THE PUERTO RICO JOURNAL OF PUBLIC HEALTH AND TROPICAL MEDICINE

VOL. IX DECEMBER, 1933 NO. 2

THE LARVAL PHASE OF UNCINARIASIS *

By BAILEY K. ASHFORD
From the School of Tropical Medicine of the University of Puerto Rico under the auspices of Columbia University
and G. C. PAYNE and F. PAYNE
Representing the Rockefeller Foundation in Puerto Rico

The Porto Rico Anemia Commission of 1904 [1] probably achieved its most valuable work in demonstrating that so widespread a scourge as uncinariasis could be halted, and that the efficiency of the agricultural laborer—its most frequent victim—could consequently be raised.

Among the valuable by-products of that seven years' campaign was the complete clinical study of the disease made from observations of the first 30,000 persons treated. It was realized that heavy infestations could produce an intense, acute form, which might often be fatal, and that from time to time persons, generally young and of fair health, could, after exposure to the wet mud of coffee plantations, become suddenly stricken with pallor, swelling and fever, and die from a severe attack of "mazamorra" or uncinarial dermatitis of the feet, such symptoms being at times accompanied by severe intestinal haemorrhage. An identical case is cited in the Report of the Commission for 1904, and this we believe to be the true meaning of the "jíbaro" or peasant term "La Bonita", considered by the victims as a separate and fearsome disease.

This acute form, fortunately unusual, can only be combated by accurate and prompt diagnosis on the part of the physician. The outstanding symptoms of a pure, unaggravated case of acute uncinariasis seem to be more or less as follows: an initial dermatitis, indefinite disturbances in the throat at times accompanied by bronchitis, a sudden unaccountable asthenia, fine, fleeting pains in the epigastrium becoming colicky upon the supervening of diarrhea, and a definite fall in blood values, with the picture of a secondary anemia. It

* This article appeared in abbreviated form in the J. A. M. A. Vol. 101: 843, No. 11. Received for publication, July 10, 1933.

should not be forgotten also, that if these infestations are sufficiently heavy an intermittent fever may develop with sudden unaccountable rises to a high temperature, and a marked leucocytosis with eosinophilia.

The story of a remarkable group infestation is told in detail in the recital of the history of Case I of the following series. A family, almost completely protected from the danger of a slowly developing uncinariasis, is in one day overwhelmed by a severe infestation while bathing in the sea —a fantastic mode of infestation this may seem to those who know that sea water, or prolonged submersion in any water, is supposed to kill hookworm larvae. Yet, in a moment, such larvae were swept off the polluted shore of a stream and out into a bay against the bodies of the bathers, effected an entrance into their skin, and produced the pictures which follow in these pages. These pictures are especially valuable clinically, as their origin cannot be confused with the underlying basic nutritional unbalance found in nearly all victims of the hookworm the world over.

In the cases which form the basis of this study an attempt will be made to combine the clinical and laboratory information.

The Initial Dermatitis.—Only one of the seven cases failed to suffer from this condition, and in all the rest, save one, it developed immediately after invasion of the skin by the larvae, its intensity seeming to depend as a rule upon the number invading. In cases III and VI infestations were not so heavy and their results not so manifest. It usually lasted about a week, but before its disappearance the throat symptoms began.

The Throat Symptoms.—A catarrhal bronchitis has been cited, especially by Calmette and Breton [2], as a frequent initial symptom in uncinariasis, but neither in our former experience nor in these cases herein recounted, was it sufficiently marked to attract attention, if it existed at all. What seems, however, to have been a fairly constant symptom was the development of a sensation of obstruction in the throat and difficulty in swallowing and speaking, unaccompanied by any striking physical signs. This symptom was present in all of the cases.

Digestive Symptoms.—In about a week from this time began the first pains in the epigastrium attributed by authors to the attack by the worm on the mucous membrane of the

upper reaches of the small intestine. Almost immediately this was succeeded by a sharp diarrhea with colic. This diarrhea was not only fermentative, but the stools frequently contained mucus and generally some blood, which was usually dark and seemed to have come from high up in the intestine. Only two cases out of the seven failed to note blood in the feces, and its absence seems to have been due to the insignificant number of worms in the intestine. In all seven cases the time of the onset of the diarrhea from the date of infestation was from two to four weeks. If blood appeared, it did so later than did the diarrhea.

At this point it might be well to note what is soon to appear a self-evident fact: that this group of cases divided itself naturally into two; first, those cases in which enough larvae had completed their cycle to set up a severe hemorrhage through their bites and blood-sucking in the intestinal canal, in addition to having, of course, an unknown population of wandering larvae in the background; and, second, those cases in which only a small percentage of larvae had been able to reach the intestine, too few to materially affect the symptomatology. This second group was characterized by a heavy population of wandering or arrested larvae in the tissues. In considering the first group, we should hold in mind for future reference the indeterminate number of larvae which had failed to complete the cycle in the human body. This group is composed of Cases I and II, and when all worms had been expelled from the intestinal canal the members of this group merged into the second.

All complained of an unusual degree of asthenia, all were pale, and all lost rather rapidly in weight.

A word here as to the pathogenesis of the diarrhea will not be amiss. As will be seen later, there is reason to suspect that some larvae still in the tissues of the body, by their death and disintegration, or, indeed, perhaps in the course of their lifetime, produce poisons affecting the blood. Now, it is difficult to explain the diarrhea in those harboring only a few intestinal worms (as, for instance, Case VII) by their local irritation. It seems far more reasonable to suppose that the elimination through the intestinal mucosa of these hypothetical larval poisons should be the real, or at least the chief cause of that diarrhea. It is somewhat doubtful, also, whether the local irritation caused by the biting of

the worms is responsible for the epigastric colics. It would seem more reasonable to ascribe this symptom also to the toxic effect of these poisons upon the mucous membrane, with its somewhat active enterocolitis. There is, however, always a certain degree of suspension of digestion in such cases, and the production of gas pains from fermentation of unabsorbed food.

There has always been a considerable amount of doubt as to whether uncinariasis *per se* causes a rise in temperature and a leucocytosis. In reality it seems to be a question more of the abruptness of invasion by large numbers of larvae than a matter of an uncompromising rule. There is no doubt, so far as these patients are concerned, that the process in acute uncinariasis is marked by fever, leucocytosis, and eosinophilia. The latter two phenomena will be discussed later. The temperature is not usually high, and is intermittent. Only at rare intervals do we see cases which interpolate a chill followed by a high temperature. Here again one must suspect the action of specific poison.

THE BLOOD.—Unquestionably the blood gives us more information at the beginning than any organ, and very especially the differential count of leucocytes. As has been said, in cases of acute uncinariasis with massive infestation. there is leucocytosis, highest in the first three months, and very gradually oscillating to a lower and lower level eventually to reach normal. But this leucocytosis is eosinophilic. Accepting the consensus of opinion that eosinophilia is the outcome of an allergy, we may readily see how foreign protein set free by the death and disintegration of wandering larvae can stimulate to very high eosinophile percentages, which percentages in these cases are phenomenally high.

The continuance of a well-defined secondary anemia with few intestinal worms, and the history of a severe skin invasion with the marked changes in the leucoytes, heretofore noted, should make us think of the retention in the body tissues of the majority of the larvae whose complete cycle has been interrupted, especially when good food and the use of iron fail to cause a rise in blood values. This larval phase of the disease must exert its influence in many cases of uncinariasis, for when one who has had to combat the disease as a physician comes in contact with the people whose daily life leads

them to acquire a larger or smaller number of larvae every time they go to work in the coffee plantation, it must occur to one that, were all of those infective organisms which enter the skin to reach the intestine, infestations would be measured, not by hundreds, but by thousands of intestinal worms.

This throws a completely new light on a disease whose intensity we have heretofore measured by the intestinal worm burden, not only in uncinariasis to which attention is now invited in its new aspect, but in ascariasis and strongyloidiasis, which recently have been considered to be more fearsome from their larval than from their adult parasitic phase.

These questions naturally rise: Are these larvae merely delayed in their journey to the intestine? How long will it take wandering or arrested larvae to complete their cycle? Do they become permanently deviated and lost in the tissue? A study of these cases makes it problematical if they ever do reach the intestine. The majority seem to die within the first three months, and there is some indication to show that their highest mortality lies at from two to four months after invasion of the skin, as seen from the usual increase in eosinophilia at this time, but some must hang on for at least a year. These seven cases have been under intense observation for nearly a year. The blood was examined completely every day for six weeks, hemoglobin percentage taken by the calibrated Sahli apparatus, the red and white cells counted, a differential count made of the leucocytes, and even a Price-Jones curve erected. From the middle of September to November this was done every second or third day, and thenceforth every week or two. We believe that few signs or symptoms have escaped us, and the whole record has been checked by a most unusually careful worm and egg count, always at the time of giving the anthelmintic, and in addition, whenever possible, in the interval between administrations of the vermifuge. In this check the matter was considerably clarified by the fact that all worms on the occasion of this remarkable invasion were of the species *Ancylostoma duodenale,* a really infrequent species in Puerto Rico. Only two of these cases yielded one or two necators, probably proceeding from previous infestations of years before, which must have been extremely slight, as they did not affect the health of the host. Whether some of these infestations had devel-

oped a relative resistance on the part of the tissues to the larvae, and thus their deviation and failure to complete the cycle, must remain a matter of pure conjecture.

Another peculiarity was the extremely small size of some of these worms, even to 1.8 mm. in length; also, there was a large proportion of males. Of the total number of worms expelled in these seven cases, 48 per cent were males, 43 per cent females, and 9 per cent unidentified as to sex.

Still another note of interest was found in the spontaneous diminution of the number of worms, four being *in copula*. Leichtenstern [3] called attention to this tendency in early cases when the worms were frequently changing position, but no attempt was made by him to give figures. This data, of course, is difficult and tedious to obtain, but we are rewarded by seeing that a no inconsiderable number is thus eliminated. In the first five cases of this series in which spontaneous elimination of worms was steadily investigated throughout a month, 5 per cent of the total worm burden was thus eliminated. Also many worms expelled were filled with blood, thus belying the statement that on separation from the intestine, or on the death of the host they immediately evacuate the blood lying in their bodies.

Thus, there seems to be a true larval phase of uncinariasis. It is indicated by loss of strength and weight, anemia, irregular fever, a definitely high eosinophilia and leucocytosis, possibly diarrhea, and a light intestinal worm burden. Indeed, there may be no worms at all in the intestine, no ova from which to make a diagnosis, and only the blood and the history of the case to suggest a larval invasion and a frustrated uncinariasis.

TREATMENT.—The keynote of the treatment is the prompt use of efficient anthelmintics, iron in large, appropriate doses, blood transfusion when the patient is suffering from profound anemia, and in the case of the pernicious type of anemia, liver extract by injection. The rest can be summed up by mentioning good food with a high content of protein of animal origin, rest, and such symptomatic remedies as may be indicated by special situations.

The use of hexylresorcinol seems well adapted to certain cases with contraindications to other anthelmintics. Hexylresorcinol is prepared in chocolate-coated pills, each contain-

ing 0.20 g. and the adult dose may be 2 g. once a week. No previous purge nor starvation diet is needed, but an after-going purge is recommended. It seems at times to produce nausea and even vomiting, but no other bad effects have been noted, nor does there seem to be record of any. In this connection we must remember Maurice Hall's wise observation that the limitations of an anthelmintic can hardly be known save after a hundred thousand well-observed administrations.

There is no treatment as yet known for the larval stage of the disease, but after de Langen's [4] and Faust's [5] experiments it is possible that some dye-stuff may yet be found to act as a remedy meriting the title of *sterilizans magna.*

Iron is of little use in cases in which larval uncinariasis is a potent cause of the anemia, which not only may account in part for the discouraging results with this remedy in the hands of the Porto Rico Anemia Commission many years ago, but indeed may speak for the conception that wandering larvae are at least an important contributing factor to the anemia. We do not doubt for a moment that worms in the intestine are a source of blood loss at any time, but we do wish to emphasize the importance of the testimony to the effect that this blood loss is far greatest when the worms are young, and that blood in the intestine, not to mention its rarity in the bodies of the worms at human autopsy, even occult blood, is only too often not demonstrable in chronic cases. But when the blood is to be built up after practically all worms and larvae have disappeared, ferruginous medication will give its usual felicitous results when used with the iron-starved anemic.

Results of Treatment.—Five of the seven cases state that they are cured, and they have gained an average of 27.2 pounds in weight, with disappearance of all symptoms save a low grade of a secondary anemia and, in one case, pronounced lack of appetite. The other two cases state that they are well, but one has gained only five pounds, and the other has lost four and three quarters. As a matter of fact, none are really cured, the blood chart of Case I being indicative of the general present condition.

CLINICAL HISTORY OF CASE I.

M. L., female, white, 11 years of age, Puerto Rican, student.

In its intellectual sense, this child belongs to one of the better families of the Island, and has always enjoyed the benefit of refined surroundings. There is no history of hereditary predisposition to any special class of disease. Dr. Ashford saw the child professionally concerning a minor complaint only a few months before her present illness, and found her normal, robust, and with a normal blood count.

CHIEF FEATURES OF ILLNESS: Diarrhea with increasingly severe hemorrhages, fever, profound pallor and prostration.

PRESENT ILLNESS: Dr. Ashford was called to see this case on August 3, 1932. Schistosomiasis had been considered on account of the hemorrhages, but as no ova of *S. mansoni* nor of any other intestinal parasite had been found, this diagnosis was abandoned in favor of a provisional one of typhoid fever, which, in spite of three negative agglutination tests, seemed a more likely diagnosis. But, in conversation with the mother, it cropped up that the hemorrhages had begun before the fever was shown to have set in, that the spleen had never been enlarged, and that no delirium or sub-delirium had ever been noted.

It seems that on June 23, 1932, the mother and patient had joined other members of the family for an outing at Luquillo, a small coast town on the north shore of Puerto Rico, noted for a beautiful bathing beach rimmed by palm trees, forming a little semi-circular bay. The bathing party on this day consisted of five, the patient, a male and female cousin, her great-aunt and a servant girl, all of whose histories are herein recounted separately. They spent all the morning bathing, and, after lunch, decided to do so in the afternoon. But meanwhile a heavy rain had come up, and on returning to the beach, they noted that a foul, stagnant stream, which in the morning had not had sufficient water in it to flow into the bay, was now pouring into the sea over the narrow strip of sand which had separated it therefrom on their morning visit. On emerging from the afternoon bath, all, save one, began to feel an intense itching over the entire body, worse, however, on the portions covered by the bathing suit, while the exposed parts were much less affected, or even, not at all. On examining themselves, they found what they described as little bites in the center of a more or less pink wheal, very thickly distributed. With the exception of the aunt, who had comparatively few, they all seemed to have an equal number of these bites. The itching continued after they reached the house, and kept them awake during the night. In all, it lasted about a week, after which the lesions became yellowish macules which persisted another week. The only one who failed to be much disturbed by the itching until next day, was Case II (M. W.).

From this point on, the symptoms will have to be recounted separately owing to minor variations.

In the case in point (M. L.), a few days after this bath, rawness of the throat developed, and swallowing became difficult, even to the point where the patient was afraid to eat. A physician was called to see the throat, but nothing was visible from his examination, although the cervical and axillary glands were swollen and painful. This condition lasted a week. A little over a week from the time of the bath, the patient began to feel very weak and sick, and two weeks after the bath colicky pains in the epigastrium developed with vomiting.

Shortly after this, July 14, three weeks after her sea bath, she took to her bed at her home in Caguas.

At this time there was a constant diarrhea, accompanied by a rapidly developing asthenia and pallor. A day or two later, the mother noticed that the stools had become black and contained blood. On questioning the patient it was found that this blood had begun to appear around the 14th of July. The amount of blood and mucus steadily increased, and on July 18 fever developed, and a physician was called. This hemorrhage had become alarming when Dr. Ashford was called in consultation, August 3. The stools were three or four in number a day, semi-liquid and fetid, but there was no tenesmus, although complaint was made of slight, cutting pains in the hypogastrium during defecation. Emetin had been injected for intestinal hemorrhage, and for two weeks there seemed to be a diminution, but at the time of the last consultation it had recurred with redoubled force, culminating in a collapse with syncope, subnormal temperature, and profuse sweating.

In this condition she was first seen by Dr. Ashford, and could be said to have been almost moribund from hemorrhage. In view of the full history as recounted (though in absence of laboratory data), he made a clinical diagnosis of acute massive infestation by hookworm, and recommended a transfusion of blood and prompt removal to the University Hospital in San Juan as soon as she should revive sufficiently to make the trip with a fair chance of reaching there alive. Three hundred cc. of citrated blood was given immediately, and with an excellent spirit of cooperation on the part of the physician who had been treating her, she was sent to the University Hospital, arriving August 6, 1932.

CONDITION ON ADMISSION TO HOSPITAL: Apart from her diarrhea, extreme pallor, prostration, and low, intermittent fever, the following additions should be made:

There was some headache, but eyes, ears, nose, throat and teeth were normal. The general physical development of the child was normal and far above the average for Puerto Rico. The cardiorespiratory system was normal, but the patient stated that she frequently suffered from "colds". The outstanding symptoms have been related, but the patient stated that for three months previous to her present illness, she suffered from sharp pains in the epigastrium soon after meals, which were relieved by bicarbonate of soda. Her other symptoms were normal.

PHYSICAL EXAMINATION: The blood pressure was 90 systolic, 60 diastolic. The weight and height could not be taken at this time on account of her physical condition. Her pallor was corpse-like, and she lay inert and apathetic, but with the intellect clear. There was no dyspnea, cough, or tremor. The superficial lymph nodes were palpable, but not enlarged. The conjunctivae were dead white, and pupils, sclerae, and muscular movements normal. Nose and ears, normal. The mucosa of the mouth was very pale; the tongue was clean. The gums and teeth were in excellent condition. Tonsils, absent. Neck, externally negative. Thorax symmetrical with equal expansion on both sides. Lungs, normal. Sounds were clear. Heart normal, but sounds were somewhat faint. Abdomen, flat and symmetrical. Spleen and liver, not palpable. No areas of tenderness or rigidity. No masses. The reflexes were normal.

It is in the white count and its differential that the most striking phenomena occur, not only in this case, but in all the others. During all of August the leucocytosis was marked, lying between 16,000 and 30,000 with a maximum of 44,000, and one fall to 8,400. Since then a gradual fall to 10,000 has taken place.

The eosinophilia has been really intriguing. During August and the first half of September, the percentage of eosinophils vibrated between about 30 and 50. Then there was an abrupt rise to a level vibrating between 50 and 75, falling gradually throughout November and December to a level lying between 20 and 40 per cent. From this point, the fall was steady to 10 per cent, where it still was on June 28, 1933. Now, to explain what happened here must be largely a matter of conjecture, but the most reasonable explanation of the phenomenon seems to be about as follows:

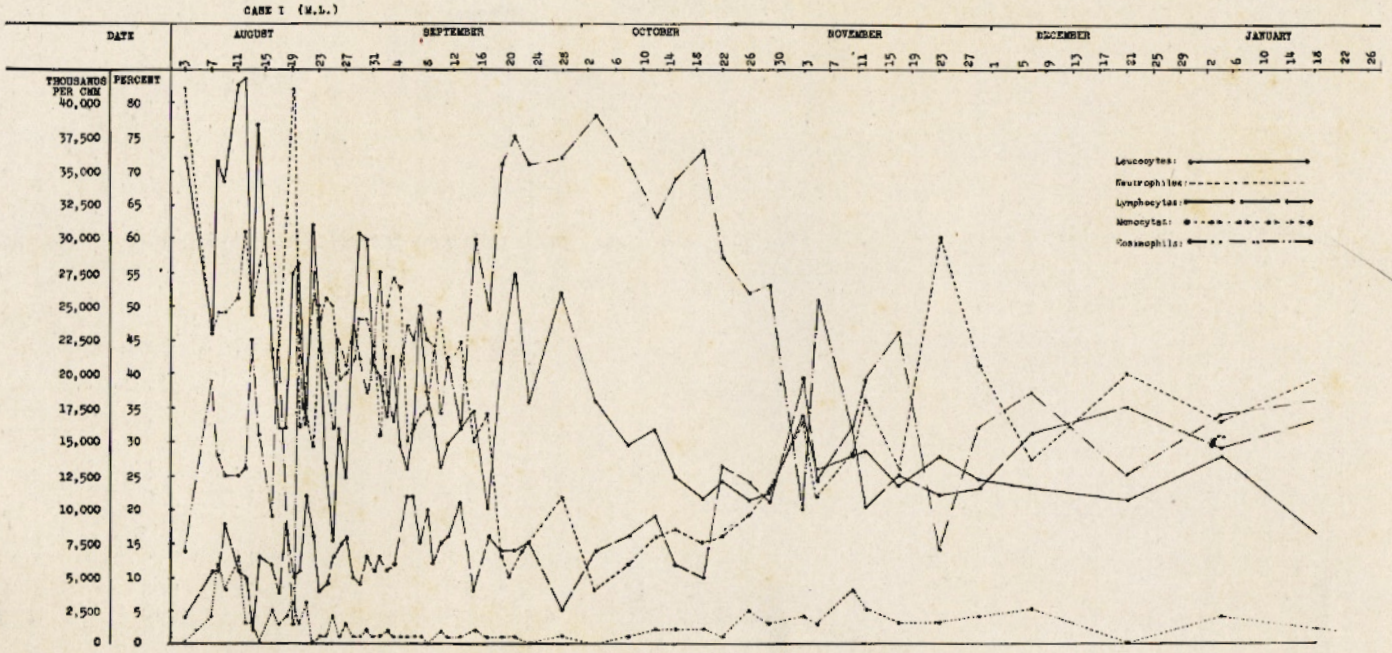
From August 3 to 31, inclusive, the 24 differential counts yielded an average of 34.6 per cent eosinophilia. During that period of time nearly all worms were expelled from the patient's intestine, or 1,395 in number. In the two months following, the twenty-six differential counts yielded an average of 54.6 per cent eosinophilia. In this latter period of 61 days, only 26 worms were expelled. After two more anthelmintic efforts in March and April of 1933, 13 more worms were expelled, and 18 days later the egg count was 2,600 per gram of feces, a Stoll calculation of 120 worms still remaining in the intestine.

There is a growing feeling that eosinophilia is a phenomenon related to the disintegration and absorption of foreign protein. It is clear that four of the five bathers on June 23, must have received about the same quantity of infestation. They all went into the water together, came out together, bathed in the same spot, had the same amount of itching and skin lesions, and suffered the same length of time thereafter. In Cases I and II, probably a relatively large percentage of larvae completed their cycle to come finally to maturity in the intestine. In Cases IV and V, the number completing the cycle must have been very small, the vast majority remaining in the tissues as wandering larvae. Case III bathed on the next day when the water was probably not so heavily loaded with larvae, and Case VI was exposed on the 23rd for only one third of the time of the others, hence their infestations were lighter. Case VII probably received a heavy infestation throughout several days. All of these last three, however, fall clearly in Group II of larval uncinariasis.

It would not be in disaccord with the clinical facts to suspect that the progressive death of more and more wandering larvae, their disintegration and absorption, should explain the high eosinophilia, and that in this case under consideration, the increase in eosinophilia in the six weeks following September 15, means that after some three months following the invasion of the skin, the larvae began to die off in large numbers.

But it is more difficult to explain the persistent oligochromemia, often becoming a mild secondary anemia, without admitting a toxin for the process of hemoglobin synthesis. One of us used to consider this process due chiefly to a hemolysin. In the light of subsequent work and new methods, it is very evident that it is probably not due to a hemolysin. In the first place, no bilirubinemia existed. On the other hand, in this case, the few worms left in the intestine after the use of anthelmintics are not sufficient to account for the secondary anemia still present by blood-sucking. Any one can see that as long as 1,448 worms are chasing each other about in the small intestine in a state of sexual exaltation, frequent changes of feeding ground, apart from blood actually abstracted, leave

CHART I



BLOOD PICTURE OF CASE NO. I, SHOWING DIFFERENTIAL COUNT FROM AUGUST 3, 1952 TO JANUARY 18, 1953

dripping wounds in the mucosa infiltrated by the anti-coagulant in the cephalic glands of the worm, and that a dangerous hemorrhage is produced, especially when we reflect that we are treating here with the *Ancylostoma duodenale* with a powerful buccal armature and sharp cutting teeth. Still, in the period following expulsion of practically all hookworms from the intestinal canal, the hemoglobin stubbornly refused to rise, and the red cell values kept tumbling down to 65 per cent or below, in spite of two months constant use of adequate doses of iron. As the daily food of the patient was known, it was certainly not due to a deficiency in copper.

To say the least, the question of a toxin acting deleteriously on the hemopoietic system is reopened by these cases.

THE FEVER: The temperature chart in this case with pulse rate has been reproduced by contraction, as the case was first diagnosed as typhoid fever. Uncinariasis is counted as an afebrile disease, but the statement of trustworthy observers in the early days that it was characterized by fever, seems to be borne out in some of these six cases of the acute stage. As a matter of fact, fever is not usually observed by those who have to treat it, as they come in contact with it usually in its chronic stage, or in those whose infestations are small, multiple, and continued over a long period of time. Such cases do not even bring out leucocytosis, and sometimes not even eosinophilia. In this case, however, and indeed, in the rest herein dealt with, these reactions to infestation come out quite sharply. The temperature is not usually high, and is generally intermittent. As will be seen in this chart, this sort of a curve is the rule, but on at least one occasion a sharp rise preceded by a chill took place, and together with the constitutional symptoms strongly resembled a malarial attack. But here the blood which had been under daily inspection had been entirely negative for the plasmodium since August 3, and at the time of the febrile movement was several times carefully searched, also with negative result. This sharp rise occurred on August 23, and in spite of the negative blood, was treated with quinine, as no chances could be taken. But a retrospect shows that in all probability it could not have been due to anything but an unusual dose of foreign protein marking the rise in the mortality of the larvae wandering about in the tissues. During July, the temperature alone was recorded while she was at home, unfortunately without annotation of the pulse rate. The average for the fourteen days of this period was for the lowest morning temperature 98.3°F; for the highest evening temperature, 100.5°F. The record for the month of August is complete for pulse and temperature, save on the first five days when the child was still at home. Respiration rate was monotonously the same, from 20 to 24 per minute, and is not recorded. The average lowest morning temperature for August was 98.9°F; the highest evening temperature was 100°F. For the eleven days in September spent in the University Hospital, the temperature was normal.

THE URINE: A long study of a series of cases in the 1905 report of the Porto Rico Anemia Commission revealed, among other things, frequent traces of albumen, some casts, and the usual urinalysis of a long-continued, slow-going chronic infectious process. But at the outset of this case the urine does not seem to have been affected. On August 10, urinalysis showed: Color, amber; appearance, turbid; specific gravity, 1015; albumen, none; sugar, none; sediment, many squamous cells; some white blood cells.

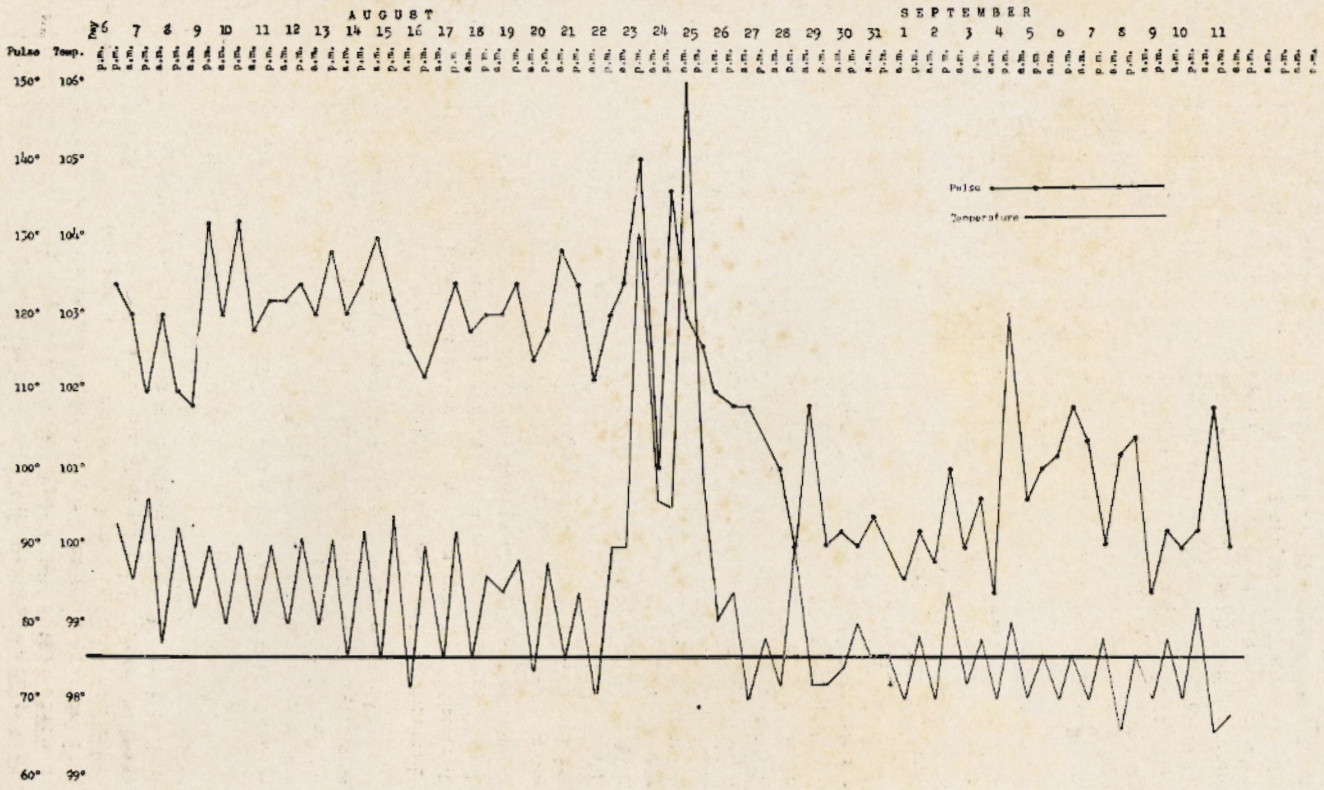
THE DIGESTIVE SYSTEM: Uncinariasis in its acute stage, when the worms are moving about in the intestine and changing their feeding ground, is apt to be marked by a considerable amount of diarrhea, often dysenteroid, and this latter description, of course, is all the more appropriate when, as in this instance, large amounts of blood-stained mucus are in evidence. From two to three evacuations a day are not unusual. There seems to be a partial suspension of digestion provoked by this helminthic irritation, and naturally, undigested particles of food will be found in the feces, whose odor is heavy and fetid, and whose color is brown or clayey, in addition to a toxic effect on the mucosa due to excretion through the bowel of the products of wandering larvae; this, however, is pure hypothesis. In this case, there was a definite tinge of black, like tar, at times mixed with red blood. The color indications of blood ran through long periods of time and demonstrated the systematic loss of large quantities of blood high up in the intestine. A curious but frequent disturbance of digestion up to the latter part of August was vomiting, with occasional pain in the lower abdomen, dizziness, and a capricious appetite with, at times, nausea.

THE NERVOUS SYSTEM: During the first six weeks the patient alternated between long periods of inertness and short emotional crises. The inertness was not marked so much by drowsiness, as by mental apathy, when she would lie perfectly conscious of her condition but without demonstrating the slightest interest in it. Then there would succeed a phase of crying or unreasonable excitement, with exhibition of bad temper over some perfectly trivial thing, such as food, with demands which could not be satisfied by us. This would be varied at times by fear of her injections, capricious refusal to take medicine and food, and so forth. When she regained her normal poise at the end of August, no trace of these mental states remained. The most important symptom, at least, the one which caused her the most distress, was a profound asthenia, here to be explained largely by the anemia, but nevertheless, a prominent feature of uncinariasis even in the absence of anemia.

THE SKIN: One of the curious features of this case was a general pruritus, which never took the form of an eruption. No traces of urticaria were ever discovered, nor was there even an increased sensitivity of the vaso-dilators on streaking the skin with the finger nail.

THE TREATMENT: The treatment has already been referred to, but will now be specified since the case came under our charge. On reaching the hospital, the patient was placed in bed and on a liquid diet. On the next day, August 7, administration of the elixir of the glycerophosphates of calcium and sodium containing 1 mgm. of strychnine to the dose was begun three times a day. On this day was also begun the daily intra-muscular injection of 4 cc. of liver extract which was sustained until the 6th of September in order not to be surprised by another failure of the gastric hormone. On the 9th of August the administration of 4 cc. of a 50 per cent aqueous solution of iron and ammonium citrate taken in orange or grapefruit juice immediately after the noonday and evening meals was begun and later substituted, as it was irritating to the stomach and produced more diarrhea, by 4 g. doses of the saccharated carbonate of iron, also in orange juice. This substitution occurred on August 26. The transfusions of blood made on the 10th and 15th of August have been described in detail and will not again be referred to. On August 12, as the child was distinctly better

CHART II

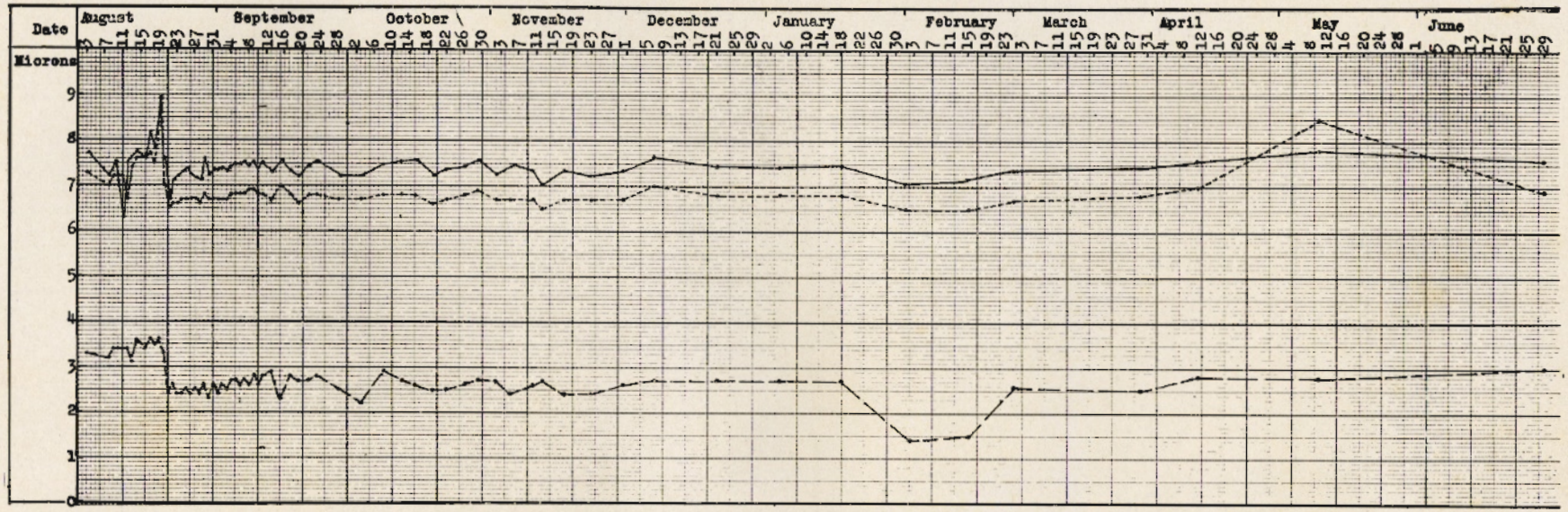


CASE I PULSE AND TEMPERATURE

CHART III

CASE I (M.L.)

PRICE-JONES CURVE



Mean ·————·

Median ·----------·

Double Dispersion —— —— ——·—

and clamoring for food, Dr. Ashford's high protein diet, used in treating sprue, was prescribed, as she had completely lost her appetite for liquids. It was only on August 16, however, that we summoned up sufficient courage to administer her first anthelmintic treatment. This has also been described in detail. Beyond causing a good deal of nausea, hexylresorcinol is believed to be the least depressive and least dangerous of all drugs for the expulsion of hookworm. But in consideration of the special features recounted in this case, a slow-acting, after-going purge was employed, chiefly because it did not increase the nausea, and also because violent purgation was feared. The dose was 5 g. of extract of cascara sagrada given in pill form an hour after the exhibition of hexylresorcinol.

On September 6 she was given full hospital diet. On September 9, the strychnine and glycerophosphates of calcium and sodium was stopped, and on the 11th she was discharged, vastly improved, although still pale. By this time she was cheerful, active, and suffered from no symptoms.

She was last seen on June 28, 1933, having gone from a weight of 77 pounds on August 30, 1932, to 105¼ pounds on this date, a gain of 28¼ pounds.

WORM AND EGG COUNT

CASE I (M. L.)

Date	Males	Females	Unidentified	Total	Egg Count per CG	Remarks
8/7/9	.....	.....	.....	.....	0	
8/10	.....	.....	.....	.....	2	Occult blood feces
8/11	.....	.....	.....	.....	7	
8/12	2	1	0	.....	.....	
8/14	6	1	1	.....	.....	
8/15	2	3	0	.....	.....	
8/16	0	1	0	17	30	Hexylresorcinol 0.8 g.
	10	6	1	17		
8/17	5	3	1	9	265	
8/18	625	107	56	788	.....	Hexylresorcinol 1.4 g.
8/19	56	52	32	140	.....	
8/20	8	8	18	34	.....	
8/21	11	11	8	30	58	
	705	181	115	1,001	.....	
8/22	0	0	0	.....	81	
8/23	27	60	0	87	.....	Hexylresorcinol 1.4 g.
8/24	30	40	24	94	.....	
8/25	8	21	4	33	.....	
	65	121	28	214	.....	
8/26	0	3	3	6	.....	
8/27	2	4	4	10	.....	
8/29	0	5	0	5	.....	
	2	12	7	21		

CASE I (M. L.)—Continued

Date	Males	Females	Unidentified	Total	Egg Count per CG	Remarks
8/30	37	63	1	101	.....	Carbon tetrachloride 1.5 cc.
8/31	6	24	0	30	.....	
9/1	2	9	0	11	.....	
	45	96	1	142		
9/2	0	2	0	2	.....	
9/3	0	2	0	2	.....	
9/4	0	1	0	1	.....	
9/5	2	1	0	3	.....	
9/6	0	0	0	0	51	
9/8	0	2	0	2	.....	
	2	8	0	10		
9/9	.....	.....	.....	.....	.....	Carbon tetrachloride 1.5 cc.
9/10	0	0	0	.....	22	
9/11	3	4	0	7	.....	
9/16	2	4	0	6	.....	Hexylresorcinol 1.4 g.
9/18	1	1	1	3	.....	
	3	5	1	9		
9/26	.....	.....	.....	.....	0	Negative for *S. mansoni*
9/29	.....	.....	.....	.....	3	
11/2	.....	.....	.....	.....	42	
11/23	.....	.....	.....	.....	64	
1/10/33	.....	.....	.....	.....	41	
1/11	.....	.....	.....	.....	71	
1/12	.....	.....	.....	.....	40	
1/13	.....	.....	.....	.....	73	
3/17	.....	.....	.....	.....	62	Carbon tetrachloride 1.2 cc.
3/19	1	0	0	1	.....	
3/20	1	1	0	2	.....	
	2	1	0	3		
4/7	.....	.....	.....	.....	52	
4/8	.....	.....	.....	.....	.....	Carbon tetrachloride 1.2 cc.
4/9	8	1	0	9	.....	
4/10	1	0	0	1	.....	
	9	1	0	10		
4/28	.....	.....	.....	.....	26	
4/29	4	1	0	5	.....	Carbon tetrachloride 1.5 cc.

CASE II

M. W., female, white, 15 years of age, Puerto Rican student. Admitted to the University Hospital August 19, discharged September 11, 1932. Mother is one of the patients in this group (Case III); father died of amebic dysentery; has one brother (Case IV), and one sister (Case VII).

CHIEF FEATURES OF ILLNESS: Diarrhea with intestinal hemorrhages. Low fever. Pallor, emaciation, and asthenia.

PRESENT ILLNESS: This child is the cousin of Case I and bathed with her on June 23 under conditions explained in that case history. No itching to speak of was noted on her body until the day after the bath, but from then on it began and lasted a week interrupting her sleep. Three or four days after this sea bath she noticed that she was hoarse and that it hurt her to swallow. This condition was accompanied by a cough, and her mother believed that she had taken cold. On June 30 she returned to her home in Río Piedras. On July 19 she began to feel very weak and had gastric uneasiness, accompanied by loss of appetite and profuse sweating. On July 22 she went to bed. On July 24 or 25 a violent diarrhea began; the stools were tarry. They occurred eight times a day, and, while there was plenty of blood, there was no mucus. The pallor which began on July 18 was now definite, and on August 6 she was sent to the Presbyterian Hospital. As she had pain in the abdomen and was pale, they gave her iron, but she states that the iron only increased the pain. No anthelmintic was given while she was there. On August 19 she was admitted to the University Hospital.

PHYSICAL EXAMINATION: Patient was poorly nourished and emaciated, but fairly well developed, alert and intelligent. The weight could not be taken on admission, as she was too prostrated to stand, but a couple of weeks later her weight was found to be 79 pounds. Skin, pale and atrophic; face, cheeks hollow and sunken; nose, prominent and sharp. Tonsils, moderately enlarged and purulent; there is a chronic follicular suppurative tonsillitis. Lungs, apparently clear. Heart, negative. Abdomen, flat and symmetrical; no masses, tenderness or rigidity. Spleen and liver not palpable. Reflexes, normal.

LABORATORY DATA: Urinalysis (August 20, 1932): Color, pale yellow; appearance, clear. Reaction, acid. Specific gravity, 1,003; albumen, none; sugar, none. Sediment, a few crystals of calcium phosphate; a few squamous epithelial cells.

Feces (August 20, 1932): Hookworm ova present; 8,000 per gram. Serology (August 20, 1932): Kahn's test for syphilis 000. Blood chemistry, (August 24, 1932): Calcium 9 mgm. per cent; chlorides 586.7 mgm. per cent.

Roentgenology (September 10, 1932): An X-ray of the chest showed both lung fields to be clear, without any evidence of parenchymatous lesion except two calcified tubercules, one at level of the third interspace in the right lung; the other at the level of second interspace near the hilum on the left side.

COURSE OF THE DISEASE: Beginning with August 19, the same orders were given as in Case I, namely, that all feces should be sent every day to the Doctors Payne for the purpose of noting the spontaneous as well as the vermifugal expulsion of worms. On August 20 only one female was eliminated but the day

before 8,000 ova per gram were present; nevertheless, on August 20 the egg-count showed only 2,800 ova per gram, a reduction which was not possible in 24 hours and which shows the fallacy of accepting the Stoll egg-count at its face value in an individual case. On August 21, 1.4 g. of hexylresorcinol was exhibited and caused much nausea, vomiting, and dizziness. But it should be noted in connection with this that the child had a large peri-rectal abscess which on this day burst and discharged a large amount of gray pus. This dose was repeated on the 23rd of August. As a result of these two administrations of hexylresorcinol, on the 21st, 481 worms were expelled, on the 22nd, 18, on the 23rd, 16, on the 24th, 7, and on the 25th, 1, a total expelled since entering the hospital of 524. It is interesting to note that 236 of these were males. From here on until the 31st no worms were spontaneously eliminated, but on that day 1.5 cc. of carbon tetrachloride was given, and 12 more worms were expelled, followed by 3 on the 1st of September, 3 more on the 3rd, and 2 more on the 4th. On September 5 she had sharp pains in the abdomen for which she had to take paregoric, and on that day quite suddenly 25 worms were spontaneously eliminated, followed on the 6th, 7th, and 8th, by 2, 3 and 1 worms respectively. On the 9th, carbon tetrachloride in the same dose was repeated, and she expelled 6 more worms on that day and still one on the 10th. On the 11th she was discharged from the hospital. But on the 15th of September she was again given the same dose of carbon tetrachloride. Twelve worms were expelled as a result, the last observation being made September 18. No more examinations of feces for spontaneous elimination of ancylostomes were made until March 25, 1933, when 1.5 cc. of carbon tetrachloride was administered. On the 25th she expelled 6 worms, on the 26th, 7, on the 27th, none. On April 22 the last dose of carbon tetrachloride was administered, 1.5 cc. and only two males recovered from the feces. Thus, in this case a total of 614 worms were expelled.

THE BLOOD: The patient happened to be admitted to the hospital on a day when the red cells made an excursion to normal, although the hemoglobin was only 34 per cent. Vague reports from the family indicate that the degree of anemia was very severe and there certainly could not have been over 2,500,000 red cells. By August 23, blood values seemed to reach their level: hemoglobin 42 per cent, reds 2,240,000. The red cells remained there until September 2, when they stepped up to the 70-per-cent level, vibrating thenceforth between 50 and 70 per cent until September 11, when a still higher level, 82 per cent, was reached. From there on the reds ran between 65 and 80 per cent, with two extraordinary pushes upward, one on the 8th of October to 92 per cent, and the other on the 29th of October to 107 per cent.

The hemoglobin crawled slowly up to reach 70 per cent on October 12; then fell to around 55 per cent, rose again to 68 per cent on December 7, and thence gently rose and fell between 65 and 73 per cent until June 21, 1933, the last reading being 77 per cent.

During much of this time, from August 27 to December, iron was administered in adequate doses. When one considers that by the 25th of August, 524, and by the 26th of September, 599 of the total 614 worms had been expelled, and that on April 24th, 1933, only 200 ova per gram were counted, blood-sucking cannot be said to have been the cause of this persistent secondary anemia, completely unaffected by iron. Indeed, although it has not been expressed in the chart, no reticulocytosis was ever seen in this case. Nor did the Price-

Jones curve ever indicate even a fleeting tendency toward macrocytosis. Indeed, there was a distinct microcytosis. The average of 5,400 cells, measured in lots of 100 on 54 successive days, was 7.32 microns; the median, 6.41 microns. The only abnormality noted was a brief initial and very feeble anisocytosis, as evidenced by the double dispersion.

In the case of the leucocytes, the total count in August ran between 18,000 and 27,000. In September, however, a little over two months from the initial bath, the count was most irregular, vibrating between 12,000 and 45,000. In October and November it ran between 11,000 and 28,000, and from December on it remained around 15,000.

From August 19 to September 2 the percentage of eosinophils rose step-like from 55 to 86 per cent, and from the latter date to November 10 remained steadily (with one dip only to 53 per cent) between 72 and 85 per cent, on two occasions reaching 87 per cent. With the exception of cases to follow, this is the highest sustained eosinophilia of which we have record, and it will be observed that it was attained only after the expulsion of five sixths of the patient's worms. Thenceforth there was a gradual decline to 50 per cent throughout November, December and January. But on the 15th of February there was a rise to 72 per cent, sustained until March 15 when there began a precipitous drop, ending in an eosinophile percentage of 33 on the 21st of June, 1933.

This very remarkable eosinophilia certainly seems to be connected in some way with the death of numerous larvae.

THE FEVER: The average lowest morning temperature from August 19 to September 11, inclusive, was 98.2°F; the average highest evening temperature was 99.4°F. The average lowest morning pulse rate was 96; the average highest evening pulse rate, 101.8.

THE DIGESTIVE SYSTEM: The stools in this case were also diarrheal, but there was less hemorrhage than in Case I. During the first five days there was an average of 4.5 stools, but thereafter generally only one a day. This case suffered greatly from diarrhea, however, before coming under our supervision. In the period of diarrhea at the University Hospital the stools were dark, full of gas, and fetid.

THE SKIN: One of the most striking changes in this case on cure was noted in the complexion. When first seen the skin was muddy and sallow and all the facial lineaments were sharpened to an almost painful degree. When last seen the face was fat and the skin clear white with rosy cheeks and the bright eyes of health and vigor. There was never any urticaria but on several occasions complaint of general pruritus, notably on September 6.

RESULTS: Clinically cured. Weight two weeks after admission to Hospital 79 pounds. Present weight June 21, 1933, 121.5 pounds. Gain 42.5 pounds.

CASE II (M. W.)

Date	Males	Females	Unidentified	Total	Egg Count per CG	Remarks
8/19/32	0	0	0	0	80	
8/20	0	1	0	1	28	
				1		
8/21	222	197	62	481	(1 pr. *in copula*)	Hexylresorcinol 1.4 g.
8/22	9	9	0	18	.....	
8/23	3	13	0	16	.....	Hexylresorcinol 1.4 g.
8/24	2	4	1	7	.....	
8/25	0	0	1	1	.....	
	236	223	64	523		
8/26	0	0	0	0	48	
8/31	5	7	0	12	.....	
9/1	0	3	0	3	.....	
	5	10	0	15		
9/3	1	2	0	3	.....	
9/4	0	2	0	2	.....	
9/5	6	19	0	25	18	
9/6	0	2	0	2	.....	
9/7	1	2	0	3	.....	
9/8	0	1	0	1	.....	
	8	28	0	36		
9/9	2	4	0	6	.....	Carbon tetrachloride 1.5 cc.
9/10	1	5	0	6	.....	
	3	9	0	12		
9/15	.....	.....	.....	.....	.....	Carbon tetrachloride 1.5 cc.
9/16/17	9	3	0	12	.....	
9/17	0	0	0	0	2	
9/30	.....	.....	.....	.....	12	
10/26	.....	.....	.....	.....	.....	Negative for *S. mansoni*
11/2	.....	.....	.....	.....	4	
11/26	.....	.....	.....	.....	3	
1/9/33	.....	.....	.....	.....	19	
1/13	.....	.....	.....	.....	12	
3/24	.....	.....	.....	.....	21	
3/25	2	4	0	6	.....	Carbon tetrachloride 1.5 cc.
3/26	3	4	0	7	.....	
	5	8	0	13		
4/21/33	.....	.....	.....	.....	2	
4/22	2	0	0	2	.....	Carbon tetrachloride 1.5 cc.
	2	0	0	2		

CASE III

M. C. de W., female, white, 38 years of age, widow, Puerto Rican. Occupation: Office clerk. Admitted to the University Hospital August 19, discharged September 11, 1932.

CHIEF FEATURES OF ILLNESS: Diarrhea. Fair degree of pallor, emaciation and asthenia.

PRESENT ILLNESS: She was first seen in Dr. Ashford's office on August 17, 1932, and stated that she was one of the bathers in the sea where Case I became infested. She had gone to Luquillo on June 1 and had bathed at this site nearly every day up to and including June 30. She stated that on none of these days previous to June 23 did it rain hard, so that the dirty brook never poured into the sea throughout this time, and she never felt any itching after these baths. In fact she did not bathe on the day on which Case I bathed, but on the day following, June 24, when the stream was still pouring into the bay. As soon as she left the water she began to feel itching which she stated lasted from 15 to 20 days. She described the lesions as little dark red points like bites all over the body where it was covered with the bathing suit. Three or four days after the itching began, she noted what she described as an obstruction in the throat like a piece of heavy mucus which she could not swallow. This eventually became an outright sore throat. About July 15, fine pains began in the epigastrium which deepened to severe pain. She also had a cough a few days after having become infested, but this cough did not seem so much like a bronchitis as an irritation of the throat. On the 5th of August she noted that her stools were the color of mahogany. Loose bowels began on July 19 and little by little developed into a real diarrhea with from eight to ten evacuations a day. The stools were black at times but the diarrhea was not dysenteroid, and there was absence of straining. It was accompanied by nausea and loss of appetite, but there was no vomiting. She rapidly lost fifteen pounds and felt extremely weak. She stated very positively that before consulting Dr. Ashford she had suffered from fever without chills.

PHYSICAL EXAMINATION: The patient was fairly well nourished and developed, but pale. She was alert and intelligent. Height 61.5 inches; weight, 108 pounds. Skin, elastic, pale and warm. Glands, the superficial lymph glands were palpable but not enlarged. Tonsils, normal. Lungs, tactile fremitus normal; the percussion note was resonant over the pulmonary parenchyma. Breath sounds were of normal vesicular quality; voice normal. Heart, normal size; action regular and fairly strong, no murmurs or thrills. Abdomen, flat and symmetrical. Spleen and liver not palpable; there were no masses, no tenderness, no rigidity, no hernia. Reflexes, slightly exaggerated.

LABORATORY DATA: Urinalysis, (August 20, 1932): Color, yellow; appearance, turbid; reaction, acid. Specific gravity, 1015. Albumen, negative; sugar negative. Sediment, loaded with squamous cells.

Feces (August 20, 1932): Hookworm ova found, and there were 2,400 per gram; but feces were negative for *Schistosoma mansoni*.

Serology: Kahn test for syphilis 000.

Roentgenology: There was no X-ray pathology in the pulmonary field.

COURSE OF THE DISEASE: On the 20th one worm was spontaneously eliminated. On the 21st and then again on the 23rd of August, 2 g. of hexylresorcinol were given. In this case hexylresorcinol seemed to have produced vomiting, weakness, dizziness, and cramping of fingers and toes. For the relief of the latter two symptoms chloral cnemata had to be employed. From the 21st to the 27th, inclusive, 61 worms were expelled. On the 30th 2 cc. of carbon tetrachloride were given, but no worms were expelled. On September 9, the dose was repeated, and one worm was expelled as a result. Again on the 17th of September 1.4 g. of hexylresorcinol was administered, but no worms were expelled. In fact, the reason can be seen in the egg-counts which ran from 100 to 500 per gram. On April 22, 1933, carbon tetrachloride was administered for the last time in a dose of 1.5 cc., and only one worm was expelled. It is very evident, therefore, that the total number expelled, or 64, about represented the ancylostome population in the intestine.

THE BLOOD: The hemoglobin hung persistently between 60 and 70 per cent in spite of three months of adequate ferruginous medication and with far too meager a population of ancylostomes in the intestine to account for it by blood-sucking. Here again, as in the previous case, we have sharp thrusts of the red cells toward normal and yet as persistent a collapse to 60 or 65 per cent erythrocyte values. Indeed, the first five months of her infestation when she had 64 ancylostomes in the intestine showed more of a tendency toward a normal red cell count than the last six months when she had almost none. The Price-Jones curve was normal save for a microcytosis during the last five months.

The leucocyte record is intensely interesting, not so much from its leucocytosis which is distinctly inferior to the others and nearly descends to the normal maximum by October, but on account of the eosinophilia. This also is inferior in height to the others, vibrating through August and September between 35 and 65 per cent. What is most important is the upward thrust on the 28th of September, about three months after skin invasion, to 75 per cent recalling a similar phenomenon of much longer duration in Case I and the other cases herein recounted, and possibly evidencing a sudden high larval mortality. From there on the eosinophilia descends, running between 20 and 30 per cent to end June 28, 1933, with 16 per cent.

There is little doubt, in view of the history and this blood record, that Case III received less of an infestation than Cases I, II, and IV.

THE TEMPERATURE: From the patient's narrative there is every reason to believe that before she came under the observation of the writers a marked febrile reaction existed, but the chart kept while in hospital, would give no suspicion thereof. For these twenty-four days the average lowest morning temperature was 98.2°F.; the average highest evening temperature was 98.5°. The average lowest morning pulse was 98.8; the average highest evening pulse was 93.

THE DIGESTIVE SYSTEM: For the first five days there was diarrhea with an average of five stools a day. These were yellow or brown, and fetid.

TREATMENT: All treatment has been detailed.

RESULTS: She feels well and weighed 114 pounds on June 28, 1933, a gain of 6 pounds.

CASE III (M. C. de W.)

Date	Males	Females	Unidentified	Total	Egg Count per C G	Remarks
8/19/32	0	0	0	0	32	
8/20	1	0	0	1		
				1		
8/21	7	13	0	20	.....	Hexylresorcinol 2 g.
8/22	4	4	1	9	.....	
8/23	10	19	0	29	.....	Hexylresorcinol 2 g.
8/25	0	0	0	0	.....	
	21	36	1	58		
8/26	0	3	0	3	.....	
8/27/30	0	0	0	0	6 & 6	
8/31	0	0	0	0	.....	Carbon tetrachloride 2 cc.
9/4, 4, 6	0	0	0	0	6 & 5	
9/9	0	1	0	1	.....	Carbon tetrachloride 2 cc.
9/17	0	0	0	0	.....	Hexylresorcinol 1.4 g.
9/26	.....	.....	.....	.....	1	
9/30	.....	.....	.....	.....	1	
10/26	.....	.....	.....	.....	.....	Negative for *S. mansoni*
11/23	.....	.....	.....	.....	1	
1/9/33	.....	.....	.....	.....	5	
1/13	.....	.....	.....	.....	1	
4/21	.....	.....	.....	.....	3	
4/22	1	0	0	1	.....	Carbon tetrachloride 1.5 cc.

CASE IV

A. W., male, white, 14 years of age, Puerto Rican, student.

Admitted to the University Hospital August 19, and discharged September 11, 1932.

His mother is Case III; his two sisters are Cases II and VII.

CHIEF FEATURES OF ILLNESS: Diarrhea with blood. Afternoon fever. Asthenia and loss of weight.

PRESENT ILLNESS: On June 1, 1932, he went with his mother and sisters to Luquillo and bathed daily in the sea with them. He noticed no itching until the 23rd, when, under the circumstances recounted in Case I, on leaving the water he began to itch all over, and noted the bites chiefly on the covered parts. For several nights he did not sleep owing to this itching. He stated that a week after the bath he felt a little ball rising and falling in his throat, followed by a sore throat and pain which interfered with talking and eating. Three weeks from the time the itching began he noted "pains in the stomach", which, though not colicky, caused vomiting and were followed by much diarrhea, about six

movements a day. On occasions blood was seen in the feces. The blood was red and watery, and very abundant. This made him quite dizzy, and as a result he spent most of his time in bed.

PHYSICAL EXAMINATION: He was physically and mentally depressed, pale and emaciated, weighing only 89½ pounds with a height of 65.5 inches. Respiratory system, normal, also nose, ears, eyes and throat; tonsils, absent. Pulse, weak and rapid. Abdomen, flat, symmetrical, and with no pain; spleen and liver not palpable; no tenderness, masses or rigidity. Skin, muddy and pallid. Profuse diarrhea, occasionally streaked with blood. Reflexes, dulled.

LABORATORY DATA: Urinalysis (August 23, 1932). Color, yellow; appearance, turbid; reaction, acid; specific gravity, 1,029; albumen, none; sugar, none; sediment, crystals of calcium oxalate.

Feces: (August 19, 1932); 4,600 hookworm ova found per gram, as well as larvae of *Strongyloides stercoralis;* negative for *Schistosoma mansoni.* Serology (August 27, 1932); Kahn's test for syphilis, 000.

Sputum examination (September 9, 1932); The patient had a severe bronchitis, and request was made for a careful examination as to (1) presence of larvae of ancylostoma, (2) for excess of eosinophils. Both were negative.

Roentgenology (September 9, 1932); An X-ray picture was taken of the lungs, but both lung fields seemed normal.

THE COURSE OF THE DISEASE: On the 19th, 20th, and 21st of August, all of the feces of this boy were saved, washed, and searched for stray worms accidentally eliminated without drugs. There was no spontaneous elimination of worms. On the 22nd and 23rd of August the patient received 1 g. on each day of hexylresorcinol, and expelled on the 22nd, 23rd, and 24th, 45 worms. From the 25th to the 29th careful examination of the washings of total feces revealed no spontaneous elimination. On the 30th the patient was given 1.5 cc. of carbon tetrachloride, and expelled on that day 1 worm, on the 31st, 4 worms, and on the 1st of September, 1 worm, a total of 6. From the 2nd to the 11th of September, inclusive, washed feces failed to show any worms. This is espe cially interesting because from September 8 on, 0.20 g. of gentian violet in chocolate-coated pills was administered daily for three weeks. This drug is said to be a specific for strongyloides, both for the worm in the intestine and the wandering larvae. It was really given with the suspicion that the severe bronchitis was due to the irritation caused by the larvae of ancylostomes in the lung, but it did not expel any worms, and it had no effect on the bronchitis. On the 17th of September, 1.4 g. of hexylresorcinol was given, and on the 17th and 18th of September, 6 worms were expelled, but it is interesting to note that on the two days previous, the 15th and 16th, 9 worms were spontaneously eliminated. On the 8th and 22nd of April, 1933, 1.5 cc. of carbon tetrachloride was administered, and 59 worms were expelled, one of them, a *Necator americanus.* Thus, in all, 125 worms were expelled from this case.

The curve of the hemoglobin and erythrocytes is quite like that of Case III, the patient's mother. The hemoglobin remained between 55 and 75 per cent, with an occasional excursion to 80 per cent, eventually rising to between 70 per cent and 80 per cent, but in the last three months falling to about 65 per cent. The final hemoglobin percentage on June 23, 1933, however, was 90 per cent. The reds kept falling precipitously from an 85 per cent to 100 per cent value

to around 55 per cent to 60 per cent, although at the end, June 21st, 1933, they were at 101 per cent. Reticulocytosis was never observed.

With one exception, when the diameter of the cell in the last week of September reached 8 microns and over, the Price-Jones curve was normal, although it is true, the double dispersion in August and September was somewhat high.

What has really happened in this case is clearly told by the leucocytes. There is no doubt whatsoever that the amount of infestation in this case did not differ materially from what happened in Cases I and II: the life cycle was broken in the tissues, the larvae began to wander, and only a few reached the intestine; hence it seems that we are in the presence of a true larval phase of uncinariasis. There was a fantastically high leucocytosis in the months of August and September. From 78,400 per cmm. it abruptly fell to 34,200; then to 14,200; then rose step-like to 56,600, and finally it fell gradually to a high normal on June 21, 1933.

But if the leucocyte count is of interest, the eosinophilia is still more so. Starting out with from 60 per cent to 70 per cent values, it fell on August 25th to 36 per cent, rising thereafter to play between 75 and 85 per cent. By October it reached nearly 90 per cent, a little over three months after invasion of the skin. By the 26th of October it tumbled to 55 per cent, and for a time played between 50 per cent and 65 per cent, only to rise again to 75 per cent in December, from which height it fell again to 53. Henceforth it maintained a value of about 60 per cent until April 29, when it began to fall, and finally reached 30 per cent on June 21, 1933.

The point is, that in lieu of over 1,500 worms in the intestine, as in Case I, there are not 100 in this case, but instead there is a tremendous eosinophilia, a marked leucocytosis, and a persistent secondary anemia to testify to the arrest of the life cycle of ancylostoma in the tissue of this particular case.

TEMPERATURE: The temperature chart indicates very clearly that the larval phase of uncinariasis is marked by a febrile reaction, and that within the curve there are distinct upward thrusts that might suggest almost any one of the common causes of fever, especially malaria. The average lowest morning temperature for 24 consecutive days in hospital, from August 19 to September 11, was 97.8°F; the average highest evening temperature was 99.3°F. The average lowest morning pulse rate for the same period was 90.2; the average highest evening pulse rate was 95.1.

THE DIGESTIVE SYSTEM: While the stools were dark, semi-solid or liquid and by no means normal at intervals, in general there was no diarrhea, although previous to his admission to hospital, the diarrhea had been a marked feature.

TREATMENT: The treatment has been detailed, and it only remains to make a few remarks on the effect of this treatment. Hexylresorcinol in common with what usually happened with the others, produced nausea. In this case, however, there was also vomiting, dizziness, and severe headache. It was on the 24th of August that this boy developed a severe bronchitis, and this, plus the constitutional disturbance due to the anthelmintic, hexylresorcinol, brought his weight down on the 29th to 85.5 pounds.

RESULTS: In common with his sister, Case II, there has been a remarkable clinical improvement. In the first place, the weight has risen from its lowest figure, 85.5 pounds, to 122 pounds on June 21st, 1933, a gain of 36.5 pounds,

and he is better in every way—in fact, normal, save for a marked pallor caused by secondary anemia which still remains, and complete loss of appetite.

CASE IV (A. W.)

Date	Males	Females	Unidentified	Total	Egg Count per CG	Remarks
8/21/32	0	0	0	0	46	
8/22	13	12	0	25	.....	Hexylresorcinol 1 g.
8/23	6	11	1	18	.....	Hexylresorcinol 1 g.
8/24	0	2	0	2	.....	
	19	25	1	45		
8/26	0	0	0	0	88	
8/28	0	0	0	0	84	
8/30	1	0	0	1	.....	Carbon tetrachloride 1.5 cc.
8/31	0	4	0	4	.....	
9/1	1	0	0	1	.....	
	2	4	0	6		
9/5	0	0	0	0	72	*Trichiuris trichiura* 1
9/8	0	0	0	0	.....	Gentian violet 0.20 daily
9/11	.....	.....	.....	.....	72 56	
9/16/17	4	3	2	9	.....	Hexylresorcinol 1.4 g.
9/17/18	0	4	2	6	.....	
	4	7	4	15		
9/26	.....	.....	.....	.....	9	
9/30	.....	.....	.....	.....	15	
10/26	.....	.....	.....	.....	.....	Negative for *S. mansoni*
11/2	.....	.....	.....	.....	43	
11/23	.....	.....	.....	.....	29	
1/9/33	.....	.....	.....	.....	62	
1/10	.....	.....	.....	.....	71	
1/11	.....	.....	.....	.....	71	
1/12	.....	.....	.....	.....	74	
1/13	.....	.....	.....	.....	56	(Second slide 56)
1/18	.....	.....	.....	.....	78	
4/7/33	.....	.....	.....	.....	70	
4/8	1	1	0	2	.....	Carbon tetrachloide 1.5 cc.
4/9	8	2	0	10	.....	
4/10	3	13	1	17	.....	
4/10	1	0	0	1	.....	I *Necator americanus*
	13	16	1	30		
4/21	.....	.....	.....	.....	No egg count	
4/22	13	3	0	16	.....	Carbon tetrachloride 1.5 cc.
4/23	6	3	1	10	.....	
4/24	1	2	0	3	.....	
	20	8	1	29		

CASE V

M. S., female, white, 26 years of age, married, Puerto Rican. Occupation, servant. Admitted to the University Hospital August 23, discharged October 23, 1932.

CHIEF FEATURES OF ILLNESS: Diarrhea, pain in the epigastrium, emaciation and asthenia.

PRESENT ILLNESS: She was brought to the University Hospital on August 23, 1932, and stated that she went with the family of Case III to Luquillo on June 1, 1932. The first day it rained hard was June 23, the day she bathed with Case I, and on leaving the water she began to have itching all over the body. This itching disturbed her sleep for several nights and lasted three or four days. Four days after this bath, she began to have severe pain in the throat and a sensation of something that could not be swallowed. She felt as though she were going to have an acute cold. This lasted more than two weeks, with pain in the chest and a good deal of cough. The pain in the stomach began when the throat symptoms disappeared. This was about the end of the first week in July. These pains were extremely severe and constant unless she took some analgesic. The day after the pain in the stomach appeared, she began to have diarrhea, with from five to seven movements a day. The stools were red like blood; at times blackish, like tar.

PHYSICAL EXAMINATION: Height, 63 inches; weight 97¼ pounds. Blood, pressure, 88 systolic, 54 diastolic. Heart, normal, but sounds weak. Skin, cool, moist and pallid, with a papular eruption over the face. Appetite lacking at time of illness. Lungs, apparently clear. Abdomen, flat; no tenderness, masses or rigidity. Liver and spleen not palpable. Reflexes, normal. Glandular system; the superficial lymph nodes were not palpable.

LABORATORY DATA: Urinalysis, (August 24, 1932): Color, yellow; appearance, clear; reaction, acid. Specific gravity, 1011. Albumen none, sugar none. Sediment, loaded with squamous cells; a few white blood cells.

Feces (August 24, 1932); 4,200 ova of hookworm per gram of feces. Cysts of *Entameba coli.*

Serology; Kahn's tests for syphilis 000.

Blood chemistry (September 21, 1932); Icteric index 1.8 Repeated September 22 and found 1.9.

ADDITIONAL INFORMATION: After her discharge from the Hospital, October 23, 1932, she was readmitted in December for the purpose of expelling a *Tenia saginata,* but the head was not expelled. The anthelmintic was male fern, and it was given through the duodenal tube, notwithstanding which she vomited nearly all of it.

COURSE OF THE DISEASE: August 23, 24 and 25 revealed no spontaneous elimination of worms. On August 26, 1 cc. of the oil of chenopodium and 2 cc. of carbon tetrachloride were administered. On this day and the next 39 ancylostomes were expelled. From August 28 to September 13, 7 worms were spontaneously eliminated. She was given on the 9th of September 2 cc. of carbon tetrachloride, but no worms were expelled as a result. On the 14th of September 1.4 g. of hexylresorcinol was administered which brought away 12 worms, four

of them *in copula*. From here on, one worm was spontaneously expelled, but it is proper to state that only from 100 to 300 ova per gram of feces were found, and often not any. The total number of worms expelled was 59.

BLOOD: Here again, we have a case similar to Cases III and IV in hemoglobin and red cells. Throughout August and September the hemoglobin vibrated between 52 and 71 per cent, but on October 20 it rose to an 83-per-cent level and was sustained, the last on June 21, 1933, registering 75 per cent. The red cells kept constantly pushing up peaks to normal level, but as rapidly these values fell to from 45 to 75 per cent of normal, showing a constant tendency to register between 60 and 70 per cent. In this case the Price-Jones curve was somewhat irregular. While it did usually give an average red-cell diameter within normal limits, on several occasions the mean diameter exceeded 8 microns. The double dispersion was constantly somewhat high.

The number of leucocytes during August and the first part of September vibrated between 18,000 and 27,000. It then stepped down to a level alternating between 10,000 and 20,000, and from September 24 on preserved a high normal. The eosinophils in the latter part of August and the first half of September vibrated between 45 and 65 per cent, with an occasional excursion upward. From that point on, they gradually descended to 15 per cent, the last reading on June 21, 1933, being 11 per cent. Thus the highest percentage of eosinophils is found after two months from the time of invasion of the skin.

TEMPERATURE: In looking over the chart of this case, we note long periods alternating between subnormal and normal temperature, and short episodes in which temperature was distinctly elevated. One such period occurred on September 13 and 14, and another, a far more important one, occurred on the 6th and 7th of October. Naturally, little inkling of this cropped up in the average per month. For August, the average lowest morning temperature was 98.2°F.; the mean highest evening temperature 98.9°F. In September the average lowest morning temperature was 97.8°F.; the average highest evening temperature was 98.8°F. For October the average lowest morning temperature was 98.2°F.; the average highest evening temperature was 98.7°F.

The average lowest morning pulse rate for the latter part of August was 84; the average highest evening pulse rate, 85. For September these values were 88 and 88, respectively, and for October, 82 and 85, respectively.

THE DIGESTIVE SYSTEM: From time of admission to hospital until September 5, there was a distinct tendency to diarrhea; often the stools, however, instead of being liquid or watery were merely semi-solid, but there was always distinct indigestion of food elements. The stools did not greatly improve in quality, although they did so in frequency for the rest of September. But from there on, diarrhea practically ceased. On the 24th and 26th of August, as well as on the 14th of September, this woman had nausea and vomiting, but only on one of these occasions was it unprovoked by anthelmintics. From time to time she complained of pain in the abdomen, especially on the 8th of September.

RESPIRATORY SYSTEM: On September 13 she began to have oppression on breathing, pain in the chest, and eventually, bronchitis with cough and expectoration. These pains in the chest lasted until October 8.

TREATMENT: Here again, we note nausea and vomiting after hexylresorcinol. On September 30, owing to the extreme lassitude of the hemopoietic system, it was decided, in spite of the secondary type of anemia, and with the additional evidence of a tendency toward macrocytosis, to use full doses of the extract of liver by intramuscular injection. This was continued until the 10th of October, but no striking results followed, and it was stopped.

RESULTS OF TREATMENT: This woman has experienced a remarkable improvement in her health. Not only has her weight risen to 120½ pounds on the 22nd of June, 1933, a total gain of 23¼, but in vitality and especially in clarity of complexion, this case bears witness to the beneficent effect on the health of being relieved of even a comparatively small number of hookworms.

CASE V (M. S.)

Date	Males	Females	Unidentified	Total	Egg Count per CG	Remarks
8/23/32	0	0	0	0	42	
8/24	0	0	0	0	40	
8/26	11	13	3	27	.....	Carbon tetrachloride 2 cc. and Oil chenopodium 1 cc.
8/27	5	7	0	12	.....	
	16	20	3	39		
8/30	0	4	0	4	4	
8/31	0	2	0	2	.....	
9/2	0	1	0	1	.....	
9/7	0	0	0	0	6	
	0	7	0	7	.....	
9/9	0	0	0	0	.....	Carbon tetrachloride 2 cc.
9/13	0	0	0	0	2	
9/14	7	5	0	12	2 pr. *in copula*)	Hexylresorcinol 1.4 g.
9/19	1	0	0	1	.....	
9/29	0	0	0	0	0	Positive occult blood
9/30	0	0	0	0	1	
10/4	.....	.....	.....	.....	3	
10/5 a.m	.....	.....	.....	.....	2	
p. m	.....	.....	.....	.....	2	
10/7	.....	.....	.....	.....	3	
10/8	.....	.....	.....	.....	3	
10/10	.....	.....	.....	.....	4	*Trichiurus trichiura* 1
10/11	.....	.....	.....	.....	2	
10/12	.....	.....	.....	.....	1	From mushy portion
	.....	.....	.....	.....	.....	5 from formed portion
10/13	.....	.....	.....	.....	2	Mushy
10/14	cultured	.....	.....	.....	6	Formed
10/15	cultured	.....	.....	.....	2	Mushy
10/17	.....	.....	.....	.....	4	
10/18	.....	.....	.....	.....	1	*Trichiurus trichiura* 1

CASE V (M. S.)—Continued.

Date	Males	Females	Unidentified	Total	Egg Conut per CG	Remarks
10/19	.....	.....	.....	.....	1	*Trichiurus trichiura* 1 No *S. mansoni*
10/20	.....	.....	.....	.....	2	No *S. mansoni*
	.....	.....	.....	.....	3	No *S. mansoni*
10/21	.....	.....	.....	.....	2	*Trichiurus trichiura* 1 No *S. mansoni*
11/19	3 live segments of *T. saginata*				1	*Trichiurus trichiura* 1
1/9/33	Liquid stool.....					
1/13	.....	.....	.....	.....	1	
4/12	.....	.....	.....	.....	.....	10 and segments of *T. saginata*

CASE VI

B. T. female, white, 56 years of age, unmarried, Puerto Rican. This case was treated in Dr. Ashford's office; first visit August 31, 1932.

CHIEF FEATURES OF ILLNESS: Diarrhea and pain in the abdomen; loss of weight and strength; anemia.

PHYSICAL EXAMINATION: Blood pressure: 135 systolic; 80 diastolic. Weight 130½ pounds; height, 66.5 inches. She is an exceptionally well developed woman and seems to have enjoyed perfect general health up to the present illness. No abnormalities were found on physical examination. She states that when she was infested by hookworm on June 23, she was perfectly well and weighed 142 pounds.

PRESENT ILLNESS: She went with the family of M. C. de W. (Case III), her niece, to Luquillo on June 1, 1932, and after the bath on June 23, just as in Case I, she emerged from the water with an intense general pruritus which lasted all of six weeks and gave her many a sleepless night. It is of importance to emphasize, however, that she remained in the water with the others for only an hour or an hour and a half on the afternoon of the 23rd of June; hence her exposure was not so great as theirs. In this case wheals developed on the skin, and from her description at first it was thought that she was depicting lesions similar to Kirby-Smith's creeping eruption, but later questioning left it less probable. In two or three days the same throat symptoms as described for the others developed, but no bronchitis. She described these symptoms as something very much unlike a "cold". She seemed to have had some accumulation of thick mucus which could not be dislodged and which bothered her considerably. In fact, not only was it an annoyance, but there was actual pain in the throat. Pain in the epigastrium and diarrhea were severe and began on July 18, lasting 15 days, but no blood was ever seen in the feces.

COURSE OF THE DISEASE: At the outset 3,100 hookworm ova per gram of feces were found. All of the excrement for 24-hour periods was collected in glass fruit jars on the day and the subsequent two or three days following the anthelmintic and promptly transported to the laboratory of the Doctors Payne.

On the 12th of September, the patient was given 2 cc. of carbon tetrachloride, and on that day, 9 worms were expelled, all ancylostomes, save one, a *Necator americanus*. On September 13, 18, and 19, no worms were eliminated. On September 21, she was given 2 g. of hexylresorcinol and one worm was expelled. On April 29, 1933, 1.5 cc. of carbon tetrachloride was given and 10 worms were expelled. On the 30th no worms were eliminated, but on May 1, one more came away, a total for this case of 21 worms.

There is little doubt that this represents only a tithe of the larvae which originally invaded this patient, and that she was suffering almost entirely from the larval, not the adult phase of uncinariasis.

THE BLOOD: That the above is true is readily seen from an analysis of the blood charts. All that has been said for the hemoglobin and red cells in Cases III, IV and V, is applicable to this one. The Price-Jones curve seems normal. The white cell count reveals a far less degree of infestation than the other cases. There was a leucocytosis of from 12,000 to 19,000 for September, and thenceforward, a high normal. The eosinophilia is more eloquent, vibrating between 25 per cent and 45 per cent during that month, and the first half of October. On the 22nd of October it rose abruptly to 62 per cent, immediately falling to 32 per cent. Henceforth it fell very gradually to 6 per cent on the 21st of June, 1933. Note especially the sudden rise in eosinophilia on the 22nd of October, nearly four months after the first invasion of the larvae.

TREATMENT: Aside from details given, this patient received 8 g. of iron daily throughout September and October.

RESULTS: This patient has become distinctly worse as far as weight is concerned, having lost, as per weight of June 21, 1933, 5¾ pounds, but states she feels better, although still thin and weak.

CASE VI (B. T.)

Date	Males	Females	Unidentified	Total	Egg Count per GC	Remarks
9/1/32					31	
9/5					31	
9/12/13	5	4	0	9		Carbon tetrachloride 2 cc. (One adult female *N. americanus*)
9/21	0	1	0	1		*N. americanus* (just a shell) Hexylresorcinol 2 g.
				10		
9/29					9	
10/26						Negative for *S. mansoni*)
11/2					52	
11/23					13	(a check count–11)
1/10/33					18	
1/11					30	
1/12					23	
1/13					19	
4/28					7	
4/29	10	0	0	10		Carbon tetrachloride 1.5 cc.
5/1	0	1	0	1		
				11		

CASE VII

R. W., female, white, 12 years of age, student, Puerto Rican. Was never in hospital. An office patient of Dr. Ashford's, admitted September 2, 1932.

CHIEF FEATURE OF ILLNESS: Pain in the epigastrium and diarrhea. Loss of weight, color and strength.

PRESENT ILLNESS: She went to Luquillo with the family on June 1, 1932, and bathed in the sea daily but had no itching thereafter. On June 19th, it was raining, but not enough to overflow the dirty stream. She stated that she dug with her hands a little channel in the sand for the water to flow into the sea. No eruption occurred on the hands, nor did she afterward feel any itching. From the 19th to the 24th, inclusive, she took no baths in the sea, but on the 25th she began bathing there again and kept it up until June 30th. After none of these baths was there itching on the body. But on the 25th of June she had a sore throat which lasted but one day. She never saw blood in her feces, but after returning to her home in Río Piedras she began to have pains in the pit of the stomach and diarrhea, as well as loss of weight, color and strength. The diarrhea was watery but not black, and there was no tenesmus.

PHYSICAL EXAMINATION: This disclosed nothing of importance. Her weight was 89 pounds.

COURSE OF DISEASE: She was given 1.5 cc. of carbon tetrachloride on September 7, 600 ova of hookworm per gram of feces having been found, but no worms were expelled. On September 17th, she was given 1.4 g. of hexylresorcinol, and 3 ancylostomes were expelled. On the next day another worm was expelled. No more anthelmintic treatment was given this child until April 29, 1933, when 1.2 cc. of carbon tetrachloride was administered, and three more worms expelled. It is of significance that previous to this dose only 200 ova per gram of feces were found. Thus the total number of worms expelled was 7.

THE BLOOD: The curve of the hemoglobin and red cells was very like that of her mother, Case III, as well as Cases IV, V, and VI. The Price-Jones curve was practically normal. The interest in this case lies almost entirely in the remarkable changes found in the leucocytes. Here we are treating with an almost pure larval stage of uncinariasis. No matter what day it was that she received her infestation, there is little doubt but that there was a heavy invasion of larvae. It has been the experience of the Puerto Rico Anemia Commission that some very heavy invasions of the skin have taken place without the slightest indication of cutaneous irritation. This is undoubtedly a case in point, for only a heavy invasion could explain the unprecedented leucocytosis and eosinophilia.

Throughout September and the first part of October we have a fall from a level of 37,000 to 45,000 leucocytes per cmm. to a level undulating clear to the end of the case between 12,000 and 9,000. The eosinophilia began with 69 per cent and rose by the 19th of September gradually to 91 per cent. It fell as gradually to 67 per cent on the 1st of October, rising again on the 22nd to 81 per cent. From here on, there was a fall to 15 per cent, with a peak in November of 68 per cent, and another in March, 1933, of 50 per cent. It is also of great importance to point out that these eosinophilic values took place after three months from the time of invasion.

TEMPERATURE: No chart was kept of this child's temperature, but she states very positively that in the first two or three months after these baths she is sure that she had fever at times.

THE DIGESTIVE SYSTEM: She had diarrhea, as did the others, and it seems to have been severe, but it was watery, never contained a trace of blood, and there was never any tenesmus.

RESULTS OF TREATMENT: This child has gained only 5 pounds in weight under treatment, and she is not much better in appearance, but like Case VI, she states that she feels much better, and of course her diarrhea and fever have disappeared. A large part of her emaciation and nervousness is due to her passion for overstudy and there is a true functional indigestion. She also has taken full doses of iron, 8 g. daily, for at least three months, but, without the slightest effect in raising the depressed values of the hemoglobin.

CASE VII (R. W.)

Date	Males	Females	Unidentified	Total	Egg Count per CC	Remarks
9/5/32	.....	.....	.....	.....	6	(Constipated)
9/6	.....	.....	.....	.....	4	(Mushy)
9/7	.....	.....	.....	.....	6	(Constipated) Carbon tetrachloride 1.5 cc.
9/8/9	0	0	0	0	.....	(Large hard mass)
9/10	0	0	0	0	.....	(Small and mushy)
9/11	0	0	0	0	.....	(Constipated)
9/17/18	2	1	0	3	.....	(Female is *A. duodenale*.) Hexylresocinol 1.4 g.
9/19/20	0	1	0	1	.....	
	2	2	0	4		
9/26	.....	.....	.....	.....	1	
9/30	.....	.....	.....	.....	4	
10/26	.....	.....	.....	.....	.....	Negative for *S. mansoni*
11/2	.....	.....	.....	.....	7	
11/23	.....	.....	.....	.....	6	
1/9/33	.....	.....	.....	.....	1	
4/28	.....	.....	.....	.....	2	
4/29	3	0	0	3	3	Carbon tetrachloride 1.2 cc.

CASE VIII

This case is offered by way of contrast, and in it we have an example of the usual type of victims of uncinariasis. His multiple infestations have occurred through the bare feet,

and have been insufficient to attract his attention on account of the small number of skin lesions, and possibly also on account of a certain tissue immunity to the irritating toxin presumably developed by the larvae. Nevertheless, this is a case, not so much of uncinariasis, as of malnutrition and protein in starvation. His declaration of a diet including a pound and a half of meat a week, eggs and milk, cannot be taken literally, but may be taken to be the dietary "highlights" of his existence, effacing the remembrance of days of nutritional unbalance. Hence, the infestation by the hookworm was just another straw to break the camel's back, and varied greatly in its character from the previously cited infestations, which fell on persons in good health, well-fed, and without any reason for anemia.

D. R. male, white, 44 years of age, single, Puerto Rican, peddler, formerly agricultural laborer who has lived in the mountains near Humacao all his life. Admitted to the University Hospital June 25, 1932; discharged August 13, 1932.

CHIEF FEATURES OF ILLNESS: Extreme pallor; asthenia and dyspnea. Chronic ulcer of the left leg. Pain and difficulty in urination; hematuria.

PRESENT ILLNESS: For the past year he has become paler and weaker, has suffered from dyspnea on exertion, weakness, palpitation of the heart, and marked constipation. He has had occasional attacks of pain and difficulty in urination, with the passage of free blood, and four months previous to entering hospital an ulcer developed at the site of a slight injury to the left leg and refused to heal. The man presented a remarkable example of eunuchoidism. The genital system was greatly undeveloped, and the hair in the armpits and in the pubic region was scanty and atrophic. He had a passive, characterless face. The flesh was flabby, and the skin wrinkled and dry. He had that curious mental submissiveness that shows in men of this type, and agreed with everyone, always seeking to avoid trouble. Day after day he lay inert in his bed, without vouchsafing any remark to anyone. His voice was feminine, high-pitched and querulous, and "broke" in speaking. With all of these psychic peculiarities he had the physical stigmata of the sexually undeveloped.

PHYSICAL EXAMINATION: Aside from being rather poorly nourished, very pale, delicately built, and mentally weak, there were certain physical findings of importance in this case. There was no apparent pain nor restlessness, cough, nor expectoration. The head was rough-hewn in contour, and he was very slow-witted. He had advanced pyorrhea. The hair was dry and thin, and he had no indications of a beard or moustache. The eyes were shifty and suspicious, and there was a general attitude of evasiveness about the man.

On June 26, 1932, this patient weighed 108.5 pounds. The bony framework was delicate, the upper extremities were disproportionately long to the trunk, and from the *symphysis pubis* to the corona of the head was 280 cm.; from the *symphysis pubis* to the floor was 294 cm. The skin was dry, and there was extreme pallor with a muddy tinge and a slight degree of edemic infiltration of

the face, especially around the eyes whose conjunctivae were dead white. His nose was strongly deviated to the right side, but the tonsils were normal. The thorax was symmetrical, and there was normal expansion. The lungs were apparently clear. The heart seemed somewhat small, and the first sound was weak, as, for that matter, was the second sound. The abdomen was negative. The ulcer on the leg was very shallow, quite superficial, about 1.5 inch in diameter, and boat-shaped. The floor was covered with moderately coarse granulations, which, in turn, were overlaid with a filmy sero-purulent exudate. It was not indurated and only slightly tender. The surrounding skin was bluish-white, but the local circulation was poor, and a constant attempt at epithelialization always fell short of accomplishment. Strangely enough, the reflexes were normal.

Laboratory Data: Roentgenology; An X-ray study of the stomach and duodenum failed to reveal any evidence of neoplastic or ulcerated processes and seemed normal. The stomach emptied well; for five and a half hours after the meal only a few mucous folds appeared coated with barium. This patient presented a marked aerocolia, especially at the flexures of the colon.

On July 22, 1932, roentgenological findings for the leg affected by the ulcer were reported as follows: "films of the middle third of the left tibia and fibula in the supine and lateral positions demonstrated periosteal thickening. The fibula presented fibrous tissue suggestive of an old healed osteomyelitis."

Urinalysis (June 27, 1932); color, pale yellow; appearance, turbid; reaction, acid. Specific gravity, 1006. Albumen, none, sugar, none. Sediment, a few uric acid crystals, but no casts.

Feces (June 27, 1932): 9,100 ova of hookworm per gram; 900 ova of *Trichiurus trichiura* per gram. There were numerous cysts of *Entameba coli*.

Serology: Kahn's tests for syphilis 000. Fractional gastric analysis (June 28, 1932):

Specimen	R	1/4	1/2	3/4	1	1 1/4	1 1/2
Total acid	7°	7°	16°	20°	13°	8°	8°
Free acid	0°	0°	5°	7°	5°	0°	0°

One cc. of histamine solution was used for the second examination, July 21, 1932.

Specimen	R	1/4	1/2	3/4	1	1 1/4	1 1/2
Total acid	15°	62°	72°	56°	42°	22°	0
Free acid	0°	42°	56°	46°	22°	22°	0

Evidently there was, therefore, either a functional inertia of the gastric secretion or a regurgitation of the duodenal contents on the occasion of the first gastric analysis performed without histamine.

In this case a careful examination of the blood was first made on June 28, 1932, with the following results: Hemoglobin 10 per cent; red cells, 1,600,000;

leucocytes, 4,900. Differential count of leucocytes: polymorphonuclear leucocytes, 50 per cent; lymphocytes, 22 per cent; monocytes, 2 per cent; eosinophils, 26 per cent.

Orders were now given to refrain from administering any of the anthelmintics used in uncinariasis, to have a specimen of feces sent to the parasitological laboratory in order to determine the number of ova per gram, and to put this man on the Ashford diet for sprue. This diet contains a pound of rare broiled steak a day, without grease, and fresh green vegetables and fruits. All cereals and added sugar, as well as lard, butter, or oil were strictly prohibited. Four cc. of a 50-per-cent aqueous solution of iron and ammonium citrate were ordered three times a day with orange juice. Finally, 4 cc. of liver extract was ordered and injected daily into the buttock. Thus, not only were the dietary deficiencies abruptly terminated, but the presumptive failure of iron for the manufacture of hemoglobin, and the possible failure of the stomach to provide the pre-ferment for the supply of the hormone stimulating the megaloblasts in the bone marrow were also taken care of. In evidence of the necessity for liver extract, it is only necessary for us to contemplate the blood examination made on July 3. While this was clearly a case of secondary anemia, still it was just on the verge of becoming an anemia of pernicious type, as the average diameter of red cells was 8.526 microns. On the basis of the macrocytosis it was certainly legitimate to give liver extract. It will be noted that no reticulocytes were found on this day.

Blood record (July 3, 1932); hemoglobin 20 per cent; red cells, 1,312,000; leucocytes, 7,100. Average diameter of red cells 8.526 microns. Reticulocytes, none. Differential count of leucocytes: polymorphonuclear leucocytes 53 per cent; lymphocytes 11 per cent; monocytes 5 per cent; eosinophils 30 per cent.

On July 6, there was a feeble reticulocytosis of 11 per cent, a little too soon for a response from liver extract, and probably due to a combination of the iron and high protein diet.

The general improvement in this man was startling. From day to day his color mounted, his strength returned, and his mentality became sharper, until on July 15, the blood revealed the following: hemoglobin 56 per cent; red cells, 4,496,000; leucocytes, 11,200. There was an average mean diameter of erythrocytes of 8.02 microns. Thus in twelve days this man had made the almost unbelievable advance in blood values of 70 per cent in erythrocytes and 36 per cent in hemoglobin, all due to a remedy for his nutritional deficiencies. Thus, fully nine-tenths of this patient's anemia and perhaps no less a proportion of the rest of the symptoms forming the clinical picture seemed alone due to nutritional unbalance.

On August 8, all of the treatment being sustained as first ordered, the blood was again examined with the following results: hemoglobin 63 per cent; red cells, 4,512,000; leucocytes, 13,200. Differential count of leucocytes: Polymorphonuclear leucocytes, 40 per cent, lymphocytes, 22 per cent; monocytes, 6 per cent; eosinophils, 32 per cent. The mean diameter of the red cells was 7.588 microns.

Now that the nature of his anemia had been explained, we were ready to expel the hookworm, which, by the way, turned out to be *Necator americanus*. On the 9th of August 2 cc. of carbon tetrachloride and 1 cc. of the oil of chenopodium were ordered and instructions given for all feces to be sent at the end of every twenty-four hours to the laboratory of the Drs. Payne for the counting

of the worms. It is of interest to note that previous to this 55,500 ova per gram of feces were found. Unfortunately, these orders were not understood in the laboratory, and instead of counting the worms in the twenty-four-hour feces on the date the anthelmintic was given, only the ova were estimated. But on the 10th (the next day), 106 females and 111 males, and on the 11th, 24 females and 27 males were counted, a total of 268 worms actually enumerated. But it is perfectly evident that at least as many more worms were expelled on that first day and lost by accident. It is certainly believed to be conservative to calculate a worm burden for this man of 500.

This case is not cited for the purpose of depreciating the role of the hookworm in producing anemia in uncinariasis, but it is merely cited on the one hand, in order to show that an intense anemia, even in the presence of many worms, is not always due alone to the hookworm. On the other hand, it brings out once more that blood-sucking and hemorrhage from wounds caused by the worms in the intestine, while they nearly cost the life from hemorrhage of at least one of the seven preceding cases when these worms were immature and actively changing their feeding-ground in the intestine, in old chronic cases, where the worms are mature and lie with their heads quietly buried in the mucosa, they probably do not ordinarily cause enough hemorrhage to account for all of the anemia present.

SUMMARY

A group infestation of seven cases of acute uncinariasis is cited in detail, showing the following unusual characteristics:

1. The symptoms were sudden, acute, and all contracted within two days and in the same manner.

2. The patients belong to the well-fed, well-to-do class.

3. The infestation was contracted during sea-bathing, the sea being polluted from a rain-swollen, over-flowing stream.

Diagnosis of uncinariasis is made.

This group is subdivided into two classes: first, those cases in which enough larvae have completed their cycle to set up severe hemorrhage through their bites and blood-sucking in the intestinal canal; and second, those cases in which only a small percentage of larvae have been able to reach the intestine, the rest remaining as a wandering or arrested group in the tissues.

Case I, belonging to the first group and acutely ill to the

condition of collapse with syncope, is described in detail, special emphasis being laid on the treatment employed.

The remaining six cases are detailed for comparison, a felicitous termination to each case being noted.

An eighth case of typical, chronic uncinariasis (unrelated to the seven preceding cases), is recounted by way of contrast —the victim being an agricultural laborer, afflicted for an extensive period, and unaware of his condition.

CONCLUSIONS

The value of these cases is in the fact that their origin lies in acute infestation which can in no way be confused with underlying basic nutritional unbalance.

Marked throat discomfort in the form of a sensation of obstruction would seem to be definite indication of an acute uncinariasis, in conjunction with other symptoms.

There is no doubt that, on the evidence of these seven cases, acute uncinariasis is marked by fever, leucocytosis, and eosinophilia, possibly caused by a foreign protein set free by the death and disintegration of wandering larvae. This same condition may be the chief cause of the accompanying diarrhea.

When continued, ill-defined, secondary anemia with few intestinal worms is found, and the condition does not abate with the use of iron and appropriate food, the serious larval phase of the disease may be considered.

No adequate remedy has yet been found for the larval stage of this disease.

REFERENCES

1. Ashford, B. K. and Gutiérrez Igaravídez, P. Uncinariasis in Porto Rico. A medical and economic problem. Senate Document 808. Washington, Gov. Printing Office, 1911.
2. Calmette, A. and Breton, M. L'Ankylostomiase. 8vo. Masson et Cie. Paris. 1905.
3. Leichtenstern, O. Einiges Über *Ankylostoma duodenale*. Deutsche Med. Wchnschr. **13**: 565, 594, 620, 645, 669, 691, 712. 1887.
4. De Langen, C. D. Anguillulosis and syndrome of the "Ideopathic Hypereosinophilia". Mededeel. van d. Dienst d. Volksgezondheid in Nederl. Indie. **17**: 515–529. 1928.
5. Faust, E. C. Gentian Violet Therapy for Strongyloides Infection. Editorial Internat. M. Digest **17**: 57–58. 1930.