive, however, in several severe cases of uncinariasis.

The Eosinophile Count in Diagnosis.

The importance of the eosinophile leucocyte count in the diagnosis of hookworm disease has been emphasized by Boycott and Haldane, and under certain conditions may be of value. They found of one hundred and forty-eight men infected with ankylostoma duodenalis 94 percent had over 8 percent of eosinophiles, and only 3 1/2 percent had less than 5 percent of eosinophiles. In eight hundred noninfected miners there were only seven cases of eosinophilia. The feces of one of those were not examined. Two showed ascaris eggs, and the other four showed trichocephalus dispar eggs. They especially recommend the eosinophile count because of the rapidity with which it can be made. They examined one hundred and eighty-three films in four days.

They themselves point out that the method is most useful only in regions where other causes of eosinophilia are rare. They say "this method could not be employed with success, for example, with an ordinary Swiss population, where ascaris is a frequent cause of a high grade of eosinophilia; still less in the tropics, where natives have more than one cause of eosinophilia in their persons besides ankylostoma. No suggestion has ever been made by us, however, that it should be used under these circumstances, nor has it been proposed that the examination of blood films should replace the search for eggs in the feces in persons in whom a prima-facie case for the presence of ankylostomiasis has been made out. The ultimate diagnosis, which is preliminary to treatment, must rest on the examination of the feces. A preliminary examination of the blood will, however, save a great deal of trouble in cases, as in English miners, where other causes of eosinophilia are practically absent."

In six hundred and ninety-three cases of hookworm infection in various degrees of which we have record of the blood examination the eosinophile count was 5 percent or over in two hundred and twelve and below 5 percent in four hundred and eighty-one. The highest count was 34 percent and the lowest 1/5 percent. The average for the entire number was 4 1/8 percent. The average for two hundred selected lowest count cases was 2 1/3 percent. It should be stated that the majority of these cases were mild infections, and indeed many of them so mild as to require the use of the centrifuge before ova were found. In four hundred and four well people, whose blood and feces were examined and no uncinaria or other eggs found, the eosinophiles averaged 2 7/10 percent. The highest was 17 percent and the lowest none in a five hundred cell count. Above 5 percent was recorded in thirty-four instances. Many cases of severe uncinariasis have not more than the normal count, as pointed out by Ashford and King, and this is true in almost all cases shortly before death. It is certain, however, that most moderate or severe cases of hookworm infection have counts above the normal. From the above and our own experience we would conclude that the chief value of the eosinophile count in the diagnosis of hookworm disease lies in the suggestion a high count makes to examine the feces when the disease has not otherwise been suspected. Eosinophilia is present in so many hookworm and other worm infections that we believe the feces should always be examined when high counts are obtained.

In this connection it may be well to call attention to the fact that a count of one hundred cells does not give a reliable estimate of the percentage of eosinophiles or any other cells found in small numbers. It is necessary to count at least three hundred cells, and preferably five hundred. Much speed can be gained by taking only the total leucocytes and the eosinophiles. Counting by twos, threes, or fives, instead of by ones, also saves time. For speed the thickest part of a spread, where the cells can be differentiated, is best.

CHAPTER VIII.

PROGNOSIS.

The prognosis of hookworm infection varies within wide extremes, depending on several factors, such as number of worms, age and constitution of the patient, possibility of getting proper food, and especially of receiving proper and timely treatment.

If the worms are few and the individual well nourished, hookworm disease does not always develop. The subject remains a carrier. Though not ill subjectively, he is, however, in a pathologic condition, and often shows, on careful examination, not only ova of the parasites in the stools, but also slight loss of weight in proportion to his age, slight lowering of the blood-coloring matter and red blood corpuscles, and eosinophilia. We believe these slight abnormalities are not without importance. If the subject is able to eat, digest, and assimilate enough proper food, and to live comfortably, he may be able to keep abreast of his contemporaries in school and college, and to hold his own at work, or in business or a profession. By six or seven years after his last infection, in most cases, he is free from parasites, these having died of old age. Under favorable circumstances the subject now recovers completely. In some cases, however, we suspect that the drain, though slight, caused by the parasites will have damaged the host, and that neurasthenia, or vascular or cardiac disease, may come on by reason of the excessive calls on the energy of the latter. For this reason, as well as for prophylactic purposes, all hookworm carriers should be sought out and treated. If they are exposed to reinfection, the risk of permanent, even though slight, damage is greater.

It is doubtful whether true immunity occurs in Caucasians. Mild cases may go on for years, the worms gradually undergoing senile changes, and therefore less potent for ill.

In moderate infections, among poor people, a lowering of physical and mental and moral strength occurs. School children so affected may not be able to accomplish more than 60 percent of required work.

The worst cases are those in which there is a heavy infection, with from one to many thousand worms. Even in well-to-do subjects these become severely affected, but among the underfed or the overworked the results are most serious. Either the patient becomes rapidly anemic, with digestive disorders, sometimes severe diarrhea with hemorrhages, anasarca, and extreme debility, or the conditions may be more chronic. Indolence and weakness lead to careless habits. Reinfection occurs from time to time. Often a whole family becomes affected more or less seriously. The wage earners lose part, or later all, of their income, the food supply becomes more scanty, and a vicious circle of poverty, weakness, and disease is established. Often doctors are far away, or even not accessible at all, and a whole family may be exterminated before the youngest children are half grown. Formerly these cases were supposed to die of pernicious malaria, of nephritis, and in some countries of beriberi. We strongly suspect, with many other southern physicians, that many cases in negroes, ending fatally and supposed to be tuberculosis, are undiagnosed cases of hookworm disease. The difficulty of getting a clear history in negroes, the rarity of physical diagnosis and sputum examination, and the similarity of the late symptoms in the disease make the confusion a very natural one.

Mortality.

The mortality of hookworm disease in America can not yet be accurately stated. The disease has not been known long enough, and the diagnosis is not attempted often enough, to furnish data of value. In Porto Rico Ashford and King estimated the death rate before systematic treatment was begun at 30 percent, which was probably not too high. In Egypt, among cases treated, Sandwith thinks 89.5 percent are cured or greatly relieved, 2.5 are unrelieved, and 8 percent die. One-third of the latter are first seen moribund, another third die of various complicating diseases, and the remaining third of hookworm disease.

In the prognosis of a given case the most useful guides are the general condition and the condition of the most important organs, the probable number of worms as shown by the fecal examination, and the possibility of proper treatment, which often depends upon the financial condition of the patient. "The destruction of the poor is their poverty" applies with particular force in hookworm countries.

Of other points, eosinophilia has some value. In severe cases, if present, it is usually a sign that the disease has not gone on to complete exhaustion of the blood-forming organs. In mild cases it often indicates periods of relative well-being. Prof. Fülleborn, of Hamburg, who had an experimental infection, told us his eosinophiles were always higher when he was feeling best.

The Porto Rico Commission, in 1904, wrote (page 84):

"The chief interest centered around the eosinophiles. There is no doubt that the following conclusions may be drawn with safety (conclusions which, by the way, were suggested in the report of the Ponce cases in 1903):

"1. Very severe chronic cases, with poor resisting power and exhausted blood-making organs, have little or no eosinophilia. Leichtenstern's remarkable case of 72 percent eosinophiles just before death does not negative this view. We had a case which died in coma, possibly due to cerebral effusion. This child was admitted with 6.4 percent eosinophiles and died with 20.8 percent.

"2. A rise in eosinophiles is of good prognostic import. Especially is this true of those who, admitted to treatment with conditions described under 1, begin to show higher and higher eosinophile counts. There are such cases, not explicable to us, where, in spite of a lack of rise in these cells, improvement does take place. It may be rather rapid, but is generally very slow.

"3. If very severe cases, presenting little or no eosinophilia, [have a] fall in their eosinophile count, the prognosis is not generally good.

"In general, good resistance to the toxin of uncinaria is expressed by eosinophilia. Our special cases, being nearly all severe, gave an average of 10.8 percent eosinophiles before any treatment was begun, and the ultimate percentage of these cells, after all treatment had been concluded, was 13.2. As forty-two of the sixty-one were completely cured at that time, and fifteen were nearly so, it is clearly seen that the number of uncinariæ *per se* has nothing to do with eosinophilia directly. As to the oft cited remark that eosinophilia and Charcot-Leyden crystals increase and fall together, there are cases which fail to show such relation.

"The eosinophiles behave in a most extraordinary way in the course of cure. There seems to be a general rise to a certain percentage, varying according to the individual, after which a fall to normal takes place. This fall to normal may occur before the patient reaches a normal hemoglobin percentage, or may be delayed until some time after cure. In this course of rise and fall, great undulations may take place in the curve, which as yet seem to be difficult to explain.

"Some very pertinent questions arise in consideration of the question of eosinophilia:

"1. Is it an evidence of blood regeneration, of increased activity of blood-making organs?

"2. Is it that eosinophiles are directly concerned in the defense of the organism against the toxin?

"There are many other theories concerning eosinophilia in general—for instance, that of Weiss, who, Ewing says, maintains 'that local eosinophilia tends to occur where there is extensive extravasation of blood, the derivatives of hemoglobin being absorbed by the polynuclear cells and deposited in the form of eosinophile granules.' "

Among other elements in prognosis, pregnancy is an unfavorable one. 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 promptly improves under thymol treatment. The offspring of untreated hookworm patients are likely to be poorly developed and marantic.

While the most severe cases are seen in early life, the disease is sometimes severe in cases that develop after 60. All complications that contraindicate treatment render the prognosis worse.

The effect of hookworm disease on duration of life is very important. Old people in the rural districts of hookworm countries seem less numerous than they are in cities, with their greater exposure to numerous adverse conditions. The Porto Rico Commission confirms this by stating that in Porto Rico, though there are more children in proportion to adults than in any other state, except South Carolina, those over 60 years are forty to the thousand, as compared with sixty-two to the thousand in the United States in general.

Intercurrent Diseases and Complications.

Like all conditions with anemia, hookworm disease is likely to be associated with many other diseases. Some of them are assisted by the anemia, and some are due to the intestinal derangements and the perversions of appetite. The following are especially frequent: gastritis, dilatation of the stomach, enterocolitis, amebic and bacillary dysentery, edema of the lungs, neurasthenia, and nephritis. The latter is very common in advanced cases. Syphilis and tuberculosis are not especially frequent, but are likely to be severe, in hookworm subjects. Rheumatic pains are not uncommon. Ashford and King recovered from the blood of such cases a bacillus, which, however, they also found in other diseases. Among other diseases frequently encountered in histories of hookworm subjects are: tonsilitis, laryngitis, pneumonia, paresis, hemiplegia, jaundice, ulcer of the stomach, conjunctivitis and trachoma, renal colic, pellagra, and elephantiasis. The last two named occur in endemic areas, and the relation is only an assisting one.

As regards pneumonia, Gregorson reports some interesting facts from Assam, where the tea-gardeners were formerly very severely affected with hookworm. Pneumonia was also very frequent, but, as the hookworm disease became less frequent under sanitation and treatment, there was a notable fall in the incidence of pneumonia. The frequency and severity of pneumonia in the southern states of America have often been noted, and no good explanation for it has been advanced. It can not be doubted that the effects of hookworm infection lower the resistance, so that depressing diseases of all kinds are more difficult to withstand. Moreover, the hookworm anemia lowers the amount of oxygen-carrying blood, while lack of oxygen in pneumonia increases the need.

Other Parasites.

It is to be expected that hookworm subjects should often harbor other intestinal parasites as well as others, as they usually live where parasites of all kinds are frequent. Many of the other entozoa, though not all, are expelled with hookworms after treatment. The following may be named: ascaris lumbricoides and ascaris caninum; bilharzia, trichinella, strongyloides, balantidium, oxyuris, diplogonoporus grandis, amebæ, fasciola hepatica, tenia saginata and tenia solium, and filaria.

Among the most frequent sequels in severe cases are: diseases of the heart, liver, and kidneys, endocarditis and arteriosclerosis, severe anemia, intestinal indigestion due to the destruction of the mucous membrane by bites and infection, and ulceration of the intestine.

Among rare results are perforation and stricture of the gut.

It should be clearly understood that the prognosis in hookworm disease is favorable in proportion to the promptness and the completeness of treatment.

In rare cases the condition is such that treatment can not be borne, or the patient is too ill to recover even if the worms are removed.

CHAPTER IX.

PROPHYLAXIS.

"In the universal treatment of persons affected lies the secret of successful opposition to uncinariasis." (Porto Rico Commission.)

Hookworm disease is theoretically one of the easiest to prevent. Its cause is known—unlike the causes of the eruptive fevers, that still remain as tests of hygienic efficiency. All the vital characteristics of the parasite are understood; it has no secondary host, like the tapeworms, that spend part of their cycle in animals widely used as food; it is not easily taken with drinking water or milk, like the germ of typhoid fever; it is not carried, to any serious extent at least, by flies or other insects, nor by the wind. In a word, it does not come to man—man goes to it.

Practically it is one of the most difficult diseases to prevent or eradicate on account of its wide extent, its intensity in favorable localities, the enormous reproductive power of the adult worm, the rapid development of the ova to the infecting stage, and the commonest method, until recently unsuspected, of infection. The very fact that the skin infection has not been known longer may be the main reason why the prophylaxis in the past has been so difficult. Wider recognition of it may bring about a greater change. Another cause of difficulty in prevention depends upon the fact that the sources of infection, their number, and danger result directly from careless or filthy habits. These, too, seem almost ineradicable, but may be much more amenable to education than they now appear.

The magnitude of the task of prevention appears from the statistics given in Chapter II. In hookworm localities practically all children and many adults have the disease, reinfection keeping it up much longer than the usual lifetime of each worm. Probably most rural negroes also are affected in all parts of the world, but often do not show symptoms. So the two classes of the population most regardless of cleanliness can do most harm by their lack of that virtue.

The problem of prophylaxis involves the following essential elements:

1. Stopping the danger of infection by exterminating the mature worms in the bodies of human beings in order to check the supply of eggs at the source.

2. Preventing the growth and existence of larvæ in the places where they develop.

3. Preventing infection by larvæ that have developed, notwithstanding the efforts mentioned under 1 and 2.

1. **Extermination of the mature worms.**—The first need for the prevention of hookworm disease is to stop it in those already affected—hookworm patients. This is a task that will naturally fall upon the physician. When the disease was unrecognized, cure was out of the question. Now that the condition is so clearly realized that the symptoms are often recognized even by laymen, and the microscopic diagnosis is easy to make, we can expect a distinct advance in the successful treatment of these important cases as soon as the people appreciate the danger now existing. Accurate recognition of the sick, careful treatment, controlled by examination of the feces, and repeated until perfect, will lessen the supply of ova to a great extent.

But not altogether. There remains the great and important class of hookworm carriers—of people either with no symptoms, or with symptoms so mild as to go unnoticed, but with from a few to a couple of hundred worms, most of which will live for several years, laying eggs in large numbers all the time, and, in hookworm localities, keeping reinfected for longer periods. These people are all the more dangerous because they are not supposed to be sick, just as a child with mild scarlet fever or diphtheria is more likely seriously to infect a whole school or community than one with a severe case that will be promptly isolated. The hookworm carriers require methods of hygienic treatment not necessary for cases of illness of obvious kinds. As they are not indisposed, they will not consult physicians; but, as they are menaces to the health of the community, it is evidently the duty and within the power of the health authorities to search them out and deal with them as if they were sick, and to see they become harmless. This not only involves a new exercise of the police power already possessed by boards of health, which seem arbitrary to those who have barbarous ideas of personal liberty, but is a task beyond the physical ability of the usual health administration as now constituted. Hookworm eradication requires an adequate sanitary organization, which would bring many benefits besides checking hookworm infection.

It would be necessary to make periodic examinations of all persons living in localities and under conditions favorable to the existence of hookworm larvæ, and to keep records of all of these; to examine all newcomers, to see that treatment is carried out to a successful degree, and that patients or carriers once cured do not become reinfected, or, if they do, to treat them again. The same authorities should organize education in regard to hookworm disease.

In localities where the population is known to the health officers—as in camps, mines, tunnel or canal workings—the inspection and treatment of newcomers could be easily accomplished. In mills and factories, employers would find it to their advantage to have the hands periodically examined and treated. A gain of 20 to 40 percent of hemoglobin, with a corresponding gain of energy, would result. In towns, villages, or country districts methods of surveillance that have not as yet been applied in America would be necessary. As regards patients, carriers, and suspects, there should always be close and cordial co-operation between practicing physicians and health authorities.

The value of accurate and careful methods under natural disadvantages has been shown in many places within the last few years, not only in the Westphalian, Belgian, and French coal mines, but especially in the island of Porto Rico, where the work of the "Anemia Commission," organized by Ashford and King, has furnished a model of efficient and economic administration.

2. **Prevention of soil infection.**—The next essential is the prevention of soil infection. In all countries about the dwelling houses, and in all mines, tunnels, or similar works where men handle earth, soil pollution from lack of care in the disposal of feces is the rule. If people with hookworms are present, the soil becomes infected, and, if the soil and climatic conditions are favorable, the larvæ develop. The Porto Rico Commission (1904) expresses the matter clearly:

"Uncinariasis is pre-eminently a filth disease. The only means of infecting the soil is by evacuation of the bowels where the ova in the feces will later develop. If latrines were generally used, uncinariasis would forever disappear. . . . [There is] absolute disregard for sanitation in this respect in the country districts. Practically all our Utuado cases stated that they deposited their feces in the open country, and had no latrine, nor even a hole in the ground, for this purpose. Our special cases there are fair examples of the average—of sixty-one persons, fifty-five had no latrine. Six generally used them, but of these four lived in town. In Bayamon a much larger percentage were more comfortably situated in life; three hundred and forty-two were questioned on this particular, and fifty-three stated they used latrines; the others, two hundred and eighty-nine, never used one. Thus the average individual living in the country, barefooted and devoted to agricultural pursuits, from time to time acquires more and more uncinariasis from infections sown by himself and his neighbors. There is a constant inflow. The time naturally comes when the parasites in his intestines die of old age, or some accident which cuts their existence."

We do not know to what extent absence of latrines exists in the hookworm area of the United States, but our own observations lead us to agree with Stiles when he says (1903):

"As we go into the country and visit the farms we not infrequently find a condition, in respect to the disposal of fecal discharges, which almost beggars description. Taking the rural districts visited during my recent trips as example, it is not an exaggeration to say that, with the exception of the planters' premises, not over half of the country houses or huts of the sand region have any privy at all; if there is one present, it is rarely properly cared for. Furthermore, it is the exception rather than the rule that it is used."

This and the resistance of the larvæ, along with favorable conditions of temperature and moisture, explain the danger of the disease. The larvæ are scattered by rains, all traces of the feces become lost, but the porous moist earth, often kept moist and protected from the sun by decaying leaves, becomes permeated with the larvæ in the encysted and infectious stage. Mines in the United States, for the most part, do not present favorable temperature conditions, though there is room for further observations in regard to the actual freedom of our miners from infection. The country is the place where practically all our American infections take place, and the great majority of infections occur near the home—in the "yard," garden, or barnyard. The barnyard is especially dangerous for many reasons. The ground conditions are often ideal for the development and existence of larvæ. Chickens, ducks, geese, and hogs scatter the eggs and larvæ in all directions. Actual feces would be avoided by people, but the invisible larvæ can not be.

The greater use of water closets or privies in towns and the universal wearing of shoes explain why hookworm disease is rarer in cities than in the country, and why the anemic countryman gradually improves after he goes to the city, and his hookworms die off and are not kept up by reinfection. Similar differences exist in general between the farm and the cotton mill, so that the anemic, poorly nourished country girl, after working for some months in the mill, shows such a contrast with her former self as one might expect under ideal conditions of country life if the conditions were reversed and she went anemic from the mill to the country. Similar improvement gradually follows when country children go to boarding schools.

For the prevention of soil infection, the use of some kind of sanitary latrine is essential. It must be easily accessible from the house or workplace, so that neither indolence nor feebleness will lead to the use of less secure localities. It must be kept clean in all parts. It must be inaccessible to animals, and must be screened to prevent flies and other insects from transporting material from it—a precaution even more valuable for the prevention of typhoid fever.

The construction may vary with the local conditions, especially as regards water supply, sewerage, and soil. When there is a proper sewerage system, water-closets are best. The ova can not develop in the sewage, or, if they do, will be swept away; and if the final disposal of the sewage is what it should be, no harm can follow.

When the nature of the ground permits, and there is no danger of contaminating wells, deep cesspools are very efficient. These can be built as septic tanks, with arrangements for flushing when desired, and for using the waste as fertilizer, as devised by Mr. Philbrick, quoted in Parkes' Manual of Hygiene.

Shallow pits or boxes are objectionable for many reasons, but sometimes offer the only method available. In such cases they should be treated every day with slacked lime, in order to disinfect not only against possible hookworm larvæ, but also against the germs of typhoid fever. Leaking of the contents must be prevented, especially washing away from heavy rains, which could scatter the larvæ.

A better arrangement is the movable pail system. In this, water-tight galvanized iron pails or buckets are kept under the seat of the closet. When a pail is put in position, as after each cleaning, a thin layer of sand is put in the bottom. Enough crude carbolic acid, diluted with twenty times its bulk of water, may be poured into the pail. The pail must be easily accessible either from the front or back. As often as necessary it is taken out, the contents buried in a pit or trench, covered over with earth and quicklime, the pail cleaned and disinfected, and replaced in position.

The contents of the pail may also be treated in a septic tank, in which case no disinfectant, such as carbolic acid, can be used. They should not be put where they can be washed away by rain, nor used as fertilizer, unless after remaining at least three weeks in the septic tank. They must not be put on a manure pile, nor left where animals can scratch over them.

These arrangements, however, do not suffice for the needs of country life, as privies near or in houses can not be util-

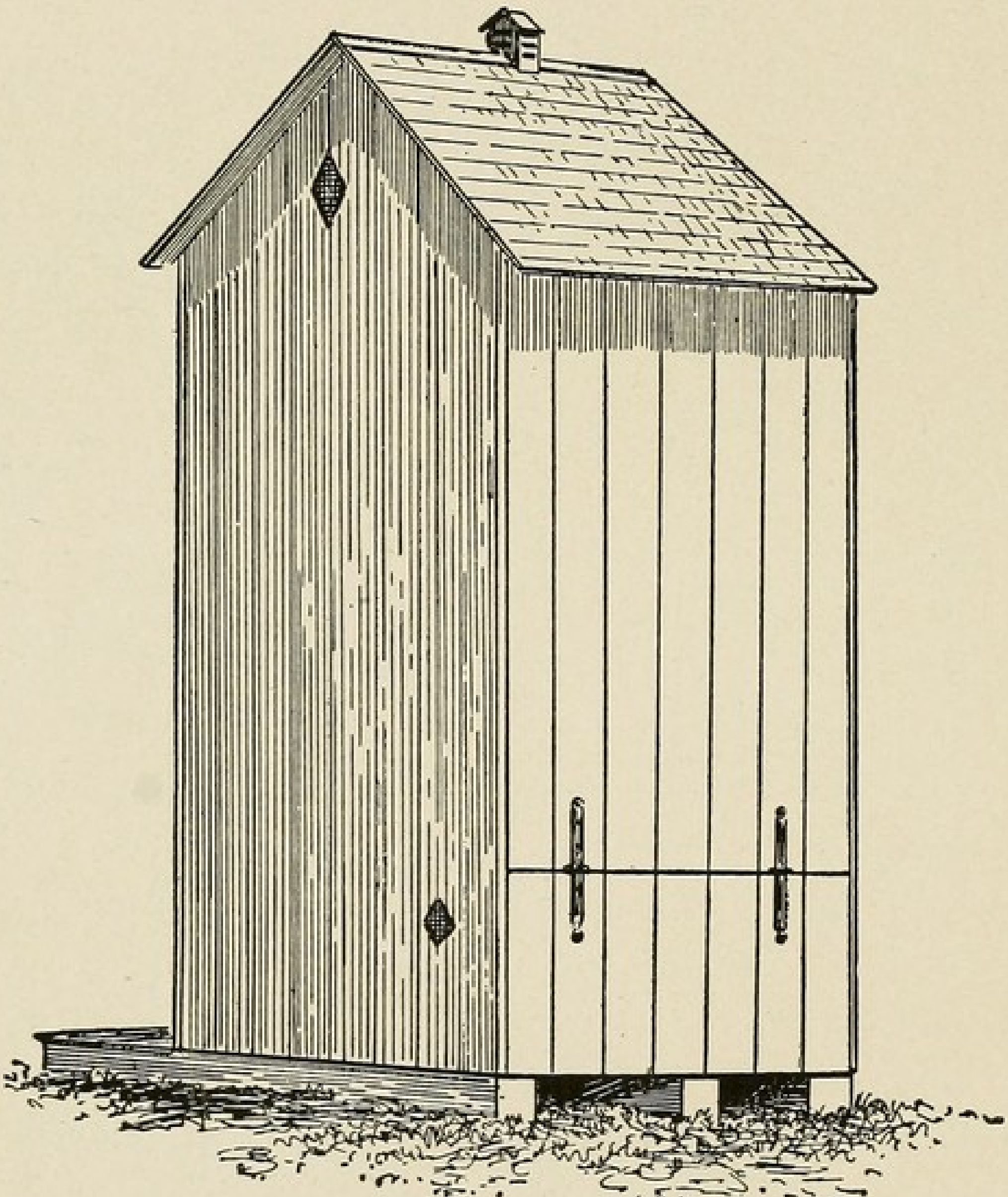

Fig. 48. A sanitary privy, designed to prevent the spread of disease. If a privy of this type were built on every farm and in every yard in villages, and if this privy were used by all persons, typhoid fever, hookworm disease, and various other maladies would almost or entirely disappear. (After Stiles.)

ized at all times by all people. It is necessary, therefore, on plantations, truck gardens, fruit or turpentine orchards, or at charcoal furnaces, and similar places to have some sanitary closet near the workmen. This may be a properly constructed privy, if the conditions warrant, or a portable privy, or a shelter of some kind over a pit or trench. In such cases it should be a rule that dry earth and, if possible, quicklime should be used with a shovel to cover the

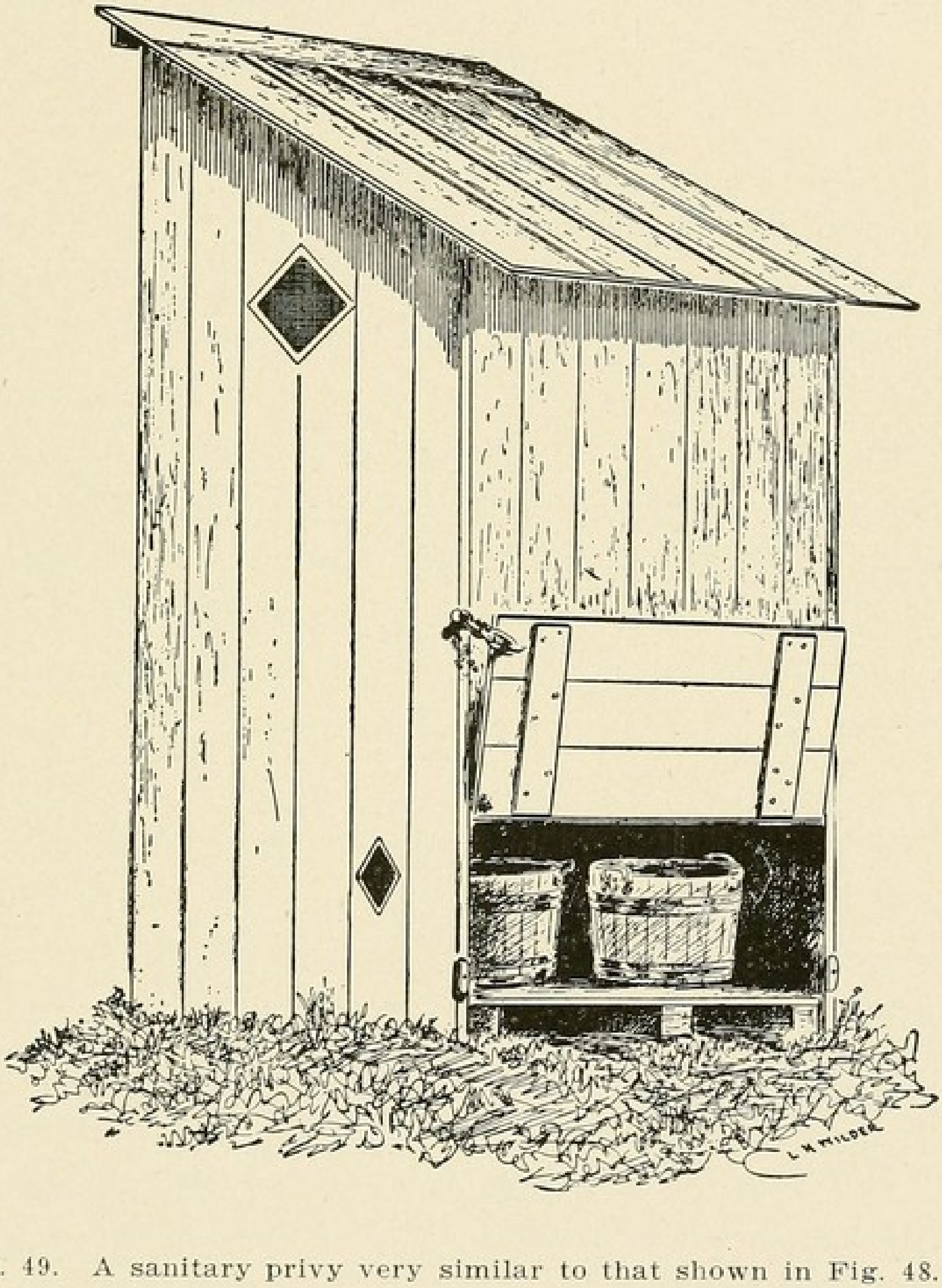

Fig. 49. A sanitary privy very similar to that shown in Fig. 48. (After Stiles.)

feces, and here, too, the danger of flooding in rainstorms must be avoided.

It is interesting to see that Moses, who gained his hygienic ideas in Egypt, the classic home of hookworm disease, ordered for his people a precaution that might still be acted upon with advantage by all who live on the land in hookworm countries. Whether it was as necessary in the Sinaitic desert as in the Nile valley may be questioned, but there can be no doubt of its usefulness in many populous cultivated lands. Moses said (Deuteronomy xxiii, 12, 13): "Thou shalt have a place also without the camp, whither thou shalt go forth abroad; and thou shalt have a paddle (or shovel, in Porto Rico the machete or cutlass, carried by every laborer, is recommended) among thy weapons; and it shall be when thou sittest thee down abroad, thou shalt dig therewith, and shalt turn back and cover that which cometh from thee."

In mines, tunnels, canal cuttings, brickyards, and similar works sanitary closets should be placed wherever there is likely to be a need for them, and their use insisted upon. In the tropical climate of warm, moist mines this is essential on account of the unusually favorable conditions for the development and continued existence of the larvæ in such places.

It is instructive to see what can be accomplished with different methods of prophylaxis on the lines described. In several mines in England, Belgium, and Germany efforts have been made on such a scale as permits useful conclusions.

At the Dolcoath mine of Cornwall, when Boycott and Haldane (*Journal of Hygiene*, vol. 9, November, 1909, pages 264—270) began their investigations in 1902, the following conditions prevailed:

"Without exhaustive search they found among the seven hundred and fifty miners employed underground fourteen men with less than 50 percent hemoglobin, and nineteen more with less than 75 percent. The general pallor of the men as a whole was very striking, and complaints of shortness of breath on climbing ladders were frequent. The disease was a material hindrance in carrying out the work of the mine. Examinations of the men who complained of no symptoms showed that practically every underground worker was infected. The sanitary circumstances of the mine were extremely unsatisfactory. There were no special arrangements for the reception of excreta underground, and the whole of the workings were extensively soiled with feces.

"Industrial efficiency was obviously confronted here with a problem of some importance. The steps taken to escape the consequences of ankylostomiasis were simple, practical, and apparently efficacious. . . . It was, in the great majority of cases, very easy to cure those actually sick by the repeated administration of appropriate anthelmintics. The effects of this treatment have been entirely gauged by the clinical results. No serious attempt has been made to ascertain whether all the worms had been killed in any particular case if the man's general condition improved so far that he was able to return to work. Having been restored to a condition of efficiency, the men, therefore, returned to work in a place which was still infected. They were, of course, reinfected again and again; any return of symptoms was noted at once and corrected by a dose of thymol. In this way actual sickness from ankylostomiasis has been practically abolished."

At the same time steps were taken to introduce sanitary reforms into the underground workings. In 1905 a special rule was established by the secretary of state for metalliferous mines in Devon and Cornwall, as follows:

"The owner, agent, or manager shall cause a sufficient number of suitable sanitary conveniences to be provided above and below ground in suitable and convenient places for the use of the persons employed, and to be kept constantly in a clean and sanitary condition, and no persons shall relieve his bowels below ground elsewhere than in these conveniences. No person shall soil or render unfit for use in any way any convenience or sanitary utensil or appliance provided for the use of the persons employed."

In 1904 such sanitary appliances were actually in use in Dolcoath in the form of loose buckets or pails, which could easily be brought to the surface, emptied, and cleaned. In 1908 "the conditions underground had been immensely improved, the pails were properly used, and it was very uncommon for the men to fail to use them. . . . We could find no feces where, as previous experience had shown, they would be most probably found. The general appearance of the men was quite different, and there was none of the anemia which had been so obvious five years before. On carefully going through two-thirds of the underground hands we found only one case of definite anemia in the person of a boy. There was only one man away from work with symptoms which could possibly be due to ankylostomiasis." Examinations showed, however, that 76 percent of the hands examined were infected, so that the improved sanitary condition had put an end to material illness, but had hardly any effect on the number of men infected. "The sanitary pail system has, therefore, evidently had a great effect in reducing the infectivity of the mine."

Boycott and Haldane compare the results with the more intensive measures taken in Belgium and Westphalia. In the latter every hookworm carrier, as well as patient, is searched out, kept away from work on compensation wages, and treated until repeated examinations fail to show any eggs in the feces. He is then allowed to return to underground work; but the workings are still infective, and he "becomes reinfected and the whole process has to be gone through again and again."

In mines, more than most other places, disinfection of the ground might seem possible, but the conditions in large and old mines are such as to make this very difficult. As has been shown in Chapter III, hookworm larvæ are difficult to attack. In the laboratory they will live more than a year. In coal water they live two or three weeks, and have been found alive in the sludge of mines closed up for ten months. They are sensitive to many disinfectants, but there is difficulty in applying disinfectants to miles of mud and water, and to wet timbers. It is also difficult to find efficient disinfectants that will not vitiate the air, or injure the boots of the men or the plant in the mine. Many substances have been tried; Belger alone experimented with 41. Ferrous sulphate in 1-percent solution is one of the most promising, and is more effective than cupric sulphate; silver nitrate, 0.05 to 0.025, and sodium hydrate or potassium hydrate in 1-percent solution kill quickly. Manganates and permanganates have a decided effect, but are too costly and oxidize too rapidly to be useful. The efficacy of sodium chloride has, however, been shown by Boycott and Haldane and by Calmette, while Manouvriez and Tirelli have shown that mines with saline waters do not become infected with hookworm, and in some mines or tunnels it might be found useful.

Boycott and Haldane admit the superiority of the German system in reducing the number of hookworm carriers. This system, as mentioned above, is one of active search for ova in feces, with treatment followed up, and education of the men. It was taken up after sanitation had been tried and failed. The failure depends, in part, upon the difficulties mentioned. In the coal mines of the Ruhr Basin in Westphalia the proportion of infected men fell as follows:

1904	13,861
1905	4,024, or 18 per 1,000
1906	3,123, or 11 per 1,000
1907	1,851, or 6 per 1,000
1908	1,171, or 3 per 1,000

In the coal field of Liége, under the care of Lambinet and Malvoz, the proportion fell from 26 percent to 4 percent in two years.

In Brennberg, Goldmann saw a reduction from 85 percent in 1895 to 8 percent in 1904.

Töth in Schemnitz (Hungary) found the miners' wages increased 60 percent after prophylactic measures were carried out.

Bruns, from Dortmund, Germany, reported a reduction in the proportion of infected miners from 35 percent to 0.1—0.2, or from 14,716 cases to 1,252.

While all these improvements have been very costly, they are profitable in the end, and they indicate the task that a country infested with hookworm has in order to become free from the tax on life and health caused by that parasite.

In the open country chemical disinfection is almost out of the question. Lime in quantities sufficient only for fertilizer would not be very efficient. In larger amounts it is one of the best, as it combines heat with disinfection. Salt and other more powerful disinfectants would either kill vegetation or be dangerous to live stock, while the cost would prohibit their use.

In hookworm countries the winter cold does not kill larvæ. Oliver froze them repeatedly, and kept them frozen for six days, but after gentle thawing they revived and gave rise to stronger and more vigorous larvæ than those not so treated.

Direct sunlight can kill them, but usually only when it dries them up. They resist the sun in northern Europe, and, although Leichtenstern could not find them in the clay of brickyards, they find in some parts of such places more favorable environment.

Drying land by ditching or drainage would do good in many places. Plowing is useful in some cases, and in others the grass may be burned over to kill the larvæ.

Sugar fields were found by the Porto Rico Commission to be rarely the sources of infection, the plowing and sun causing the death of the larvæ. Tobacco fields also are only slightly dangerous.

The larvæ are killed in deep or moving water, but can live for long periods in shallow water along the edges of streams—just the places that are used for wading, or in some countries by washerwomen and water-carriers—and in small puddles. Moist earth—especially if sandy, so as to retain moisture, or shaded by vegetation—offers ideal conditions for the life of larvæ, and should be treated accordingly in hookworm countries.

3. **Prevention of infection by larvæ.**—On account of the difficulty of preventing the life and development of larvæ in places where men, women, and children work, it is essential to lessen the danger of infection by education. We believe that the problem can never be solved without this. From the history of some other sanitary movements in America it is possible that the importance of this will not be recognized by health officers and legislative bodies. It is interesting to see the views of Ashford and King, formed among a people that might be considered even less capable than our own of education in matters of sanitation. Stating that education would make unnecessary the laws regarding latrines, they tell how laborers in Porto Rico annoyed their foreman by asking for latrines, and from that

island, with its melancholy history of ignorance and oppression, they write:

"Law is not the instrument best fitted to compel a man to be clean and live up to the rules of hygiene. Legislation concerning such matters would lie dormant in the statute books until people learn to appreciate the philosophy and spirit that originate such measures."

Every one living in a hookworm country should be taught the essential facts about hookworms and their effects. Actual specimens, charts and diagrams, illustrations of patients before and after treatment, and clear descriptions should be available and used frequently by health officers, school teachers, and all others who may have the authority or opportunity.

It is a reflection on the common sense of the country that we have for years been spending time and money teaching school children the evil effects of alcohol, tobacco, pork, and coffee, while the children were in many cases being killed by hookworms before they were tempted to drink whisky or even to smoke. It is especially important here to emphasize the fact that skin infection is the most serious danger—the method of infection par excellence, as it has been called. Formerly much stress was laid upon mouth infection, which, though rare on the whole, may occur. People should, therefore, be warned against soiling the mouth with muddy hands; eating with muddy hands; eating muddy vegetables or fruit; drinking muddy water, or drinking from muddy receptacles; accidental swallowing of water while bathing; earth eating; carrying home muddy clothes that might soil the hands of wife or child; cleaning muddy boots; crawling of children on the earth, which they put into their mouths; handling mud-bedraggled dresses;

eating of sweets made in dirty houses. The danger is especially great with wet or moist earth. But it can not be too often repeated that in the great majority of cases in America ground itch is the origin of hookworm infection.

It is fortunate that most people living in hookworm districts know ground itch by that name or one of its synonyms, and realize where and how they contract it. If such people could be taught that ground itch is the usual beginning of hookworm disease, the skin lesion would assume an importance far greater than it now has, and it should be much easier to induce methods of prevention. In our opinion the first and most important measure to be undertaken in the crusade against hookworm disease in America is wide dissemination of the facts regarding ground itch, conveying the information that when ground itch is prevented there will be no hookworm disease.

Where ladders are used in infected mines, the workmen must be warned against the danger of infection either through the skin of the hands and arms, or the mouth by putting infected food or the fingers into the mouth. Mine timbers have been found infected as high as a meter above the ground.

Gardeners, and those who handle vegetables or fruit that may be infected, should be warned about hand or hand-to-mouth infection.

Bathing in common in tubs should not be practiced by workmen, such as miners, or country children. Shower baths should be used.

In all occupations—such as mining, farming, or gardening—where hookworm prevails, placards and other notices should be posted, warning the hands against the danger of skin infection, as well as of soil or water contamination in general.

In hookworm localities the habit of going barefoot should be avoided. The danger of a single experience, as in wading, should be clearly understood. Those who work in infected soil—as in mines, tunnels, or fields—should realize the danger of defective boots. It is also possible that boots soaked for hours in hookworm infected water may be penetrated by larvæ. Bass found kid gloves could be penetrated, and Tenholt found that old boots harbored the larvæ. Various substances have been recommended for the treatment of boots, such as grease or water-proofing material.

The larvæ sink so rapidly in water that drinking from deep pools does not involve much danger.

CHAPTER X.

TREATMENT.

Ground itch is usually treated by somebody other than the physician, or not at all. Of the home remedies may be mentioned bathing the feet in hot salt water, mullein tea, "red oak ooze," application of peach tree leaf poultices, various salves and ointments, including application of fresh turpentine from pine trees, etc. Another favorite remedy, especially for the fissured toes, is to tie around them a wool cord saturated with tallow. Bentley recommends in the papular and early vesicular stages of the disease the application of a strong solution of salicylic acid in collodion or alcohol. This will cause the eruption to dry up, and cut short the attack of the disease to one or two days. If pus has formed, the pustules should be opened up and disinfected with pure carbolic acid, silver nitrate, or nitric acid. When great swelling occurs, it may be necessary to make a few free skin incisions and then to use hot foot baths.

Dalgetty advised the application of a strong solution of lime and sulphur, or a strong phenyl (benzol) solution; also recommended as a wash, 10 parts, with soap 5 parts, and water to make 100 parts; or the affected area may be painted with coal-tar to prevent infection with pyogenic bacteria.

Stiles quotes the following from an anonymous writer in the *Journal of Tropical Medicine* (1900):

"The indications are to get the case as soon as possible; to carefully cleanse the foot by soaking it in warm antiseptic solution; then open the vesicles with sharp-pointed scissors, snip the loose skin away, and finally wash the parts with carbolic acid solution (1 to 40), and treat the resulting ulcer with carbolic acid, phenyl oil, zinc ointment, etc., according to circumstances. The soaking, washing, and dressing operations are repeated once or twice daily, and healing takes place in eight or nine days in favorable cases."

The larvæ remain in the skin so short a time before they get into the deep circulation, and entirely out of reach of local remedies, that it is not practical to make applications that would even promise to affect them. Only symptomatic treatment, therefore, is to be instituted. The most distressing symptom is terrible itching, which often causes the patient to do considerable harm by scratching, producing raw, inflamed areas, especially in the folds between and beneath the toes. Deep fissures may occur. These often become infected and pus is formed. Any antiseptic soothing application may be of service for the itching and to prevent secondary infection. The following is recommended:

℞ Salicylic acid..............................5 grains.
Zinc oxide ointment........................2 drams.
Vaseline ....2 drams.
Mix.
Sig.: Apply locally, twice daily.

It is especially important to keep the foot bandaged or covered to prevent scratching and rubbing. Frequent hot bathing seems to hasten the healing process. This is probably due to the increased circulation induced, hastening removal of the toxic substances causing the irritation.

The laity should be taught that the common "toe itch" or ground itch is not a trivial matter, but that a physician should be consulted at once. Proper advice and treatment at this time may prevent the development of severe disease later. An important function of the physician called to treat a case of ground itch is to urge the patient to spit out everything coughed up for several days afterwards, explaining that swallowing the sputum probably means swallowing larvæ of dangerous worms.

Treatment Before Ova Appear in the Stools.

Whether treatment to kill worms in the intestinal canal should be instituted before they have had time to mature and begin laying can not be stated positively. Ashford and King say they know of many cases in which thymol given previous to maturity of the worms failed to expel them, and believe with Leichtenstern and other German writers that this may be due to the better protection given the small worms by mucus and folds of mucous membrane. If we recall the development of the worms in the gut, little or no result could be expected from treatment until after the infection had existed for several days at least. Though it has been shown experimentally that larvæ may reach the lungs in three hours, it may require considerably more time for them to reach the bowel, as is shown in Chapter III, and when they do reach it they are still in the encysted condition, in which they are able to resist chemical agents wonderfully well. They were found by Looss nine, ten, and eleven days after infection in blood cysts and still in the encysted condition. Lambinet states that the encysted larvæ are not killed in a 2-percent solution of corrosive sublimate after an exposure of six hours, nor in a 25-percent sulphuric acid solution in three-quarters of an hour. We do not know of any experiments to determine the effect of thymol on encysted larvæ, but from the foregoing we think it is not likely to kill them. Bruns concluded, after months of laboratory experimentation with every sort of chemical disinfectant, that none has yet been found to kill the encapsuled larvæ so surely that it can be practically used.

At least as early as about fourteen or fifteen days after infection the worm is provided with a buccal capsule, whereby it attaches itself to and feeds on the mucous membrane. From this time on the parasite is just as much exposed to the action of drugs as it is after maturity and egg production are established. Our personal experience does not permit us to speak with certainty on this point, but we believe from the above facts that treatment should be begun fourteen or fifteen days after the infection, and that satisfactory results will follow. The same treatment should be instituted after an attack of ground itch as if eggs were present in the stools. Two or three courses of thymol or beta-naphtol should be given about one week apart. This, we believe, would get rid of most, if not all, of the worms before they reach maturity and have done much harm. The stools should be examined at the proper time, and from two to three months after the attack of ground itch, for eggs of any worms that may have escaped previous treatment.

Treatment of Hookworms in the Intestine.

It is important to understand the conditions that must be met in the treatment of hookworm infection. The worms, three-eighths to three-fourths of an inch long, lie in the small intestine, especially the jejunum. The head and sometimes one-fifth or more of the body of the worm is buried in the mucosa, and the whole body surrounded and protected by any food that may be in the gut, but especially by thick and tenacious mucus, which is almost always present. The normal amount of mucus is increased by the irritation produced by the feeding of many worms. Remedies used against the worms affect or kill them by local action, and the first step in the treatment is to remove this protection of chyme and mucus, so the drug may come in contact with the worms. To secure an empty alimentary canal is not easy. One who has had occasion to examine stools passed after the bowels are supposed to have been thoroughly emptied by a purgative must be impressed with this fact. Sometimes large evacuations, containing recognizable food remains, occur. The upper portions of the gut can be pretty thoroughly freed from food material by a large dose of some salts—Rochelle, Epsom, or Glauber's. On theoretical grounds, and as the result of clinical experience, we believe that sodium sulphate dissolves and removes the intestinal mucus best. Many believe that calomel or calomel and podophyllin are better. The Porto Rico Anemia Commission tried podophyllin extensively for the initial purge, but concluded that it had no advantage over sodium sulphate, and that its drastic action may be harmful to weak patients. It is highly recommended by German writers for its destructive action on the worms when given in large doses. In the usual doses, up to 3 centigrams (1/2 grain), it has no such action. Lambinet recommends jalap and calomel as a preliminary purge. Lutz gives 1/2 gram (7 1/2 grains) calomel and 2 grams (30 grains) alcoholic extract of senna leaves one-half day before beginning the specific treatment (thymol). Sandwith does not give any preliminary purgative, considering it unnecessary. Dieminger considers the preliminary purge unnecessary, especially when male fern is the anthelmintic employed. By having a patient abstain from everything except the most easily digested diet, like milk, for twenty-four hours, and giving an ounce of sodium sulphate at least four hours after the last feeding, the upper bowel is usually pretty well cleared of food and mucus. More certain results can be had by giving another similar purgative twenty-four hours before this one. Ashford and King did not consider preliminary dieting practical with their Porto Rico cases, or especially needful. Almost all other authors advise light diet or fasting the day before specific medication is employed. It may not be practical in many instances, we admit, but we believe it is always advantageous if there is no distinct contraindication. After the preliminary preparation, the drug selected to kill or expel the worms is to be given as soon as the peristalsis from the purgative has ceased, usually six to eight or ten hours. Thymol, beta-naphtol, and male fern are the drugs most often employed. Thymol, first used against ankylostoma duodenale by Bozzolo, is by far the most generally used in America and England, and, in view of the almost invariably satisfactory results obtained when properly administered, it seems all that could be desired.

Dose of Thymol.

The dose of thymol for internal use, according to the United States Dispensatory, is 2 to 10 grains. It is only slightly (1:1,100) soluble in water or the gastric and intestinal juices, and therefore little absorption occurs when it is given undissolved and on an empty alimentary canal. Used as a vermifuge, it is not intended to be absorbed, and is used in much larger doses. Up to 8 grams, or 120 grains, a day have been taken for several days without disturbance of digestion or intoxication.

Leichtenstern recommended two or three doses of 30 grains each at two-hour intervals for several days; Giles, 25 grains in alcoholic solution morning, noon, and night; Scheube, 60 to 120 grains, divided into four doses, administered one and one-half hours apart and followed in twelve hours by a purgative; Lutz, 30 grains, repeated once or twice at two-hour intervals; Mosler and Peiper, 30 to 150 grains in three to six doses during the day; Sandwith, 1 gram (15 grains) of thymol at 6 p. m. and another similar dose the next day at 6 a. m. At 8 a. m. about 1 ounce (30 grams) of magnesium sulphate is given. The patient is on fever diet the first day, but gets his full dinner at noon the second day. Manson gives 30 to 120 grains of thymol in divided doses within three or four hours.

Ashford and King do not believe it necessary or justifiable to administer more than 60 grains of thymol at a time, or to repeat oftener than once a week. Sandwith says the same thing.

Sixty grains to an adult is the amount almost universally employed in this country for a course of treatment of hookworm disease. The dose for children should be in proportion to the size or apparent age. Ashford and King's table of doses, which we recommend, is as follows:

Ages.	Grains.
Under 5 years old in size	7½
5 to 10 years old in size	15
10 to 15 years old in size	30
15 to 20 years old in size	45
20 to 60 years old	60
Over 60 years old	30 to 45

Unfavorable conditions—such as great weakness, extreme anemia, diarrhea, cardiac depression, pregnancy, and dropsy—may require a still smaller dose than that indicated by the size.

Mode of administration of thymol.—It is customary to give the drug in two or three "broken" doses, and to give them one or two hours apart in order to prolong the presence of the thymol in the upper bowel.

Thymol occurs in coarse crystals. As it acts only when in contact with the parasites, it is more effective if finely powdered. This can be done in a few minutes in a mortar with pestle, or on a slab with a spatula. It tends to pack together under pressure, or in the mucus in the intestine. To prevent this, sugar of milk or other inert soluble substance should be mixed with it. Lindeman suggests equal parts of thymol and sugar of milk, and we find that this insures the proper crumbling or breaking up of the contents of the capsule or wafer when the latter is dissolved.

We have often found in the stools of patients who have taken thymol, coarse lumps, and a few times the entire contents of a tightly packed capsule.

Thymol has a pungent, acrid taste, and burns the mouth and throat. It should, therefore, be given in cachets, wafers, or capsules. A No. 0 capsule will hold, without packing unduly, 5 grains of thymol of the mixture of equal parts of thymol and milk sugar.

When necessary to administer it to children who can not swallow capsules or wafers, it may be satisfactorily given suspended in mucilage of acacia or some simple syrup. Burning, nausea, and even vomiting may be caused by the presence of the pungent thymol in the stomach. Vomiting can usually be prevented by determination on the part of the patient, by lying on the right side to hasten the passage of the medicine through the pylorus, and by refraining from drinking much water. After the thymol has presumably had time to pass the part of the small bowel where the worms are—that is, two or three hours—it can not longer be of service, and should be gotten rid of by another brisk purgative of salts to prevent its absorption. As thymol is soluble in oil, castor oil should never be used for this purpose. The purgative is not to move out the worms, but specifically to move out the thymol. All the worms passed are dead, and not much would be gained by hastening their removal from the bowel after they have been killed. Sufficient thymol may be absorbed to be harmful if allowed to remain long enough. Besides oils, other solvents—such as alcohol (tinctures, whisky, wines, brandy, beer), ether, glycerine, turpentine, acetic acid (vinegar), chloroform—and large amounts of water should be avoided.

Patient to remain in bed.—On account of the increased tendency to vomit and the marked increase of toxic symptoms from thymol when patients are up, all of them should be required to remain in bed until the thymol is moved off. Either the bedpan or commode should be used in the room. We have seen several patients get up and walk about against this instruction without experiencing the slightest inconvenience, but Sandwith says that before adopting this precaution several instances occurred in which patients were brought back from the water-closets collapsed or fainting.

Diet during thymol treatment.—In order to have the alimentary canal remain clear while the thymol is present, absolutely no food or drink should be allowed, except water, from the time the preparatory purgative is given until the purgative following the thymol has acted well. If the patient is very weak and feels faint, or if the burning in the stomach is excessive, a little warm broth or coffee may be allowed. We do not employ these, however, except very rarely. When one or two free movements have occurred after the last purgative, the patient may begin to eat, and his diet need not be restricted unless there is some special indication. He waits now several days, usually a week, before taking another course. In the interval the diet should be full and the most nutritious compatible with the patient's digestive ability, which is usually good.

Selection of time for giving treatment.—For apparent reasons, Sunday is a very convenient day on which to give the treatment, especially to working people, school children, etc., as recommended by Stiles. It is also convenient to give the preparatory purge at night and to begin the thymol early the next morning. The patient then loses little sleep the first night, and finishes the treatment before the next night.

We give our patients the following instructions, the doses being for an adult:

All of Saturday have milk or other light diet.

Saturday, 8 or 9 p. m., take sodium sulphate, 1 ounce.

Sunday, 6 a. m., 20 grains thymol.

Sunday, 7 a. m., 20 grains thymol.

Sunday, 8 a. m., 20 grains thymol.

Sunday, 10 a. m., 1 ounce sodium sulphate.

Until 4 p. m. do not eat or drink anything but water, and but little of that. Remain in bed.

After 4 p. m. rise and eat what you want and do whatever you feel like doing.

Thymol may affect the patient unfavorably in three general ways—by intoxication, by irritating the kidneys, and by irritating the stomach and intestine.

Thymol intoxication symptoms.—The effects of absorption of a large amount of thymol are headache, weakness, dizziness, tinnitus, nausea; rapid, weak pulse, and sometimes sweating of the face or body; cyanosis of lips and fingers. The temperature in one instance fell 5 to 10 degrees F. Frequently none of these symptoms are felt until the patient gets out of bed. The intensity of the symptoms must, of course, depend on the amount of thymol absorbed and the individual susceptibility. Thymol is soluble in alcohol and volatile oils, and these should be rigidly interdicted. In fact, the patient should be instructed absolutely not to swallow anything except water, and to drink only a small quantity of that. Many cases of intoxication are due to drinking too much water. The importance of this is often overlooked. Thymol is sufficiently soluble in water, about 1/2 grain to the ounce, for the patient to absorb a toxic dose if he drinks large quanties of water. The infrequent occurrence of toxic symptoms from thymol given in the doses mentioned is suggested by the fact that the authors have treated several hundred cases without ever seeing more than a little dizziness and weakness as a result. We have heard, however, of alarming symptoms, but not of any fatal cases. In one instance a family of four children was poisoned by the usual doses of thymol calculated according to their ages. The symptoms were weakness, dizziness, fainting, and unconsciousness. One child fainted when returning from the water-closet and the other three got out of bed and came to her assistance, but each one fainted, and it was necessary to carry all four of them back to bed. All had been given castor oil two hours after the last dose of thymol, and the one who fainted first had eaten a slice of bread and butter. In six hours afterward they were all in the yard playing. Two days after the poisoning the urine was examined and found free from albumin. We have several times noted that patients who complain of dizziness and other symptoms of intoxication seem to recover and feel well remarkably early after the purgative acts well and food is taken. They are usually able to get up at once, and, though unpleasant recollections of the recent experience remain, the symptoms have entirely disappeared.

Recently a university student treated by our colleague, Dr. Gage, took 60 grains of thymol and two hours afterward a drink of whisky to "wash down" the dose of salts. There followed several free movements during each of this and the next three days. The patient was up and felt fairly well, but a little weak. On the fifth day he had a mild collapse, with dizziness and severe headache lasting a few hours. Eructations tasting strongly of thymol occurred frequently. During the next three days several dysenteric stools were passed. It was eight or ten days before the patient felt entirely well in his head and in his bowels. The eructations of thymol and mild collapse five days after it had been taken indicate that it had not been eliminated in this instance, in spite of several free bowel movements.

Pregnancy contraindicates the administration of thymol, except under the greatest care, for fear of producing abortion, which it occasionally does. Nephritis and considerable edema are also contraindications.

Ashford and King note that in very edematous patients the effect of large doses of thymol is particularly harmful. By the next day the edema is much increased and often involves the brain. Albumin and casts are increased in nephritic cases when large doses of thymol are administered.

We saw, however, a very severe case of hookworm disease in a child of 16 who had 60 percent of moist albumin by the Purdy acetic acid and ferrocyanide test when she was given 30 grains of thymol. No untoward results were noted, and 2,760 uncinariæ were expelled. Three days after the thymol was given the urine showed only 18 percent of albumin by the same test. The effect of thymol on the normal gastro-intestinal canal is occasionally burning epigastric pain, nausea, and vomiting, and more or less diarrhea. If diarrhea or dysentery already exist, they are promptly aggravated by large doses. In several instances we have seen loose bowels, lasting two or three days, follow administration of thymol. One case had six to twelve movements a day for six days. The rectum and anus are irritated by thymol passing out with the feces, and, if hemorrhoids or fissures are present, this symptom is much increased.

The degree of debility must be taken into account when considering the size of the dose for a given case. A very weak subject should receive not more than 15 to 30 grains the first dose, which will usually relieve him so that he can resist a full dose next time. Some English writers do not believe the small doses accomplish much, but actually large numbers of worms are sometimes expelled as a result of them.

The Porto Rico Anemia Commission treated 112,580 cases of hookworm disease during the years 1904 to 1907 inclusive, all, except relatively few, with thymol, and after this extensive experience advise placing the thymol in the hands of patients to carry home and take according to directions. Boycott and Haldane, as well as many other recent writers, have had no dangerous symptoms such as were described by some early observers, probably from giving oil or alcohol after the thymol.

Treatment of toxic symptoms produced by thymol.—Cardiac stimulants, such as a hypodermic of a small dose of morphine (1/6 grain) and atrophine (1/120 grain), or strychnine (1/30 grain), or digitalin (1/100 grain), are of service in combating toxic symptoms. Hot coffee has been recommended for the weakness sometimes present. It is customary with some to give strychnine and digitalis for a day or two preceding the day thymol is given. This seems unnecessary, except with extremely weak patients. Alcoholic stimulants or tinctures by mouth must be rigidly avoided on account of the danger of dissolving and rendering absorbable more thymol. One of the most important things is to keep the patient lying down. If fainting occurs, the head should be lowered, as in fainting from other causes. The irritation to the kidneys by thymol, if properly given, is negligible unless much is absorbed. Even then the irritation rapidly subsides without treatment after the drug is stopped. The diarrhea sometimes occurring after the thymol administration soon passes off without requiring treatment. If treatment is demanded, it should be along general lines.

Results to be expected from thymol in expelling worms.— The first course of thymol properly given usually gets rid of 80 to 90 percent of all the worms present. So good a result is obtained only when proper preparation, etc., are observed. One of the secrets of successfully treating intestinal parasites of all descriptions is to secure an empty alimentary canal before the specific drug is given. This is so important that we do not doubt that it is often much better to give a purgative on Friday night as well as on Saturday night. There are, no doubt, other factors that prevent marked success in some cases, such, for instance, as the rapid carrying down of the thymol by peristalsis to below the location of the worms. For this reason it is desirable not to begin the thymol until peristalsis from the purgative has ceased. It should, however, be given soon afterward and before the worms are again protected by the mucus, which soon forms. Cases are often met with in which no eggs are found after one course of thymol, a fact known to German miners seeking work. In many more a few remain until three or four courses are given, and in a few cases six to eight or ten courses are required to get rid of all of them. It can be said, however, that, if persisted in, thymol will always succeed. It is even a better specific for hookworm disease than quinine is for malaria.

In a very extensive experience reported by Ashford and King, 97.8 percent of those who expelled all their uncinariæ received thymol five times or less. Of these 41.8 percent expelled all after one treatment, 32.1 percent after two treatments, 14.2 percent after three treatments, 6.8 percent after four treatments, and 2.8 percent after five treatments. Of 4,474 cases which received thymol, 81.1 percent expelled all uncinariæ, but, subtracting 507 who never returned or ceased to return after two or more treatments, this percentage rises to 91.5 percent. Sandwith cured 95 percent of 185 cases of ankylostomiasis with five or less doses of thymol. The cures in the 185 cases were effected in the following manner:

Number cured.	After number of treatments with thymol.
42	1
58	2
43	3
25	4
9	5
4	6
2	7
2	8

It would seem, therefore, that the old world hookworm is about as easy to expel as the American variety.

In our own experience about one-half of all cases have been cured of all their worms with three courses of thymol; several have required five, six, and seven treatments, and one required ten full treatments. In the case already mentioned, 2,760 worms were expelled after one treatment, but the highest number counted in any other case was 1,054.

We have often been impressed with the fact that many, in this country at least, do not fully appreciate that the treatment must generally be repeated several times before all worms are expelled. The complaint is made that, though some worms are expelled after a course of thymol, the patient is not cured. We would reply that few other diseases are cured by a single day of treatment.

Repetition of treatment.—On account of the irritation to the alimentary canal and kidneys produced by thymol, most authors agree that it should not be repeated oftener than once a week, unless there is some special indication for it. We have, however, several times given a course of thymol every third or fourth day for several times, and have not seen any harm result therefrom. We believe it is a good plan to give three treatments one week apart, and, after waiting about a week, to examine the feces for ova. Usually in mild or medium cases none will be found. If any are found, treatment must be repeated. It must be remembered that sometimes ovulation is suspended temporarily after thymol has been administered, and, if symptoms persist, the feces should again be examined in three or four weeks after the last treatment. The result of the treatment can thus be best determined.

Other Methods of Treatment.

Beta-naphtol.—Beta-naphtol, as advocated by Bentley, is given with the same precautions, preparation of patient, and the same after-treatment as with thymol. Colbert had one patient who expelled 4,016 worms from one dose of beta-naphtol. Beta-naphtol, however, seems to act well only when the preliminary purgation and fasting have been carried out thoroughly. If food is taken, very poor results are often obtained. Ashford and King concluded that thymol was superior to beta-naphtol where the patient was not under control, and state that they were obliged to abandon the use of the latter for walking patients on this account. They speak of several instances in which, after repeated doses of beta-naphtol were given, eggs were persistently present in the feces, which cleared up after a single dose of thymol. Bentley states that he abandoned thymol two years before to use beta-naphtol, and has used it in several thousand cases with excellent results. The dose is one-half that of thymol—viz., 30 grains for an adult. It frequently is successful in expelling worms, but in many patients who took their medicine at home the Porto Rico Anemia Commission found the number of worms expelled far less than when thymol was administered. On the other hand, a comparison of forty hospital cases treated with thymol and thirty treated with beta-naphtol, in which the number of worms expelled was carefully determined, shows the results from each drug to be about equal. The finding of the commission shows the following percentages of all worms in the intestinal canal of the patient that were expelled:

	Percentage of total number of worms expelled.
After 1 dose of thymol	76.85
After 1 dose of beta-naphtol	72.24
After 2 doses of thymol	90.17
After 2 doses of beta-naphtol	88.12
After 3 doses of thymol	95.28
After 3 doses of beta-naphtol	93.67
After 4 doses of thymol	96.57
After 4 doses of beta-naphtol	96.47

Beta-naphtol is more irritating to the kidneys, and sometimes sets up considerable nephritis. There is already albuminuria in many cases of uncinariasis, and it seems unwise to select a drug irritating to the kidneys. Unpleasant dizziness often results from its use. It is, however, less depressing than thymol. Its cost is only about one-tenth that of thymol.

Oleoresin of male fern.—Male fern has been used for a very long time as an anthelmintic in treating tapeworms, and has recently been much used on the continent of Europe in ankylostomiasis. Of 21,612 cases treated in Westphalia by Bruns it failed to expel all the parasites in only 1.5 percent, and in only 15 to 30 percent of cases was it necessary to give a second dose. He records, however, four cases of blindness resulting from its use. Tenholt cured 95.8 percent of his cases with three doses. Lambinet gives a purge of calomel and jalap powder the night before, and on the following morning "Duhourgan's teniafuge francais," which is ext. filic. mas. 4 grams, chloroform 3 grams, ol. ricini 40 grams. This is given in two doses, with an hour's interval, and repeated the next day. Töth recommends 45 to 75 grains filix mass, with a glass of liqueur, every day for four or five days. Dieminger noted icterus, gastritis, and gastro-enteritis in some cases, as has also been noted by Töth and others.

Leichtenstern says that 150 grains should not be exceeded.[3] Ashford and King tried ethereal extract of male fern in Porto Rico, and say that in some cases in which the parasites were resistant to thymol this gave good results and in others it did not. They suggest that the deleterious effect of the hot climate of Porto Rico on the drug may have been responsible for the variable results obtained. In their 1905 preliminary report they say: "The highest number of uncinariæ expelled by either of these preparations (solid extract and fluid extract) was eight, while a subsequent administration of only three-fourths of the usual dose of thymol brought away 3,686, and this in the very same case." It seemed to cause more dizziness and nausea, and patients complained that they felt sicker and weaker after it than after thymol. The drug is very variable in its potency, and, though we have not experimented with it in this disease, we believe that its use will be limited, by its much greater cost and other objections mentioned, to cases that have failed to be cured by thymol or beta-naphtol. The same preliminary treatment is to be given, and 75 to 150 grains of oleoresin of male fern administered in two divided doses one hour apart.

Eucalyptus.—Phillips recommends eucalyptus oil combined with chloroform and castor oil. The following is divided into two doses and given one-half hour apart:

Ol. eucalypti	2.5 grams.
Chloroformi	3.5 grams.
Ol. ricini	41. grams.

This is not easily administered, and is very nauseating, but has the advantage of causing live worms to be expelled.

Podophyllin.—Podophyllin is recommended by Neumann, who thinks a certain amount of inflammation of the intestine favorable, if not indispensable, for expulsion of the worms. It is not very toxic, but irritating to the mucous membrane. He gives two pills a day of 0.045 milligrams of the active principle for four days, and, if ova still persist, he gives male fern.

Other Drugs.—The following other drugs have been mentioned by various writers:

1. Juice of ficus doliaria, 3 to 6 teaspoonful doses; much used in Brazil.
2. Powdered areca nut.
3. Jorrissen's preparation (a costly one)—terpine 1/2 gram, levigated sulphur 2 grams, condurango powder 1 gram.
4. Infusion of bark of acacia anthelmintica.
5. Oil of peppermint.
6. Kerosene oil.
7. Guaical carbonate.
8. Thymotal.

General Treatment.

Anemia.—The same general principles of the treatment of anemia from other causes apply also to the treatment of this, the most constant and the most prominent symptom of hookworm disease. The most important measure is, of course, to remove the cause, but, inasmuch as this often requires three to six weeks, and the patient must rebuild his blood during and after this time before he is back to normal health, the question arises as to what treatment may be made use of to hasten blood formation. Pure air, sunlight, and nutrition are the most important factors. The class of people affected, except miners and tunnel workers, are blessed with air and sunlight. In most cases the removal of a large portion of the worms is promptly followed by increased appetite, and when the digestion and assimilation are good, as they usually soon become, nutrition is increased far above that required for a normal individual. We do not believe special dieting necessary, or even appreciably beneficial, for mild or medium cases, but that liberal general diet should be allowed. Very severe cases, with weak digestion and assimilation, are no doubt benefited by a wise selection of easily digested, nutritious diet suited to the individual case. An abundance of good general diet is what is required for most rapid recovery. If we recall the fact that not only is the blood below normal in hookworm disease, but many of the other body tissues as well—bone, muscle, nerve, hair, skin, etc.—the importance of a general mixed nutritious diet becomes apparent.

The anemia in most cases is of the secondary type, with low hemoglobin and low color index, which is generally benefited by administration of iron, one of the essential elements in hemoglobin. Very mild and mild cases probably are not appreciably affected by iron, but all moderate and severe cases should take some form of this drug in the interval between thymol treatments. We admit, with all other writers on this subject, that the importance of iron in the treatment of hookworm disease, compared with specific treatment against the worm, is very small. We also believe that recovery from almost any grade of hookworm anemia will follow expulsion of the worms as certainly without as with iron treatment, but that it will generally be more or less hastened thereby. In fact, the anemia is benefited decidedly by iron, either alone or combined with bitter tonics, without any specific treatment being directed against the worms. Many patients with chronic severe uncinariasis give the history of taking iron tonics or reduced iron year after year. They get run down, weak, and more anemic every spring, but get sufficient relief from iron to carry them through the summer, never, however, getting entirely well. Looking back over an experience of many years spent in a section of country heavily infected with this disease, we recall several families that we now know were severely infected, and that bought year after year their supply of reduced iron, which was kept in the country stores. We recall that another method of administering iron was to place some nails, or iron scraps and scales from the blacksmith shop, in a bottle with vinegar, with or without some bark and herbs added, for a bitter tonic. Some old man or old woman of the neighborhood, frequently a grandmother of several families, was supposed to know best how to make these "spring tonics," which generally contained iron. Since the country has settled up, and railroads and towns, and drugstores and more doctors and patent medicines have come in, there is far less of this self-medication, but the point we desire to make is that iron is sufficiently beneficial in hookworm disease, without the worms being treated, to direct the patients themselves to continue to use it.

The history of Dr. T. B. Ford, who practiced for many years in a heavily infected section of Mississippi, is interesting in this connection. Dr. Ford (now retired) was a close observer, and much cleverer than the average country practitioner. Long before hookworm disease was diagnosed in this country he had learned that there was a specific anemic disease, the cause of which he did not know. He could not cure it, but it was always benefited by iron and quinine pills, which he made up himself. They were made of reduced iron, quinine sulphate, and extract of gentian. He frequently varied the proportions to meet, as he thought, special indications, but, as we remember it, each pill contained from one-half to one grain each of the iron and quinine. The disease was so prevalent in that country, and the benefit derived from "Dr. Ford's iron and quinine pills" so apparent, that they were known by the laity for thirty or forty miles around to be a specific remedy for this unknown disease.

There is evidence that iron hastens blood reconstruction and none that it interferes with it, or is otherwise harmful; therefore some form of iron should be given in moderate or severe anemia cases. Stiles believes that it should not be given between the first and second treatments with thymol, in order to impress on the patient the fact that the thymol is actually the source of benefit and must be continued. The patient usually improves so much during the first week that any skepticism he may have had as to the correctness of the diagnosis is dispelled. The same principles would govern the selection of the form of iron here as in the treatment of any other secondary anemia. Blaud's pills, five grains, t. i. d., and iron (reduced), quinine, and gentian, 1/2 to 1 grain of each, t. i. d., are recommended. Sandwith gives 7 1/2 grains of sulphate of iron t. i. d., the best results being obtained when this is preceded by extract of bone marrow for about a week.

A few cases of long standing and usually severe hookworm disease develop the pernicious type of anemia, with high color index, and are not benefited by iron, as would be expected. Many of them recover very slowly, or never return to a perfectly normal blood condition. They are benefited by arsenic in the form of Fowler's solution, and should take five to ten drops t. i. d. over long periods of time, with occasional short intervals of rest. Such a case, age 24, first seen four years ago, gave a history indicating hookworm disease since early childhood, and the feces showed what we considered a mild infection, which was confirmed by the expulsion of twenty-four worms following 60 grains of thymol, after which no eggs could be found on several examinations extending over six weeks' time. The blood condition at different times and the treatment is shown by the following table:

CHART 1.

Date.	Hemo-globin.	Red cells.	Color index.	Eosinophiles, percent.	Treatment.
May 4, 1906	48	2,010,000	1.2	18	Thymol and Blaud's pills.
May 11, 1906	45	2,100,000	1.1	16	Thymol and Blaud's pills.
May 25, 1906	52	2,250,000	1.2	11	Thymol and Blaud's pills.
July 6, 1906	43	1,910,000	1.1	..	Fowler's solution.
Sept. 14, 1906	50	3,214,000	0.8	8	Fowler's solution.
Feb. 6, 1907	62	4,116,000	0.8	4	Fowler's solution.
Nov. 12, 1907	71	4,860,000	0.7	2	Treatment discontinued.
Jan. 21, 1908	84	4,920,000	0.9	4	Treatment discontinued.
July 11, 1909	81	4,741,000	0.9	1	Treatment discontinued.

There were present a few normoblasts, poikilocytosis, and anisocytosis all the time until the arsenic treatment was begun. It will be seen from the chart that there was no gain until the arsenic was begun, regardless of the fact that all the worms had been expelled and the patient took Blaud's pills all the time. That the patient did not have pernicious anemia is indicated by the nearly normal blood for over two years. We have seen several patients showing this type of anemia, and always making slow or no improvement after curing them of their worms. In fact, we know four cases still anemic, notwithstanding that two of them were cured of their worms more than two years ago. Such cases demonstrate that hookworm disease may in some way damage the blood-making organs to an extent and in a way that makes recovery impossible. Fortunately, such cases are relatively very few in this country. The only way we know to recognize them certainly is by proper blood examination.

Improvement After Treatment.

There are indeed few diseases in which treatment is followed so promptly and so certainly by unmistakable improvement and recovery as is proper anthelmintic treatment in hookworm disease. This is one of the few specifics in medicine. The improvement in severe cases is marvelous. A child with 15 or 20 percent hemoglobin, pale, "tallow-faced," one-fourth, one-third, or even one-half under weight, undeveloped, dyspneic, and languid, can be seen to gain weight, height, and color almost daily, and often within two or three months be converted by a few doses of thymol into a red-faced, hardy, healthy-looking child. He often grows more in one year after treatment than he had in the previous five, or even ten, years. Nature seems to try to make up for lost time, and, though the child may never attain the size he would have attained if he had not been infected, the gain is great and rapid. Among the important factors determining the length of time necessary for a patient to regain his health and completely recover, and whether complete recovery can result, are: the severity of the disease, the age of the patient, and individual recuperative powers. It must be remembered that hookworm disease may be produced by any number of worms from one up to the lethal dose, sometimes as high as four or five thousand. This very variable number of worms, as well as other factors, necessarily gives rise to differences of intensity. One patient may be so badly affected as to require months to recover or to preclude complete recovery, whereas another may return to full health in a few days. We have long been impressed with the influence of age on the recovery from hookworm disease, young or growing patients always gaining much more rapidly than adults. We shall say more about this below under "height and weight." Individual recuperative powers are here of much importance, as in many other diseases. Two individuals cured of their worms and having equal amounts of hemoglobin, of equal weight and the same age, will often not return to the normal at anything like the same rate.

Blood.—The blood charts shown below are selected from those published by Ashford and King, and some of our own, to show the rate of improvement in the blood during treatment. It will be noted in most of the charts that the number of red cells increases faster than the hemoglobin, and that they usually go considerably above the normal 5,000,000 long before the hemoglobin has reached normal. It will also be noted that the eosinophiles come down more slowly than the gain in red cells or hemoglobin. In fact, they often remain high after the blood is otherwise normal. We know of several instances in which the eosinophile count has been above 6 percent six, eight, and ten months after all worms were expelled, and one instance of 17 percent two years after successful anthelmintic treatment.

It may occur, as is shown in chart 4, that the eosinophiles may increase for some time as the blood improves, especially in those severe cases in which the stimulus is sufficiently great to exhaust the eosinophile-making ability, which again revives after a part of the worms are gotten rid of.

CHART 2.

Date.	Hemoglobin.	Red cells.	White cells.	Eosinophiles.
May 8	33	2,868,000	13,200	16.8
May 16	36	2,991,040	5,000	22.4
May 23	38	3,960,000	5,200	16.4
May 30	36	4,384,000	3,200	17.6
June 6	50	4,000,000	9,200	8.6
June 13	56	4,541,600	5,200	14.8
June 20	62	4,360,000	9,800	10.8
June 27	67	5,261,600	7,200	8.8
July 4	66	4,152,800	8,800	9.0
July 11	76	6,866,400	6,400	6.0
July 18	83	7,635,200	6,200	...
July 25	83	7,035,200	7,400	4.8
Aug. 1	82	5,176,000	4,000	5.6
Aug. 8	75	5,924,000	5,000	8.6
Aug. 15	101	5,164,000	7,800	8.8

CHART 3.

Date.	Hemoglobin.	Red cells.	White cells.	Eosinophiles.
May 17...........	28	3,480,000	7,400	10.
May 24...........	29	3,024,000	7,200	8.
May 31...........	30	3,864,000	5,000	8.8
June 7...........	50	3,981,600	11,600	4.
June 14...........	54	5,786,400	4,200	8.8
June 21...........	66	5,355,200	5,800	10.4
June 28...........	90	6,195,200	6,400	12.
July 4...........	103	6,088,000	17,800	6.4
July 21...........	115	....	.....	...
Aug. 2...........	95	....	.....	7.2
Aug. 3...........	92	....	.....	8.8
Aug. 4...........	92	....	.....	6.4
Aug. 6...........	85	....	.....	6.

CHART 4.

Date.	Hemoglobin.	Red cells.	White cells.	Eosinophiles.
May 12...........	20	3,195,520	6,400	.8
May 19...........	28	2,804,000	5,000	4.8
June 26...........	38	4,075,620	3,400	6.8
June 2...........	38	4,626,400	3,800	4.8
June 9...........	41	5,901,600	4,400	4.
June 16...........	46	5,817,600	4,400	7.2
June 23...........	49	6,016,000	5,000	8.
July 30...........	55	5,964,000	6,400	21.2
July 7...........	67	6,466,400	7,600	12.2
July 14...........	76	6,295,200	11,200	9.2
July 21...........	82	6,017,600	6,600	9.6
Aug. 28...........	83	6,364,000	4,400	8.
Aug. 4...........	90	6,630,400	8,800	2.2
Aug. 4...........	104	6,724,000	7,800	1.6

CHART 5.

Date.	Hemoglobin.	Red cells.	White cells.	Eosinophiles.
May 13...........	27	2,306,640	6,200	2.
May 20...........	19	1,688,000	5,000	.4
May 27...........	25	1,804,000	3,800	4.1
June 7...........	27	2,964,000	4,800	..
July 13...........	30	2,977,600	8,600	.8

CHART 6.

Date.	Hemoglobin.	Red cells.	White cells.	Eosinophiles.
May 13...........	14	1,226,400	4,200	8.4
May 20...........	21	1,746,640	5,000	4.4
May 27...........	21	2,084,400	5,600	2.8
June 3...........	22	2,504,000	4,000	3.2
June 10...........	22	2,377,600	3,600	2.4
June 17...........	32	2,555,200	2,800	3.2
June 24...........	52	4,461,600	4,200	3.2
July 1...........	41	3,528,800	4,200	2.8
July 8...........	65	4,870,400	8,200	1.2
July 15...........	78	4,852,800	4,200	5.6
July 22...........	78	4,352,000	5,600	3.2
July 29...........	68	4,417,600	6,200	3.2
Aug. 7...........	95	5,092,800	8,200	4.8
Aug. 14...........	109	5,190,400	10,800	2.

CHART 7.

Date.	Hemoglobin.	Red cells.	White cells.	Eosinophiles.
May 14...........	16	1,531,200	7,800	18.3
May 21...........	31	2,133,280	6,200	14.4
May 28...........	27	2,666,400	11,600	18.4
June 4...........	35	3,880,000	9,800	28.4
June 11...........	36	3,315,200	7,400	22.
June 18...........	50	4,181,600	14,800	17.2
June 25...........	59	5,238,400	11,200	46.
July 2...........	56	5,288,800	7,400	22.
July 9...........	55	5,195,200	11,200	32.4
July 17...........	64	5,461,600	8,600	40.
July 23...........	64	5,786,400	4,800	18.
July 30...........	84	5,440,000	9,600	24.4
Aug. 6...........	90	6,688,000	6,800	26.
Aug. 14...........	101	5,928,800	10,200	28.4

CHART 8.

Date.	Hemoglcbin.	Red cells.	White cells.	Eosinophiles.
Nov. 14...........	25	2,457,500	5,035	16.
Nov. 22...........	35	2,987,500	3,050	12.
Nov. 28...........	50	3,603,125	2,431	21.
Dec. 8...........	65	4,050,000	2,083	20.
Dec. 15...........	65	5,005,600	3,024	18.

CHART 9.

Age 14. Thymol once a week, no iron.

Date.	Hemoglobin.	Red cells.	Eosinophiles.
May 19.............	34	3,671,400	19.
May 26.............	45	4,430,000	14.
June 2.............	61	....	..
June 9.............	60	5,200,000	6.
June 16.............	63	5,904,000	9.
June 23.............	82	....	6.
June 30.............	100	5,409,500	8.

CHART 10.

Age 32. Thymol. Cured of worms after two treatments. Blaud's pills.

Date.	Hemoglobin.	Red cells.	Eosinophiles.
Nov. 19.............	72	4,950,000	12.
Nov. 26.............	78	....	6.
Dec. 19.............	85	5,640,000	10.
Dec. 28.............	104	6.120,000	4.

CHART 11.

Age 16. Mild case. Thymol. Cured first course. No iron. 81 worms collected.

Date.	Hemoglobin.	Red cells.	Eosinophiles.
March 6............	86	5,100,000	4.
March 19............	94	6,244,000	4.
April 2............	96	5,450,000	..

CHART 12.

Age 17, female. Thymol. Mild infection, pernicious anemia type. Fowler's solution after first two weeks. History indicates hookworm disease all her life.

Date.	Hemoglobin.	Red cells.	Eosinophiles.
March 13............	55	2,340,000	6.
March 29............	51	2,422,000	3.
May 3............	63	3,215,000	6.
June	..	....	4.
June 19............	61	4,752,000	4.
Sept. 22............	88	5,420,000	..

This case illustrates the slow (seven months) improvement usually made by this kind of anemia. Chart 1 shows another case of this kind, in which it took nearly two years for the blood to become approximately normal. Though severe cases may require several months to return to a normal blood condition, it is our belief that the average case in this country reaches a normal red cell count and hemoglobin index in one to three months, and very many mild cases within one month.

Height and weight.—The growth in height is in proportion to the amount of reduction and the age of the patient. When patients are not more than two or three inches below what they should be, this is usually gained if they are not over 20 years old. When over 20 they may still grow, but it is doubtful whether they ever reach the height due them. In fact, we have seen many cases grow several inches in height and several pounds in weight after they were 26 to 28 years old. One man 27 years old married while yet a boy in size and appearance, and moved to town. Within a couple of years he had grown so much that it was often remarked that married life had made a man of him. This occurred before we knew of hookworm disease, but subsequent familiarity with the disease and an opportunity to examine the man's brother, and the knowledge that another brother had died of undoubted hookworm disease, explain the cause of his dwarfing. The gain in weight is even more rapid sometimes than the gain in height. A 16-year old boy under our observation gained twenty pounds in weight and grew two inches taller in two months. Captain J. F. Siler had one patient who gained thirty-five pounds in one month. The foregoing were severe infections, but we have often seen remarkable gains in weight and general feeling by patients who had very mild infections. One man gained nine pounds in one month after expelling only nineteen worms. Another man, 35 years old, gained nineteen pounds after getting rid of a mild infection.

Patients with severe disease and childish voices at 18 to 20 or 22 years old will usually have change of voice within two or three months.

Pubic and axillary hair that have not started begin to grow within two or three months if the patient is of proper age. We have observed the beard to begin to grow at 29 years, and we believe it may later than this.

The mammæ of girls develop rapidly in dwarfed patients, and we have observed this after 24. No doubt this can occur even later if the worms are gotten rid of.

At the end of our chapter on treatment we wish to emphasize that we must not lose sight of any other diseases the patient may have when we are considering his treatment. Curing hookworm disease may often benefit, but will not cure, other diseases present.

REFERENCES.

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