The Milroy lectures : on ankylostoma infection, delivered before the Royal College of Physicians of London on March 2, 7, and 9, 1911 / by A.E. Boycott.

With the authors compliments

Note for new cat

The Milroy Lectures

ON

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BY

A. E. BOYCOTT, M.A., D.M. Oxon.

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ANKYLOSTOMA INFECTION.

LECTURE I.

Delivered on March 2nd.

MR. PRESIDENT AND GENTLEMEN,—Taking the world as a whole, with the possible exception of the malarial organisms, ankylostoma is, I suppose, responsible for more unhappiness and inefficiency than any other parasite, and, for the most part indirectly, for no inconsiderable number of deaths. Practically all tropical countries are permeated with the worm, and in places where the conditions for its propagation are not unfavourable it may reduce four-fifths of the population to a continual state of chronic ill-health which is only terminated by their premature decease, commonly from some secondary affection. Under circumstances where the prevailing conditions are more or less inhibitory, though most people may be infected, yet in relatively few is the dose of parasite so big or the resistance of the host so small that any demonstrable illness is produced. An individual in whose bowels ankylostoma is living and whose tisssues are shown to be reacting to its presence by changes in the bone marrow, may be said to be infected with ankylostoma in the true sense. But if there are no subjective or objective signs of illness one cannot reasonably say that he is suffering from the disease ankylostomiasis. It is necessary, therefore, to distinguish between cases of ankylostoma infection without illness and cases of ankylostomiasis as sharply as the fact that the one must grade imperceptibly into the other will allow; and to recognise that the latter comprise a variable, and often very small, proportion of the total number of infected individuals.

From the point of view of preventive medicine the worm

carrier, owing to his mobility and the fact that his appearance and habits excite no apprehension, is in many ways a more important person than the sick man who is laid by the heels with his anæmia and dyspnœa. I have, therefore, taken "Ankylostoma Infection" as the title of these lectures rather than "ankylostomiasis," and by the latter term I shall refer only to illness due to ankylostoma. We have, unfortunately, no convenient terminology in current use denoting the distinction between "Wurmträger" and "Wurmkranken," "ankylostomés" and "ankylostomiasiques."

In this country ankylostoma is restricted to a very small area—the underground workings of the metalliferous mines in Cornwall; and the persons exposed to infection number in all only some 6000. There is no clear record that any death there has been due to uncomplicated ankylostomiasis. It may therefore well seem presumptuous on my part, whose only personal experience of the parasite has been in Cornwall, to attempt to deal with an infection which, as I have already indicated, attains dimensions of massive importance in the tropics. As a matter of fact, however, the segregation of the saprophytic phase of the parasite to a special and restricted area, and the fact that only a limited proportion of the population is exposed to the possibility of infection, afford opportunities for the study of many of the questions involved which cannot be obtained where infection is intensive and generally disseminated both on the earth and in the people. In the tin-mines of Cornwall, and the coal-mines of Northern France, Belgium, and Westphalia, ankylostoma is confined to subterranean workings, and only those who work in mines run the risk of being infected. The surface in the neighbourhood is, *quâ* ankylostoma, sterile, and the general population live free from infection. In most respects these are the ideal conditions which one would desire to lay down in any experimental inquiry into an epidemic infection; they are seldom realised so satisfactorily in the natural history of disease.

In reference to the personal observations which we have made in Cornwall and in connexion with Cornish cases of ankylostoma infection [1] it should be understood, though their names are not always mentioned, that whatever of interest has come out of these inquiries is mostly due to Dr. J. S. Haldane, reader in physiology in the University of Oxford, and Mr. R. A. Thomas, manager of Dolcoath Mine. To a somewhat less, but by no means small degree, these investigations have been assisted also by Dr. S. G. Scott and Professor J. Cadman.

[1] The literature will be found in the Journal of Hygiene, vol. iii. (1903), p. 95; vol. iv. (1904), pp. 73, 437; vol. v. (1905), p. 280; and vol. ix. (1909), p. 264. And in Parliamentary Papers, Cd. 1318, 1902; 1843, 1903; 2066, 1904; 2091, 1904; 4820, 1909.

The Life-history of Ankylostoma.

The life-history of ankylostoma seems to be now satisfactorily established. The adult worms, male and female, live in the small intestine of man. They eat away at the mucous membrane to which they are attached, with their heads buried more or less deeply into the mucosa and sometimes the submucous tissue. The eggs are laid here in prodigious numbers, and pass out of the human body to begin the saprophytic stage of their existence in the stools. As seen in the ordinary sample of fresh fæces which has been outside the body for several hours, the eggs have generally divided once or twice, so that two or four cells are visible within the transparent shell; unsegmented eggs are not uncommon. Under favourable circumstances development proceeds rapidly through a morula stage to a little worm which hatches out in one or two days; if conditions are unsuitable this period may be prolonged to a week or ten days or even several weeks. The larval worm, after escaping from the eggs, continues its rapid development, moults three or four times,[2] and in four to ten days, according to circumstances, reaches a definite stage—the full grown larva. At this point it is an individual, without any sexual differentiation, about 0·6 mm. long, and is provided with a stout chitinous[3] sheath, inside which it can move about pretty freely. Hence the term "encapsuled larva." Unless it has an opportunity of becoming parasitic no further growth takes place and the full grown larva will continue its saprophytic phase without any further alteration for at least many months. If, on the other hand, it gains entrance to the human body, further progress is made, sexual differentiation becomes manifest, and in about six or seven weeks the adult worm is living in the small intestine.

In the life-history of all parasites it is important to know at what stage or stages multiplication of individuals takes place, and especially whether any increase occurs during any saprophytic phase. For it is clear that it is better worth while to plan one's attack, if any direct attack is desirable, upon the multiplying rather than upon the resting stage. In the case of ankylostoma there is, I think, no doubt that there is no multiplication except during the parasitic phase. The view—first propounded by Giles in his admirable study of kala-azar, and subsequently supported from time to time by

[2] I do not suppose the number of moults is indefinite or immaterial, but I do not know exactly how many there are. My own observations indicate at least three.

[3] The hard parts of the skin of such animals are commonly described as "chitinous," but not necessarily in all cases in any more precise sense than that in which strong soap solutions or silicic acid are called "gelatinous." Bondouy (Archives de Parasitologie, vol. xiv. (1910), p. 1), at any rate, has shown that the skin of the horse strongyle (*Sclerostoma equinum*) does not consist of chitin—i.e., does not yield glucosamin on decomposition.

various other observers—that ankylostoma larvæ may become sexually mature, and reproduce themselves outside the body, seems to be founded on erroneous observations. Those who have supported the theory of heterogenesis have not sufficiently appreciated the extraordinary prevalence of small nematode worms throughout nature, not parasitic—as far, at any rate, as the higher mammals are concerned, though some of them appear to have important pathogenic relations to plants. Many of them have larvæ which are indistinguishable from those of ankylostoma, especially when in their earlier stages, and on superficial examination their eggs are very similar, though, as far as my experience goes, generally distinguishable on careful comparison. Such nematodes may be found anywhere; they are particularly abundant in fæces which have been lying on the ground in hot moist places, such as mines, where ankylostoma is prevalent. In examining such fæces immediately after collection, and from time to time after subsequent incubation, sexual forms, and then a fresh generation of eggs and larvæ, will often be found; this occurrence is liable to be the more misleading if the fæces are derived from a person infected with ankylostoma, and are found to contain eggs and larvæ which resemble, and in many cases doubtless really are, those of the human parasite.

I have made many attempts to observe the development of sexual forms in cultures of fæces from infected persons, taking care not to introduce any obvious source of contamination, such as earth or the like, and keeping the cultures under aerobic and anaerobic conditions, and with various food materials in different amounts, but in every case without success. The admixture of a little garden earth will often result in the appearance of worms which proceed to become sexual and multiply. Even if occasionally sexual reproduction were observed in fæces which had been effectually protected from contamination, as Ozzard[4] and others appear to have done, I confess that I should interpret the phenomenon as being due to the person having swallowed the eggs of some of the free-living nematodes. Considering the degree to which these animals infest all nature, it seems likely that man must from time to time ingest them or their eggs in fair numbers. Leiper[5] has lately recorded a remarkable instance in which these deceptive little worms appeared in an old laboratory jar.

Apart from the question of heterogenesis, these considerations indicate that one must be extremely cautious in identifying any nematode larvæ which may be found loose in the world as being those of ankylostoma; one cannot, for instance, obtain any evidence as to the infectivity of a place by observations on the prevalence of such larvæ. The

[4] Brit. Med. Jour., vol. ii., 1909, p 779.
[5] Ibid., vol. ii., 1909, p. 1332.

only test that I know of which will help to identify ankylostoma larvæ from others which are morphologically closely similar is to keep them under observation and see that no sexual differentiation occurs.

The nematode *Strongyloides intestinalis* is often found along with ankylostoma; one or two cases were seen in Cornwall. The eggs of the sexual parasitic generation (*Anguillula intestinalis*) hatch inside the body and pass out in the fæces as larvæ, which give rise to a sexual saprophytic generation (*A. stercoralis*). It is possible that this has been sometimes mistaken for a sexual saprophytic phase of ankylostoma.

Modes of Infection.

Up to 1898 it had always been assumed that the only path of entrance of ankylostoma in the human body was the mouth and alimentary canal. Looss,[6] however, then suggested that infection might take place through the skin, afterwards showing that larvæ could penetrate human skin, producing a local reaction, and that men and dogs could acquire the disease by the cutaneous route. Experiments made on man by C. A. Smith, Pieri, Herman, Bruns, Tenholt, and others confirmed these observations. Personally I produced an infection in Professor J. B. Leathes by applying a few full-grown larvæ to the skin of his forearm for a couple of hours. There were a slight local reaction and some itching. As he wrote to me, "*σκωληκόβρωτος ἐγιγνόμην*," but in the sequel he did better than Herod, and had no symptoms of illness, though definite signs of infection in the form of an increase of eosinophile leucocytes appeared four weeks later; eggs were found in the stools after 50 days. This experiment is, I think, particularly conclusive, since Leathes was at the time working in a chemical laboratory in London, and had never been exposed to any possibility of natural infection. The larvæ used for the experiment were a single batch bred for the purpose from infected fæces in another part of the building with which Leathes had no contact. In the building itself no other ankylostoma material had ever been dealt with.

Of the possibility of larvæ passing through the skin, and ultimately reaching the bowel, there is therefore no doubt. There are also reasons to believe that this is, in nature, by far the most important method of infection. The local reaction due to the larvæ themselves is variable, erythema and urticaria, sometimes hardly perceptible, but though there may not be much to see there is generally a good deal of itching. Scratching and secondary infections from the dirt which accompanies the larvæ often result in the appear-

[6] See Zeitschrift für Klinische Medizin, Band lviii., 1906.

ance of furuncles, which are such as impress themselves on the subject's memory. Hence the "ground itch" or "coolie itch" of Assam, the "mazamorra" of Porto Rico, the "bunches" of Cornwall. The Cornish miners knew long ago that the agent which lived in Dalcoath Mine, and ultimately led to anæmia, was also the cause of their skin troubles; they were perfectly clear that "bunches" preceded shortness of breath and that the two had some etiological connexion, and produced cogent topographical evidence that one did not occur without the other. I am free to confess that for my own part, having failed to infect myself through the skin, I neglected their epidemiological evidence and was not very much interested in the long tales they had to tell of how they had scratched themselves all night after working in particular parts of the mine, and later on became short of breath. But they evidently knew more about it than I did, and I have often wondered since how many lessons the general consensus of popular opinion has to teach experimental parasitologists.

The obvious difficulties in the way of mouth infection with the stale remnants of human fæces raise the possibility of ingestion being able to give rise to an infection as widespread as that which obtains with ankylostoma under favourable circumstances, where 95 per cent. of the population may harbour the worm. There do not, however, seem to be any conclusive reasons for doubting the importance of mouth infection on this score. Infection with ascaris and trichocephalus certainly takes place by the mouth, since the eggs do not hatch outside the body. All Chinamen are said to have trichocephalus and 70 per cent. of the patients in Paris hospitals[7]; it occurs in as many as 8 per cent. of the random patients in Guy's Hospital,[8] a fact which shows that even in and about London people must swallow the remnants of human fæces more frequently than a consideration of their habits and sanitary circumstances would suggest. Ascaris is rare enough in this country, but occurs in half the agricultural population in Switzerland,[9] and freely in most tropical countries. Of Cornish tin-miners four-fifths have trichocephalus and a quarter ascaris, the frequency of infection with ankylostoma varying from 10 to 90 per cent.

It seems almost impossible that mouth infection among civilised persons should be so frequent, but the facts do not seem capable of any other interpretation. On the other hand, it seems unlikely that the severity of ankylostoma infection, and especially the frequency of reinfection, are compatible with the hypothesis that all the worms are swallowed as larvæ. There is no parallel in bacterial infections, since

[7] Chantemesse and Rodriguez: Bulletin de l'Académie de Médecine, vol. lix., 1908, p. 407.

[8] Journal of Hygiene, vol. v., 1905, p. 274.

[9] Galli Valerio: Centralblatt für Bakteriologie, Orig., Band xliv., 1907, p. 531.

these can multiply in the body, whereas one ankylostoma larva cannot, if swallowed, give rise to more than one adult worm in the intestines. Most infections with trichocephalus and ascaris seen in this country are slight; but, as in hot countries where the segregation of fæces is imperfect, in Cornish miners some very heavy infections are seen.

In Cornwall, in Porto Rico, and in other places where inquiry has been made, with Egypt as a marked exception, nearly all cases of ankylostoma infection give a history of a skin eruption, characteristically associated with excessive itching in its early stages and often occurring in repeated attacks. Those who fail to recollect any such incident cannot be considered as necessarily examples of mouth infection, since it is known experimentally that the local changes at the point of entrance may be very slight, especially if secondary infections are avoided. But though the skin is doubtless the usual and the important path of entry, there are no reasons for doubting the possibility of mouth infection. Leichtenstern showed that infection follows after swallowing adult larvæ, and I was myself infected in this way through an accident with a pipette. The work of Looss on dogs and of Schaudinn on monkeys has shown that larvæ penetrating the skin get into the veins and ultimately lodge in the lungs, whence they pass up the trachea and down the œsophagus to their definitive home. Some such sojourn in the tissues may be necessary for development; if so, it may be presumed that larvæ which are swallowed escape from the upper part of the alimentary canal and then go through much the same course as those which enter through the skin. But at present there is no evidence showing that this is the case, and that larvæ when swallowed do not go on straight into the bowel.

Experimental skin infection is not always successful. Pieri, Grassi, and Galli-Valerio, for example, had several failures. I tried repeatedly to infect myself in this way, but with no success, using both cultures containing many adult larvæ and infected fæces obtained in Dolcoath Mine.

Ankylostoma can only gain an effective entrance to the human body in the stage of the full-grown larvæ. Eggs or young larvæ are not infective when swallowed, nor can they pass through the skin. The full-grown larva, with its protective capsule, develops a perfect passion for going through small holes. If water containing such larvæ is filtered through ordinary filter-paper most of them are found in the filtrate. I do not think anyone has ever determined what happens if adult worms are swallowed. Their fate is of no practical importance. The fact that eggs and young larvæ are not infective is, however, most significant, since it means that the fæces of an infected person do not become infective till after the lapse of at least four days, and an individual cannot re-infect himself by immediate contamination as appears to occur with oxyuris.

Duration of Infectivity.

The time-relations of the various stages of development require some notice. From the fresh egg to the full-grown larva may take as little as four days or as long as a couple of months, according to circumstances, the chief factor being temperature. The full-grown encapsuled larva has a moderate natural death-rate when kept under artificial conditions in the laboratory, but out of a good brew a great many are alive at the end of 12 or 15 months, as Looss, Oliver,[10] and I have found, and I daresay would survive a good deal longer. It is a fair assumption that in nature they may live two or three years. This is the less remarkable when we consider that they do not grow or reproduce themselves, and hence have a low metabolism and require very little food. From the time when adult larvæ get into the body till eggs can be found in the stool varies between six and ten weeks,[11] and seems to be the same whether the larvæ are swallowed or get in through the skin. Lambinet[12] showed with dogs that the period was the same whether the larvæ of the dog ankylostoma (*A. caninum*) were applied to the skin, injected subcutaneously, or swallowed.

The duration of life of the adult worm is, no doubt, liable to much variation. In countries infested with the disease opportunities for reinfection are so numerous that it is difficult to obtain satisfactory data. It must also be remembered that recovery from ankylostomiasis by no means necessarily means that the individual is no longer infected. In Cornwall circumstances are better arranged, for there is no chance of reinfection unless the underground workings of the mines are visited. A good many men, after becoming ill with the disease, have abandoned mining altogether. In three such cases we found eggs in the fæces six, four, and four years respectively after the last possible exposure to infection; two of the men were quite well, one was still anæmic. In a good many cases the worms die out in a year or two, or, at any rate, become so few in number that ordinary routine examination fails to find any eggs in the fæces. The recent observations of Bruns, to which I shall refer later, show that the difficulties of accurate diagnosis under these circumstances are considerable. Stiles[13] examined children in the Charleston Orphan Asylum, where infection could almost certainly be excluded, and found that three were still infected after six years' residence. Ashford,[14]

[10] The Lancet, vol. i., 1910, p. 356.

[11] Looss, 71 days; Pieri, 70 days; Smith, 45 days; Bruns, 46 and 53 days; Boycott, 50 and 55 days.

[12] Bulletin de l'Académie Royale de Médecine de Belgique, Jan. 28th, 1905.

[13] Public Health and Marine Hospital Service, U.S.A., Bulletin 10, 1903, p. 58.

[14] Anæmia in Porto Rico, 1904, p. 51.

Porto Rico, in a similar institution found, among 45 girls, four who were infected after four years.

Taking the whole saprophytic and parasitic cycle together, the time from the first infection of one individual to the establishment of an infection derived from him in a second person may vary from seven weeks to at least six years. The recipient of infection does not himself become infective for about seven weeks. An infected place may become infective four days after eggs have been deposited there, and may remain infective for at least a year.

The Two Causative Organisms.

From the parasitological point of view, the specificity of the causative organism constitutes an integral part of the conception of the individuality of an infective disease ; the medical mind pays attention rather to the congeries of symptoms ; while to the epidemiological sense the circumstances which condition prevalence in place and time more particularly appeal. The classification and nomenclature of diseases must necessarily vary with the particular trend of the systematist concerned ; the real difficulty obviously begins when a compromise has to be made between the different principles which I have indicated without diverting an undue amount of time and trouble into the barren fields of terminology. With complete knowledge the parasitologist, the physician, and the epidemiologist will, no doubt, all find their lines of thought in harmony, but meanwhile one has to recognise that there is some inconsistency in having one disease, ankylostomiasis, which may be caused by either or both of two parasites which are specifically or, as some would have it, even generically distinct. In 1902 Ashford and Stiles showed that most of the ankylostomiasis in the southern regions of the United States and in Porto Rico was not due to *Ankylostoma duodenale*, but to a hitherto unrecognised species, *Ankylostoma* (*Necator*, *Uncinaria*) *americanum*. *A. americanum* is distinct enough from *A. duodenale:* the worms themselves are smaller, the eggs rather longer and narrower, the mouth has no recurved hooks, and the genital armature of the male is different. Since its original discovery it has been found in all parts of the world. If sufficient search were made it is pretty certain that both species would be found everywhere that ankylostomiasis is prevalent. On general grounds one would surmise that in any given locality one of the two species is probably autochthonous, and that the other has been introduced. *A. americanum* has not been identified in Cornwall, probably because comparatively few adult worms have been collected for detailed examination. Where both species are abundant individuals are often doubly infected ; thus in Panama

Whipple,[15] in 273 necropsies, found 39 with *A. duodenale* alone, 49 with *A. americanum* alone, and 25 with both. As far as is known, there is no clinical variation in cases of ankylostomiasis which can be correlated with the causative species of parasite. It is possible that the extraordinary divergence of the experience of different observers on certain points—the presence and abundance of blood in the stools, the relative efficacy of various anthelmintics, and so on—would be explained by taking into consideration this question of species. So far, however, no one seems to have started from the point of view that duodenaliasis should be distinguished from americaniasis. The term uncinariasis which is in use in America was born of the zoological passion for antiquarian research; it does not signify a specific infection with *Uncinaria americana*, but is synonymous with ankylostomiasis. In passing, one can only express one's relief that no organised attempt has been made to apply the law of priority to the nomenclature of disease.

Both species are restricted to man and probably the higher apes; experimental infections have been achieved occasionally in monkeys, and, as far as the earlier stages are concerned, in dogs and guinea-pigs. Other animals have ankylostomes of their own; dogs, cattle, sheep, seals have each their own species, none of which are naturally infective for man. Other parasitic nematodes (strongyles), which are widely distributed in domestic and other animals, have eggs which on casual inspection resemble those of ankylostoma; hence the notion that man might contract the infection from horses, and the statement lately printed in a reputable journal that the human parasite occurs in hens and other domestic animals.[16]

The Symptoms of Ankylostoma Infection and Ankylostomiasis.

The skin symptoms associated with ankylostoma infection are of two kinds. 1. Resulting from the irritation caused by the larvæ penetrating the skin, there may be a local erythema or urticaria, varying greatly in severity in different cases, and often, from secondary infections, going on to pustules and furuncles. It may be that the organisms causing these secondary infections—in the cases I have examined they were staphylococci—are actually carried into the subcutaneous tissues on the larvæ; this is the less probable if, as is stated, the larvæ leave their outer skins behind them when they penetrate the hair follicles. 2. At any time after infection,

[15] American Journal of the Medical Sciences, vol. cxxxviii. (1909), p. 40.

[16] Journal of Tropical Medicine, vol. xii., 1909, p. 333.

sometimes months or years after the subject has been removed from any chance of a fresh invasion, attacks of generalised urticaria may occur, as with hydatids and *Filaria medinensis;* in other cases a general pruritus, without any local changes, causes a good deal of trouble

During the first few weeks after infection there may be a slight bronchial catarrh and trivial pains in the upper part of the abdomen which bear no relation to the taking of food. These symptoms are no doubt due to the worms passing through the lungs in the course of their development, and to the irritation which they cause when they first reach the bowel. Manouvriez, describing the anæmia of coal-miners in France in 1878 without any idea that it was a parasitic disease, draws attention to the regular occurrence of urticaria and boils, and notes that a bad attack is generally accompanied by bronchitis (*catarrhe des gourmes*). Leathes also noticed a slight catarrh soon after his experimental infection.

These symptoms in the skin, lungs, and bowels may be very slight and may easily escape notice, so that an infection may readily become established without attracting the recipient's attention. In a certain number of cases, however, the individual becomes anæmic, and the severe symptoms which constitute the disease ankylostomiasis supervene. Various writers have described symptoms in ankylostomiasis which are not due to the anæmia, but represent, in their opinion, a direct toxic action of some product of the worm on the economy. Siccardi [17] has recently strongly urged that some such explanation is required for the occurrence of nervous symptoms (easy cerebral and muscular fatigue, apathy, melancholia, amblyopia with a central scotoma) in infected persons who are not anæmic. As a rule, however, these symptoms are not prominent, and are overshadowed by the dyspnœa, dyspepsia, and general upset of all the organs of the body, which may reasonably be ascribed to the anæmia. That a toxic substance is absorbed into the body is, however, clearly shown by the occurrence of urticaria and by the almost constant response of the eosinophile leucocytes in the bone marrow.

The incidence of anæmia in infected persons appears to be determined by three factors—individual susceptibility, dose of infection, and frequency of infection. It is significant that the proportion of infected persons who are anæmic is in general parallel with the proportion of the whole population who are infected, especially in the sense that severe anæmia is seldom found unless the infection is very prevalent. Thus in Cornwall, in Dolcoath Mine, 95 per cent. of all underground hands were infected, and about 5 per cent. of those infected were ill to a material degree; in Grenville 15 per cent. and in Tincroft mine 10 per cent. were infected, and

[17] Archives de Parasitologie, vol. xiii., 1910, p. 555.

there was only a single case of illness in 800 men. In the Belgian coalfield 4 per cent. of the men are now infected, and cases of severe anæmia are unknown. In Porto Rico, on the other hand, where the whole agricultural population was infected, about half had less than 50 per cent. hæmoglobin, and suffered from a severe grade of the disease.

If, then, the prevalence of infection is slight, the incidence and severity of illness will be correspondingly low.[18] This relation does not necessarily hold for bacterial infection, where the infective agent can multiply inside the body. With ankylostoma this, of course, does not occur, and the evident connexion between prevalence and severity points clearly to the quantity of infection being an important factor in determining illness and correspondingly reduces the significance of individual susceptibility. Abundant contact with larvæ means, as a rule, that most people will be infected, that the proportion who receive large doses will be considerable, and that frequent reinfection will occur. It is difficult to separate the two last factors, for each reinfection swells the total number of worms in the body. There are, however, certain facts which indicate that the same total of worms will be more effective in causing anæmia if it be taken in divided doses rather than in a single massive infection.

It has been frequently observed—and in Cornwall the evidence is particularly clear—that if an anæmic person is removed from the infected place he often rapidly improves, and may recover completely without any specific treatment. Some natural decrease in the number of worms must go on, but at least as many may still remain when the anæmia has disappeared as are found in anæmic individuals who are constantly exposed to reinfection. This suggests that the maximum effect of infection is exerted soon after the worms reach the intestine, and that subsequently, as far as that particular batch is concerned, the host becomes relatively immune. Further, that frequent reinfection is a potent factor in producing the more severe grades of anæmia, apart from the contributions which are in this way made to the total mass of infection.

Of individual susceptibility we only know that some individuals do not become ill, though they harbour many worms and are exposed to infection and reinfection equally with very sick persons. As regards the supposed racial immunity of negroes, the exact observations of Ashford [19] suggest that the blacks, with an equal dose of worms, are as susceptible to anæmia as others, but that under the same circumstances of exposure they do not become so heavily infected. If the influence of variations in habits can be excluded, this indicates a resistance to infection rather than

[18] There are, of course, exceptions.
[19] Anæmia in Porto Rico, 1905, p. 10.

a resistance to the consequences, a relative immunity to the parasite and not to its poisons. There is, however, no definite evidence that anybody is definitely resistant to infection in the sense that ankylostoma will not live in him. With free exposure to larvæ, in only 2 to 5 per cent. of individuals is infection not discovered; this might easily be accounted for by defective diagnosis.

The Pathology of Ankylostoma Anæmia.[20]

The anæmia of ankylostomiasis may reach a very severe grade, cases with 15 to 30 per cent. hæmoglobin being common in heavily infected places.[21] Thus, of the 61 cases described in detail in the second report of the Porto Rico Commission, 46 had less than 30 per cent. and 18 less than 20 per cent. hæmoglobin. Estimations of the total quantity of hæmoglobin in the blood show, however, that the percentage content of hæmoglobin does not correspond to the actual deficiency, owing to a considerable increase in the plasma and the total volume of the blood. In the following table are given the results of determinations made by the carbon monoxide method[22] of Haldane

—	Hæmoglobin per cent.	Total hæmoglobin: grammes.*	Blood volume cubic centimetres.	Relative number of red cells in whole blood.
Normal	100	400	3000	100
Ankylostoma No. 1 ...	44	311	5160	102
,, No. 2 ...	47 41	357 331	5520 5880	106
,, No. 3 ...	49	316	4620	128
Chlorosis	40	354	6480	173
Pernicious anæmia ...	26	179	5160	32
Anæmia from hæmorrhage	33	175	3900	73
Polycythæmia	162	1360	6000	400

* The assumption is made that 1·34 cubic centimetres of oxygen combine with 1 gramme hæmoglobin; the actual determinations are made in terms of oxygen capacity.

[20] Anæmia denotes a deficiency in the concentration (not the total quantity) of hæmoglobin in the blood.

[21] Records as low as 9 or 10 per cent. hæmoglobin are suspicious; the Fleischl instrument reads too low at the bottom of the scale. The worst case we had in Cornwall had 17 per cent. on the Haldane-Gowers hæmoglobinometer.

[22] The experimental proof that this method gives substantially correct results will be found in the Journal of Physiology, vol. xxxiii., 1906, p. 493, and the Journal of Pathology, vol. xiii., 1909, p. 256.

and Lorrain Smith on three Cornish cases; for comparison I give the corresponding averages for normal persons (Haldane and Lorrain Smith); for cases of chlorosis, pernicious anæmia, and anæmia from hæmorrhage (Lorrain Smith); and for cases of splenomegalic polycythæmia (Boycott and Douglas). The figures are all corrected for variations in body-weight and are expressed as for a standard individual of 60 kilogrammes.

On the whole, therefore, in ankylostoma anæmia there is comparatively little shortage of hæmoglobin, nearly the whole of the anæmia being due to an increase in plasma. The condition, indeed, is a hydræmic plethora like chlorosis, and quite different from pernicious anæmia and anæmia from hæmorrhage, in which there is a more or less grave defect in the total quantity of hæmoglobin in the blood.

The colour index is characteristically low, and becomes lower as the grade of anæmia becomes more intense. Hence the total number of red cells in the body may be greater than normal. In a case of moderate severity—40 per cent. hæmoglobin—the morphological changes in the red cells are very few. There is some variation in size, most of the abnormal cells being too small, and a little poikilocytosis, but one does not find any marked signs of active regeneration of red cells (polychromasia, punctate basophilia, nucleated red cells), presumably because the whole blood contains about as much hæmoglobin as, and actually more red cells than, normal. In severe cases such changes appear in varying degrees, because, with a great increase of plasma, the rate of circulation cannot be sufficiently accelerated to carry an adequate quantity of hæmoglobin through the lungs in unit time. In all these particulars there is a great similarity to chlorosis, and a sharp contrast with pernicious anæmia. Occasionally in ankylostomiasis, as in anæmia from malaria and malignant disease, blood formation becomes more embryonic, and large cells with a high colour index are found.

In the relation of symptoms to the degree of anæmia there is a further similarity between these two states of hydræmic plethora. It is characteristic, and has been noted by Ashford and others, that in ankylostomiasis a pretty severe degree of anæmia may be associated with a surprising capacity for work. Thus in Cornwall men with less than 40 per cent. hæmoglobin were doing their regular work in the mine, and of men with between 40 per cent. and 50 per cent. hæmoglobin our notes record "feels quite well," "no symptoms," though their occupation entails a great deal of muscular effort. In the same way a chlorotic anæmic to the same degree will be fairly active, while cases of pernicious anæmia are obviously very sick people by the time their hæmoglobin has fallen to 40 per cent.

Some Theories as to the Cause of the Anæmia.

As already noted, our cases of ankylostomiasis had a real deficiency of hæmoglobin amounting to about 15 per cent. Without further information it is not possible to say whether this is due to the fact that they were working men, and on the whole decidedly less well nourished than the laboratory workers who furnished the "normal" data,[23] or whether there is actually some loss of blood from, or destruction of blood within, the body, which would account for a deficiency of this degree. Most observers have assumed that the blood volume is unaltered, so that the concentration of hæmoglobin in the blood is a measure of the total quantity; in other words, that a patient with 20 per cent. on the scale of the hæmoglobinometer has only one-fifth of the normal amount of hæmoglobin in his whole blood. They have therefore sought for reasons why so much blood should disappear.

The original idea was that the worms themselves suck blood.[24] This they undoubtedly do, for blood may be found in their alimentary canal, though, as a rule, in only a proportion of the worms obtained by the action of anthelmintics or post mortem. It is, however, not certain that this represents the natural condition. Whipple has pointed out that the worms may be observed to void blood, and it is possible that the empty individuals are to be accounted for in this way. Looss is of opinion that the normal food of ankylostoma is the mucous membrane, and that they only take in blood accidentally when they happen to penetrate a vessel. They do not seem to make much headway in digesting red corpuscles; on the other hand, it may be chiefly plasma that they are after. Many observers have expressed a natural hesitation in believing that such severe anæmia can result from the abstraction of such small amounts of blood; for, whether the worms digest it or not, the quantity must be small, else blood, or remains of blood, would be constantly present in the stools.

Actual enumeration shows more bites than correspond to the number of worms found post mortem. It has therefore been suggested that the worms often let go their hold on the wall of the bowel to take a fresh grip elsewhere, and that their old bites continue to bleed. In support of this hypothesis Loeb and Smith[25] found that extracts of the head-end of the worm inhibit coagulation of the blood, as also did

[23] L. Smith's observations on a few hospital patients not suffering from anæmia support this interpretation (Transactions of the Pathological Society of London, vol. li., 1900, p. 311).

[24] Cf. "The Vampire of the South," by Marian Hamilton Carter, McClure's Magazine, vol. xxxiii., 1909..p. 617.

[25] Proceedings of the Pathological Society of Philadelphia, vol. xxx., 1904, p. 173. Centralblatt für Bakteriologie, Orig., Band xl., 1906, p. 740.

Noc.[26] If this accounted for the anæmia, the stools ought to contain obvious quantities of blood. Sometimes they do, as may occur in any severe anæmia, and with massive infections with ankylostoma produced experimentally in dogs (Looss), but in the majority of cases blood is very seldom found.

Others have sought to show that blood is destroyed inside the body, and in this connexion have described the occurrence of hæmolytic substances in the bodies of the worms. Weinberg[27] found a hæmolysin in the allied nematode of the horse (*Sclerostomum equinum*), Preti,[28] Noc, Alessandrini,[29] and Calmette and Breton various similar substances in *A. duodenale* and *A. americanum*. Noc and Blasi[30] describe isohæmolysins in the serum. Loeb and Smith found no hæmolysin, but Whipple[31] found a very weak hæmolysin in *A. duodenale*, *americanum*, and *caninum*. Whipple thinks, however, that it is very unlikely that this weak hæmolysin can have any relation to the anæmia of ankylostomiasis. He points out that extracts of trichocephalus may be equally hæmolytic; cases of trichocephalus anæmia have been described,[32] but their etiological connexion with this common parasite is extremely doubtful. Whipple also found that ankylostoma may be embedded in the mucous membrane of the human intestine in small cysts filled with blood, and that this blood is not hæmolysed—almost conclusive proof of his contention that such hæmolysins as are present are quite negligible.

Even if hæmolysins were present in large amounts they could not be regarded as being the cause of the anæmia unless evidence of actual hæmolysis in the body were obtained. No such evidence exists. The amount of iron in the liver is normal[33] instead of being much increased, as it is when excessive destruction of red cells occurs (pernicious anæmia, malaria); and determinations of the total amount of hæmoglobin in the blood show that only about one-tenth is missing altogether; this might easily be accounted for by the small amount lost by the sucking of the worms and the bleeding of their bites

A certain number of cases when quickly improving show some degree of polycythæmia, the red cells rising to between 6 and 7 millions per cubic millimetre.[34] This is clearly the same phenomenon as is well known in chlorosis, and is due

[26] Annales de l'Institut Pasteur, vol. xxii., 1908, pp. 896, 955.
[27] Ibid., vol. xxi., 1907, p. 798.
[28] Münchener Medizinische Wochenschrift, Band lv., 1908, p. 436.
[29] Il Policlinico, vol. xi., 1905, p. 541.
[30] Annali d'Igiene Sperimentale, vol. ix., 1909, p. 449.
[31] Journal of Experimental Medicine, vol. xi., 1909, p. 331.
[32] Deutsche Medizinische Wochenschrift, 1902, p. 468; 1905, p. 95.
[33] Rake: Journal of Pathology, vol. iii., 1896, p. 107. Hopkins: Guy's Hospital Reports, vol. l., 1894, p. 349. Ryffel: Journal of Pathology, vol. xiv., 1910, p. 411.
[34] See, e.g., the cases in the appendix to Anæmia in Porto Rico, 1904.

to a rapid concentration of blood containing in all too many red cells of a low colour index. Weinberg and Leger[35] are, however, ingenious enough to see in it an indication of the effect of repeated small doses of hæmolysin, which, as Cantacuzène[36] showed, may stimulate the marrow.

A good number of worms acting for some time can cause ultimately a marked degree of sclerosis of the intestine, with atrophy of the mucous membrane. It is difficult to see how this can have much to do with producing the anæmia, though the probability of some impairment of nutrition and delay in recovering from the effects of the anæmia must be considered.

The essential change in the blood, therefore, is an increase in plasma, with a secondary, compensatory reduction in the colour index. There is probably also a small defect in the total amount of hæmoglobin, which may be attributed to the local action of the worms in the bowel. The response to this loss may be imperfect owing to the prolonged oxygen starvation of the marrow itself.

[35] Bulletin de la Société de Pathologie Exotique, vol. i., 1908, p. 229.

[36] Annales de l'Institut Pasteur, vol. xiv., 1900, p. 378.

LECTURE II.

Delivered on March 7th.

The Diagnosis of Ankylostoma Infection.

Mr. President and Gentlemen,—In the presence of well-marked anæmia, the only essential in the diagnosis of ankylostoma infection is that the possibility of a parasitic anæmia should be in one's mind. The disease was long unrecognised in Cornwall because it never occurred to anyone that it might be ankylostomiasis ; it might, indeed, with some luck have gained a footing in medical literature as "Dolcoath anæmia," the chief characteristics being that it was confined to men working underground and that it was completely refractory to iron and arsenic. One case, at least, whose chief symptoms were dyspnœa and palpitations, went through the hands of several London consultants, whose opinions varied between dyspepsia and cardiac neurosis. Directly the idea that ankylostoma might be at the bottom of the matter occurred to anyone—in the present instance, to J. S. Haldane—the stools were examined and found to be full of eggs, and so the mystery was cleared up. In the same way in Porto Rico in 1899 one-third of 36,000 deaths were due to "anæmia," which was supposed to be caused by poor food and unhygienic conditions ; it was only towards the close of that year that Ashford found that the condition was constantly associated with an eosinophilia, was by this led to examine the fæces, and so demonstrated that this enormous mortality was due to ankylostomiasis. The fact that the parasite occurred in the Southern United States had been known to the curious for a long time before Stiles in 1901 drew attention to the fact that it was the cause of serious endemic disease among the whole agricultural population.

In definite cases of ankylostomiasis there is no difficulty in making the definitive diagnosis of ankylostoma infection. The eggs are quite different from those of any other human parasite and occur in the stools in large numbers. If confusion arises, it is generally from some of the vegetable remains which one finds with all sorts of queer objects (mites, snails' tongues, &c.) in fæces. It is, however, obvious that it is not always easy to decide whether all or some of the illness in any given case of infection is due to the worm. This is especially difficult where, as, for example, in Assam, nearly all the natives are infected, and other

diseases, such as malaria and kala-azar, are common enough. Quite recently, for example, Noc[2] has pointed out that in Cochin-China the difficulties of estimating the share of ankylostoma in causing illness are such that he inclines to the view that the parasite has a considerable share in producing "beri-beri." In Cornwall the chief source of difficulty in this connexion is miner's phthisis, the symptoms of which are by no means always free from ambiguity. The effect of anthelmintic treatment is the most useful test.

Methods of Detecting Eggs in Fæces.

The difficulties of diagnosis are, however, considerable when infection is slight and no obvious anæmia is present. Accurate examination of the blood by the Haldane-Gowers hæmoglobinometer may be of assistance. With apparently healthy adult males any reading below 85 per cent. should excite suspicion. As a rule, plenty of eggs will be found in the fæces of even slightly anæmic cases and in many of those who have their full quantum of hæmoglobin. If few worms are present the discovery of eggs may be very difficult. Such a condition occurs especially in persons who have received specific treatment and from whom it is desired to expel absolutely every worm. In the ordinary way fæces are examined microscopically for eggs by smearing up a small piece, with the addition of water if necessary, into a sufficiently thin film on a glass slide. In the cases we are considering eggs will be found in such a preparation only by luck, and many infected stools will be passed as normal. Most of the fine mud can be removed by emulsifying a piece of fæces of the size of a nut and vigorously shaking up with water in a test-tube three-parts full. After standing for ten minutes all the eggs have fallen to the bottom and most of the supernatant fluid can be poured off. By repeating this process three or four times any eggs present can be obtained mixed only with the larger fragments, and the chance of finding them is very much better. Still further separation can be effected, as in Bass's method,[3] by taking advantage of the specific gravity of the eggs (about 1100). By washing with a solution of calcium chloride of specific gravity 1050 (12 per cent. hydrated salt) two or three times after washing with water, a good deal of light material can be got rid of, and by subsequently adding calcium chloride of specific gravity 1250 (55 per cent.) the eggs can be floated to the top and so separated from the crystals and heavy débris. Centrifugalisation saves time. Thus in one series of 315, 79 (25 per cent.) infections were found by direct examination and 38 more (12 per cent.) after washing.

[2] Annales de l'Institut Pasteur, vol. xxii., 1908, pp. 896 and 955.
[3] Hookworm Disease, 1910, p. 175.

The most accurate method of finding a few eggs appears to be cultivation and discovery of the larvæ. A convenient method of procedure is as follows. In the bottom of an ordinary 4 in. Petri dish make a pile of circular pieces of blotting paper about 2½ in. wide and ¼ in. high. Fill the dish with water nearly up to the level of the top of the papers and cover the island of paper with a thick layer of the fæces; incubate at 30°–36° C. for from five to seven days. When the larvæ hatch they swim away from the fæces into the water, which remains almost clear, and by centrifugalisation two or three can be found without much difficulty.

At the International Congress on Industrial Diseases held at Brussels in September, 1910, Bruns, who is in charge of the laboratory work in connexion with ankylostomiasis in the Westphalian coal-field, stated that of men with slight infections only 40 per cent. were diagnosed by direct microscopic examination, 55 per cent. by microscopic examination after gravity separation of the eggs, and 99 per cent. by the method of culture. This means that of every 99 men found infected by the culture method only 55 were diagnosed by microscopical examination, and that with every 99 positive by culture one case occurred which was negative to culture and positive to microscopic examination. There is no evidence to show how many cases of infection were not revealed by any of the methods. It is well known that some samples of stools are so noisome that the eggs will not hatch in them, so that the culture method cannot be regarded as infallible, though it is undoubtedly the best process available under all circumstances.

Other sources of error arise from the fact that the stools of an infected person may contain no eggs. It has already been pointed out that in experimental infection a period of from seven to ten weeks elapses after larvæ have entered the body before eggs are found in the stools.[4] Taking the shorter period as that which would most probably apply to large natural infections, there is therefore a considerable time after infection when examination of the fæces will necessarily prove negative. Eggs will also be absent if only male worms are present in the bowel;[5] it is inconceivable that under these circumstances enough worms should be present to cause any material illness, and such individuals are of course innocuous to others. It is also a matter of fairly common experience that eggs may not be found for a few days after anthelmintic treatment, but may reappear a week or two later. It is possible to explain these cases by an assumption that the eggs which ultimately appear have been laid by worms which were not fully developed and had not reached the intestine when

[4] Lambinet (Deutsche Medizinische Wochenschrift, 1904, p. 1848) showed that with *Ankylostoma caninum* in dogs the interval is only three weeks. Is the rate of development of the parasite proportional to the rate of metabolism (duration of life) of its host?

[5] A single male ascaris is not infrequently found post mortem.

treatment was administered. But in many instances so recent a reinfection can be excluded with considerable certainty, leaving only the usual and reasonable explanation that the shock of anthelmintic drugs temporarily paralyses oviposition.

Another source of failure to find eggs in the fæces produced for examination by an individual suspected of infection has been introduced along with schemes of compulsory examination and treatment which have for their object the exclusion of infected persons from certain places—e.g., the underground workings of a mine. If such procedures prove objectionable—as in fact they do—it is obvious that fæces which contain no ankylostoma eggs are likely to become an article of commerce, and it has actually occurred in the coalfields of Belgium and Westphalia that infected workmen have presented for examination stools which were passed by somebody else. Hence policemen were set to supervise the personal production of samples for examination.

While, therefore, in many cases the diagnosis is simple enough, there are a good many circumstances which render the examination of fæces fallacious. These are especially frequent when infections are relatively slight and become of considerable practical importance when it is sought to establish some system of quarantine.

Eosinophilia.

The only point on which a diagnosis might be made in the first two or three weeks after infection is the skin eruption which marks the entrance of the larvæ. In characteristic cases and under conditions of exposure to infection a diagnosis might well be based on this alone, sufficiently positive, at any rate, to justify precautionary measures of quarantine. During the next four or five weeks examination of the blood may be of the greatest assistance. Most cases of ankylostoma infection show a considerable increase in eosinophile leucocytes in the circulating blood, and this increase is definitely perceptible about three weeks after infection. The following table shows the results of blood examinations made after experimental infections by the skin (Dr. Leathes) and by the mouth (myself):—

Skin Infection.

Days after infection.	Eosinophiles per cent.
0	2·0
14	7·4
21	3·0
27	14·4
43	13·4
44	20·8
48	35·6
50	Eggs found.
52	44·8

Mouth Infection.

Days after infection.	Eosinophiles per cent.
0	3·4
8	2·6
14	10·0
36	24·0
41	33·6
48	40·4
55	Eggs found.

In neither case was the slightest illness produced beyond the most trivial abdominal discomfort. Eggs were very few and far between, and it was only by prolonged examination of thoroughly concentrated samples that they were found at all. Indeed, in my own case daily examinations gave negative results about two days out of three, and both cases would, I am sure, have been, except by accident, passed as free from infection after examination of the ordinary film of unwashed fæces. It will be seen that by a fortnight or three weeks after infection the blood was obviously abnormal; eggs were not found till more than seven weeks had elapsed. Bruns and Müller [6] after experimental skin infection found 5 per cent. eosinophiles after three weeks, 10 per cent. after four weeks, and 25 per cent. after five weeks, eggs being found on the fifty-third day.

The facts which have been ascertained with regard to the general correlation of an eosinophilia with ankylostoma infection are as follows. Of 148 infected men in Cornwall (*A. duodenale*) the percentage of eosinophiles in a differential count of 500 leucocytes on a stained blood film varied between 3 and 73 per cent.: 5 had less than 5 per cent., 4 between 5 and 7 per cent., and 139 showed more than 8 per cent., of whom 123 had more than 10 per cent. and 49 more than 20 per cent.; the average of the whole number was 18·2 per cent. Experience shows that anything over 8 per cent. can be called a definite eosinophilia, figures between 5 and 8 per cent. being suspicious, but not necessarily abnormal. The most marked reaction seems to occur in young people who have been only recently infected and may not have become anæmic at all.

No.	Age.	History.	Hæmoglobin.	Leucocytes.	Eosinophiles.	
			Per cent.	Per mm.³	Per cent.	Per mm.³
1	23	1 month.	80	56,000	66·2	37,000
2	18	6 months.	98	20,600	56·2	11,500
3	17	6 ,,	50	44,000	72·7	32,000

In such cases there is a veritable eosinophile leucocytosis comparable to that which occurs in trichinosis. In cases of longer standing the number of eosinophiles may be much less, and in cases which have reached a severe degree of anæmia may be even less than normal. No marked examples of this were observed in Cornwall, but the careful work of Ashford with *A. americanum* shows clearly that the responsivity of the marrow may be depressed or almost destroyed by long-

[6] Münchener Medicinische Wochenschrift, vol. lii., 1905, p. 1484.

continued severe anæmia. Thus in one series[7] 21 per cent. had less than 5 per cent., and only 61 per cent. more than 8 per cent., all the patients having less than 50 per cent. hæmoglobin. In another series of severely anæmic cases 40 per cent. had less than 8 per cent. eosinophiles when first seen. An absence of eosinophilia was found in Porto Rico to indicate a bad prognosis. Dealing with men who were not anæmic, Bruns[8] in Westphalia, with *A. duodenale*, found 8 per cent. with less than 5 per cent. eosinophiles and 84 per per cent. with more than 8 per cent., the corresponding figures for Cornwall being 3 per cent. and 94 per cent., though the two series are not directly comparable since in Westphalia the men under examination had been treated on one or more occasions. In Belgian coalminers, Herman and Dascotte[9] found less than 5 per cent. in 18 per cent. of 200 cases, and over 8 per cent. in 65 per cent. Unless the reaction to *A. americanum* is altogether different from that with *A. duodenale*—and the Porto Rico results are against this supposition, the vast majority of worms there being *A. americanum*—the blood-counts of Dock and Bass[10] are inexplicable. In 693 infected persons the count gave less than 5 per cent. in 481 (69 per cent.), the average being 4·1 per cent. Most of the cases were very mild.

The effect of treatment on the eosinophilia is very irregular. In the majority of cases, starting with a marked eosinophilia, the leucocytes gradually come to normal or thereabouts as the worms are expelled and the patient recovers. In very anæmic persons treatment may produce an eosinophilia which subsequently declines. In others, again, the eosinophilia may persist long after all worms have been destroyed. The following examples illustrate these points :—

Case I.			Case II.			Case III.		
Date.	Hb. %.	Eosin. %.	Date.	Hb. %.	Eosin. %.	Date.	Hb. %.	Eosin. %.
May 8th ...	33	16·8	May 12th...	20	0·8	Oct., 1902 ...	48	16·0
,, 16th ...	36	22·4	,, 19th...	28	4·8	Nov., ,, ...	43	18·0
,, 23rd ...	38	16·4	,, 26th...	38	6·8	Aug., 1903...	64	—
June 13th ...	56	14·8	June 9th...	41	4·0	Dec., ,, ...	92	14·8
,, 27th ...	67	8·8	,, 30th...	55	21·2	Feb., 1904 ...	96	13·4
July 11th ...	76	6·0	July 7th...	67	12·2	May, 1905 ...	95	11·2
,, 25th ...	83	4·8	,, 21st...	82	9·6			
Aug. 15th ...	101	8·8	Aug. 4th...	90	2·2			

[7] American Medicine, vol. vi., 1903, p. 391.
[8] Münchener Medicinische Wochenschrift, 1905, No. 6.
[9] Bulletin de l'Académie Royale de Médecine de Belgique, vol. xxii., 1908, p. 75.
[10] Hookworm Disease, 1900, p. 180.

The third case shows particularly well how a marked enosinophilia may persist for at least two years after expulsion of the worms. The man had been dosed several times, and repeated search failed to reveal any eggs. We examined also in Cornwall four men who had given up underground work some years previously, and in whose stools no eggs could be found; their blood showed an eosinophilia of from 11 to 22 per cent.

Eosinophilia, therefore, is of no value in gauging the results of treatment or in ascertaining whether the worms have died out from an infected person. But under certain circumstances it may be of considerable help in diagnosis. It is, in the first place, obvious that other causes of eosinophilia must be absent, or at any rate infrequent. The causes of eosinophilia other than ankylostoma are: (1) true paroxysmal asthma; (2) pemphigus and the bullous eruptions of the dermatitis herpetiformis group; (3) other animal parasites—i.e., bilharzia, ascaris, oxyuris, trichina, filaria, and tænia.[11] Of these bilharzia and trichina alone give a marked eosinophilia with anything like the regularity seen in ankylostoma infection. Trichocephalus,[12] by far the commonest intestinal worm in this country, gives no definite reaction The data recently collected by Schloss [13] show the frequency with which worm infections cause eosinophilia in children in the United States :—

Worm.	Number of cases.	Eosinophilia.		Highest eosin. count.
		Over 8%.	Over 10%.	
Trichocephalus...	31	0	0	6·4
Oxyuris	23	5	3	14·0
Ascaris...	6	2	0	9·2
Hymenolepis	20	7	4	22·6
Tænia saginata	3	2	1	13·2
Total	83	16=19%	8=10%	—

In 83 infections, therefore, only 16 (19 per cent.) had a definite eosinophilia. Blood examinations are, however, not much use for diagnostic purposes in places such as the tropics, where worms are very prevalent, except in so far that the absence of an eosinophilia in a reasonably robust subject may be taken to exclude ankylostoma infection with a fair degree of certainty. But in this country the method is

[11] Journal of Hygiene, vol. iv., 1904, p. 466.
[12] Ibid., vol. v., 1905, p. 278.
[13] American Journal of the Medical Sciences, vol. cxxxix., 1910, p. 675.

of great practical utility. Worm infections are not common, and as a matter of ascertained fact eosinophilia is distinctly rare in the general population. To investigate this point blood films were obtained from 158 underground workers in uninfected coal, lead, and tin mines, and from surface workers at Dolcoath. Their differential counts contrasted with those of Cornish miners infected with ankylostoma were as follows :—

Percentage of eosinophiles.	Infected miners.		Non-infected miners.	
Less than 1 per cent.	0		29	
1 per cent.	0		49	
2 ,,	0	3·4%	32	91·2%
3 ,,	4		23	
4 ,,	1		11	
5 ,,	2		5	
6 ,,	1	2·7%	5	7·0%
7 ,,	1		1	
8 ,,	7		1	
9 ,,	9		0	
10 ,,	40		0	
15 ,,	34	93·9%	0	1·8%
20 ,,	22		1	
25 ,,	8		1	
More than 30%	19		0	
Total examined	148		158	
Average eosinophiles %	18·2		2·5	

The figures for infected miners suggest that any figure above 8 per cent. may be regarded as indicative of infection. Of the three cases above this figure among the men not infected with ankylostoma, one (8·4 per cent.) had trichocephalus and oxyuris, the other two (23·8 and 25·6 per cent.) trichocephalus and ascaris; all three came from Levant mine, where worm infections are very common.

In holding an inquisition for ankylostoma this method of examination is therefore very useful. It is easy to obtain blood films from the men, and any question of fraud is excluded. I do not know what sort of response one would obtain if one descended on some mine in this country where the terrors of ankylostoma were unfamiliar, and asked 100 men to produce samples of fæces for examination, but I imagine that at any rate a great deal of time would be consumed before such an examination was complete. The same number of men can be examined by the blood film method in a few hours. It is quite unnecessary to count all the films; after a little practice the obviously negative and positive cases can be separated by a short inspection of the slide. As a further proof of the pudding, I give the results of a search recently conducted, in conjunction with Cadman, in likely places for ankylostoma. Films were obtained from a good

proportion of men working underground in hot and wet mines; samples of fæces were subsequently obtained from any cases showing more than 8 per cent. eosinophiles.

Locality of mine.	Number of men examined.	Number positive.
Midlothian	94	1 : 15% : Trichocephalus.
Fife	89	0
Fife	24	0
Lancashire	22	0
Yorkshire	57	0
South Wales...	120	0
,, ,, ...	52	0
,, ,, ...	52	1 : 9·5% : Trichocephalus.
Isle of Man	109	2 : 11% Trichocephalus; 24% : man disappeared.

In all, then, of 619 men, four showed an eosinophilia; on further inquiry none of these had ankylostoma. The method is particularly useful in an inquiry for latent infection, since the reaction is best marked in the young and lusty who are not anæmic—the people, that is, who are least liable to be suspected of infection; and, as pointed out above, it may be very well marked in extremely slight infections, appearing in a recognisable form after infection several weeks before there is any chance of finding eggs in the stools. It is possible that precipitin and Bordet-Gengou reactions may prove of service in diagnosis as they have in other worm infections.

The Conditions which Determine the Prevalence of Ankylostoma Infection.

One has learned so much in recent years about the direct transmission of pathogenic parasites from host to host, that one recognises something exceptional in the case of ankylostoma, where the chief circumstances which influence development outside the body are those which condition the prevalence of infection in man. Some parasites, such as the gonococcus or spirochæta pallida, have no life outside the bodies of their special host; others, as trypanosomes, malaria organisms, and cestode worms, oscillate between two different animal hosts; others, again, though apparently capable of no inconsiderable saprophytic life, like the diphtheria bacillus, the typhoid bacillus, or the meningococcus, depend in the main on living animals for the continuance of their existence; organisms which have an active, proliferative, saprophytic life, such as the tetanus bacillus, are now known to be in the minority among the infective agents of important human diseases. In ankylostoma, on the other hand—and the same is, of course, true of the other common nematode parasites ascaris and trichocephalus—the sapro-

phytic phase is of fundamental importance. Since the eggs cannot develop during the parasitic phase, since they cannot again enter the parasitic phase till they have become definitive ("encapsuled") larvæ, and since the larvæ cannot become sexual and multiply without changing the saprophytic for the parasitic phase, it is obvious that the conditions which determine, in the saprophytic phase, the development of the eggs into larvæ are as fundamental to the propagation of ankylostoma as is the existence of a host in which a multiplication of individuals takes place. Its existence in nature is to ankylostoma what the mosquito is to the malarial parasite, or *Limnæa truncatula* to the liver fluke. The influence of various physical circumstances on the life of ankylostoma may be grouped under the following heads :—

1. *Oxygen.*—A free supply of oxygen is necessary for the growth of the embryo, and in its absence the eggs do not hatch and die in a few days. Eggs, therefore, cannot possibly hatch in the intestine. They will very rarely hatch if they are covered in an open dish with a layer of ordinary tap water about an inch deep, though this contains oxygen to begin with and does not offer any great obstacle to diffusion. Even if the water is stirred by bubbling hydrogen through it they seldom hatch, though a fair proportion develop if a good stream of air is kept passing through the liquid. Eggs, therefore, will not hatch if fæces are passed into a good volume of water, nor will those in the interior of fæcal masses make much progress. The eggs are not, however, killed by deprivation of oxygen in less than about 10 days; at low temperatures they would probably survive longer. The young larvæ, as might be expected, also require a free supply of oxygen while they are growing rapidly, though they thrive well in water, but when they become full grown and encapsuled they develop some of the remarkable anaerobic capacities shown by adult intestinal worms, and apparently derive the energy required for their very active movements by fermentation rather than by direct oxidation, as shown by Weinland in his study of the metabolism of adult ascaris.[14] At this stage they will live for at least two or three weeks, wriggling about all the time, in hydrogen or nitrogen at room temperature; in parallel experiments at 37° C. they died in about 24 hours.

2. *Moisture.*—At any stage of development from egg to encapsuled larvæ desiccation at ordinary temperature is very soon fatal. Hence some degree of wetness in the place where infected fæces are deposited is necessary for the development of infectivity. Ankylostomiasis never prevails very extensively in dry places. In this connexion it should be remem-

[14] Zeitschrift für Biologie, vol. xlii., 1901, p. 55.

bered that really dry districts are uninhabitable, and that the holes and corners in which fæces are apt to be deposited in nature are liable from their situation to be rather specially damp, if only because they are sheltered and evaporation hindered. The influence of vegetation in preventing the surface of the earth from drying is of considerable importance. Thus in Porto Rico the sugar fields are not nearly so heavily infected as coffee and banana plantations. The former are ploughed up every year and the surface is freely exposed to the sun after the crop is harvested, while the coffee bush itself produces shade and in its turn is always shaded by some other tree. The ground beneath banana plants is densely shaded, and the mass of decomposing leaves and stalks remains wet for a long time after rain, and forms an ideal medium for the protection of the larvæ.

In mines the influence of moisture is equally well marked. The rise and progress of ankylostoma infection to the proportions of a serious epidemic in the Westphalian coal pits followed the introduction of watering the roads to prevent dust explosions. The following figures show how the prevalence of infection increased, watering being begun in the last six months of 1899:—

Year.	Number of collieries infected.	Number of cases reported.	Cases per 10,000 miners working.
1896	15	107	6·4
1897	31	113	6·2
1898	23	99	4·9
1899	26	94	4·4
1900	40	275	11·7
1901	63	1030	40·6
1902	66	1355	52·9

Active measures against the disease were commenced at the end of 1902, when a careful survey revealed about 18,000 infected men (9·1 per cent.). The gold mines in South Africa are almost quite dry, and though about half the native labourers working underground are already infected when they first come to work there is no evidence that infection tends to spread, and there have been few, if any, cases of the white miners acquiring the disease there. In Cornwall all the mines are more or less wet, but those which have a considerable proportion of dry roads and galleries are among the less heavily infected. Many coal pits in this country are too dry for the development of the larvæ. The recognition of the importance of coal-dust in the causation and propagation of underground explosions may, however, lead to the introduction of water sprinkling, with the result that in this respect conditions may become favourable. The alternative plan of having "dustless zones" on the roads is much to be preferred from the present standpoint.

3. *Temperature.*—The effect of cold is not altogether certain. My own experience is that the eggs die if kept for a few days near freezing temperature, and Stiles and Bruns [15] obtained the same result. Bruns also found that freezing kills the larvæ in an hour or two. Oliver,[16] on the other hand, finds that infected fæces may be frozen and the eggs still remain capable of hatching, and that larvæ may be buried in snow for six days without necessarily losing their vitality. The lethal effects of high temperatures on eggs and larvæ are well shown in Bruns's experiments. (Next table.)

Fæces in nature can hardly become heated as high as 48° C. (118° F.) unless they are at the same time being dried. It may occasionally happen that so hot a place occurs underground with an atmosphere saturated with moisture; such would be of no practical importance since men could not work there.

Effect of Heat on Eggs.

Temperature.	Duration of heating in minutes.					
	1	2	3	5	10	15
47° Centigrade.	+	+	+	+	+	+
48° ,,	+	+	+	+	+	+
49° ,,	+	+	+	+	−	−
50° ,,	+	+	+	−	−	−
51° ,,	+	+	+	−	−	−
52° ,,	+	+	−	−	−	−
53° ,,	+	−	−	−	−	−
55° ,,	+	−	−	−	−	−
58° ,,	−	−	−	−	−	−
60° ,,	−	−	−	−	−	−

\+ = Eggs subsequently developed into encapsuled larvæ.
− = No development.

With encapsuled larvæ Bruns obtained the following results:—

Temperature.		Temperature.	
48° Centigrade...	Alive after 30 min.	53° Centigrade...	Dead after 2 min.
49° ,, ...	,, ,,	54° ,, ...	,, 1 ,,
50° ,, ...	Dead after 20 min.	55° ,, ...	,, 1 ,,
51° ,, ...	,, 5 ,,	56° ,, ...	,, 1 ,,
52° ,, ...	,, 3 ,,	60° ,, ...	,, 1 ,,

[15] Klinisches Jahrbuch, vol. xii., 1904.
[16] THE LANCET, Feb. 5th, 1910, p. 357.

Experiments in which the eggs and larvæ are kept continually at the same temperature show, however, that a less degree of heat is distinctly detrimental. At 36°–38° C. (97°–100° F.) the eggs often die without hatching; a few larvæ generally hatch out in about 24 hours and as a rule rapidly die away, only a very few surviving to the infective stage. Encapsuled larvæ which have been reared at a lower temperature have, in my experience, always died in a few days at 37° C., though they will live under the same conditions at room temperature for more than a year. The further development which they undergo when they gain entrance to the human body must be associated with a change in their temperature relations. Conditions probably seldom occur in nature which would make these facts of great practical importance. If fæces are dried the eggs and larvæ are killed in any case; if they remain moist their temperature will be reduced by evaporation if the air is not too humid. There is no inhabited part of the world where a temperature approaching 98° F. prevails for any length of time associated with a high relative humidity; such a combination would hardly be compatible with human life.[17] In mines restricted areas of the workings may be as hot and wet, but this is very uncommon. In Levant Mine in Cornwall some of the deeper galleries have a temperature of 93° F. with saturated air. At Schamrock Mine, in Westphalia, Meyer found that 15 per cent. of men working at about 20° C. (68° F.) were infected; 56 per cent. between 20° and 25° C. (68°–77° F.) and only 28 per cent. between 25° and 29° C. (77°–84° F.); but it is difficult to be certain that all the other circumstances were identical.

At the lower end of the scale the development of ankylostoma is also definitely limited by temperature. I have twice succeeded in hatching eggs and growing the larvæ to the encapsuled stage in an incubator in which the temperature was generally 15·9° C. (60·6° F.) and never exceeded 17° C. (62·5° F.), but such experiments do not always succeed either as regards hatching of eggs or development of larvæ. The lowest point at which really free and full development of the majority of eggs is to be expected is placed by Bruns at 20° C. (68° F.), and this is in accordance with my own experience. The encapsuled larvæ live very well at 15° C.

The widest possible range of temperature is therefore 15° C. (59° F.) to 38° C. (100° F.), but the range which is suitable for the great majority of eggs to hatch and larvæ to develop and continue to live when they have reached the encapsuled stage is restricted to the interval between about 20° C. (68° F.) and about 32° C. (90° F.).

As might be expected, temperature has a marked influence

[17] Journal of Hygiene, vol. v., 1905, p. 494; Journal of Pathology, vol. xiii., 1909, p. 62.

on the rate of development. At 35° C. (95° F.) free larvæ may appear in 24 hours and encapsuled larvæ in four days; at 16° C. (61° F.) the eggs take three to seven days to hatch and encapsuled larvæ may not be present for a fortnight. Taking all the circumstances into consideration we should suppose that the optimum temperature for the saprophytic phase of ankylostoma is somewhere about 27° C. (80° F.).

These experimental observations are fully in accordance with the observed epidemiological facts. The annual isotherms of 16° C. (61° F.) mark fairly accurately the limits of the distribution of infection of an epidemic degree about the world. Thus the disease is prevalent in the Southern but not in Northern United States, in Spain and Italy but not in France or Germany, in Queensland but not in Victoria. For obvious reasons the correspondence cannot be expected to be very exact, but we should expect that infection might be extensive anywhere where the mean annual temperature was over 60° F., while in cooler climates nothing beyond sporadic cases would occur. The following table shows the mean monthly and annual temperatures for a number of

Mean Monthly Temperatures (°*F.*).

—	Infected.					Not infected.						
	Trinidad.	Calcutta.	Brisbane.	Georgia, U.S.A.	Naples.	Melbourne.	Scilly Isles.	London.	Paris.	Chicago.	Berlin.	Aberdeen.
January	76	65	77	44	47	67	46	38	36	23	31	38
February	75	70	76	47	49	67	46	40	38	25	32	38
March	77	79	74	56	51	65	46	42	43	35	37	40
April	79	85	70	63	57	60	49	48	50	46	46	44
May	79	85	64	72	64	54	52	54	55	57	55	48
June	79	84	60	78	71	50	57	60	62	66	62	54
July	78	83	58	80	76	48	61	63	65	72	65	57
August	78	82	60	79	76	51	61	62	64	71	63	56
September ...	79	82	65	75	71	54	59	58	58	64	57	53
October	80	80	70	64	63	57	54	50	50	53	48	47
November ...	80	72	73	54	54	61	50	43	42	39	38	42
December... ...	77	65	76	47	49	65	47	39	37	29	33	38
Annual	78	78	69	63	61	58	52	50	50	48	47	46

places in which infection does and does not occur. Thus the West Indies (represented by Trinidad), Assam (Calcutta), and the Southern States (Georgia) are all notorious foci; in Queensland (Brisbane) there is widespread infection, and

a considerable amount of ankylostomiasis occurs in Italy[18] (Naples). In Victoria (Melbourne), on the other hand, the disease is not known, nor does it occur in the Northern States (Chicago), nor among the general population in France, Germany, or England.

It is pretty clear, then, that the disease does not gain a foothold under circumstances of temperature which experiment has shown to be not incompatible with the development of infective larvæ from the egg. Thus in this country it appears from the Greenwich Records for the 50 years 1841–1890, that the mean daily temperature is, on the average, over 60° F. on 71 days in each year, the mean maximum over 60° F. on 162 days, and over 70° F. on 85 days; the temperature exceeds 70° F. on 85 days, 80° F. on 14 days, and 90° F. on one day. In July, 1859, the thermometer rose above 80° F. on 21 days, and in July, 1868, on 20 days. As a matter of fact, if one leaves infected fæces in the open air in London in the summer one may after a time find encapsuled larvæ in them, though not in all samples. Oliver has observed the same thing in Newcastle. One would not expect to find ankylostoma rampant in this country owing to the effective control of fæcal contamination, but experience shows definitely that infection equally fails to spread in uncivilised countries of like climate. But such spread is not impossible. A certain number of cases have been known for many years to arise in the brickmakers[19] in the Cologne district, and there is at least one case where infection was acquired in New York by a boy who played in his father's brickyard in which were workmen who had brought the worm from elsewhere.[20] There does not seem to be any known infection in the neighbourhood of Chicago, although the summer there is very hot, and during the two months in which the mean monthly temperature is over 70° F. eggs would readily hatch and quickly develop into infective larvæ.

The only localities in North-Western Europe in which ankylostoma can thrive and make any headway are the underground workings of mines. Most mines are warm, and many hot, from a variety of causes. As pointed out by Haldane,[21] these high underground temperatures are due, in the first place, to the natural temperature of the earth, which increases with the depth from the surface by about 1° F. for every 60 ft. Thus the mean annual temperature on the surface in Cornwall is about 50° F., and the natural temperature of the

[18] Of 1200 patients in the hospital at Pavia in 1909 Marti found 76 cases of ankylostomiasis.

[19] The temperature in such places may well be a good deal above the screen records in the neighbourhood.

[20] W. R. Stone: Medical News, vol. lxxxii., 1903, p. 680. A second case is recorded by H. Brooks, Medical Record, vol. lxxvii., 1910, p. 191.

[21] Report on the Health of Cornish Miners, Parliamentary Paper, Cd. 2091 (1904), pp. 93, ff.

rock at 1800 ft. is about 80°, and at the greatest depth at present reached in Dolcoath mine (500 fathoms = 3000 ft.) about 100°. As far as this source of heat is concerned the mines will go on getting hotter as they get deeper. A certain amount of heat is also produced by the men, animals, lights, and explosives underground, and the incoming air is warmed by compression as it comes down the downcast shaft. The most important source of the generation of heat underground is, however, the oxidation of the minerals as they are exposed to the air. There are good reasons for thinking that the chief process of this kind going on, both in coal and metalliferous mines, is the oxidation of iron pyrites. According to some, heat is also produced by the shearing and straining of the strata when they are disturbed and are capable, as in coal-pits, of a certain range of movement, but it is doubtful whether this possible source of heat is of any quantitative importance. On the other hand, the temperatures which would in this way be reached are actually diminished to a greater or less degree by the cooling effect of the ventilating current of air which operates partly by taking up heat from the rock and, which is more important, by evaporating water out of the workings. Hence the actual temperature of any place underground will, depth and other conditions being equal, depend largely on the volume of ventilation ; the downcast shafts and intake roads will be cooler than the upcast shafts and return roads, and dead ends without any through ventilation will be especially hot. A mine may also be cooled a good deal by the percolation through the strata of surface water, which is ultimately pumped out from the bottom.

In considering the effect of underground temperatures on the propagation of ankylostoma, it is important to note that there is relatively little variation at different seasons of the year, except near the intake of fresh air.

In Cornish mines considerable areas of the underground workings are over 70° F. In Dolcoath mine, for instance, a good deal of the deeper galleries have a temperature between 75 and 80°, and in places where fresh rock is being opened up by tunnelling temperatures of 98° or thereabouts are not uncommon by reason of the high natural temperature of the virgin rock and the absence of any effective ventilation. In Levant mine, where the ventilation is very imperfect, the temperature where much of the work is now being done is over 80°, and in some places as high as 90°. In other mines, however, which are not so deep and better ventilated temperatures are much lower (60–70°). The temperature of coalpits in this country varies in the same way, and it is impossible to make any general statement on the point, if only because the temperature varies so much in different parts of the same pit. There is, however, no doubt that as far as temperature alone is concerned there are many places in British coal-pits where ankylostoma would get on very

well. In their exhaustive report [22] on the ventilation of coal-mines Professor John Cadman and Mr. E. B. Whalley incidentally give a number of data relating to 43 collieries which were not selected as being particularly hot. In 30 temperatures of over 70° F. were observed, in 12 of which the thermometer recorded over 80°, and in 2 more than 90°. In another series of 20 collieries in North Staffordshire, temperatures over 70° were observed in 15, and over 80° in 5. In Westphalia in about two-thirds of the collieries the temperature is less than 70°.

In the case of mines there is particularly clear evidence that ankylostomiasis does not become prevalent if the temperature is below about 70° F., though we know that experimentally infective larvæ may develop at 61°. Tenholt's figures for the Westphalian colliery district in 1901 show this very well.

Temperature about working face.	Number of collieries.	Number of men employed underground.	Number of cases of ankylostomiasis.	Cases per 1000 men.
Below 63° F. (17° C.) ...	67	36,033	20	0·6
63°–68° F. (17°–20° C.) ...	84	68,604	25	0·4
68°–72° F. (20°–22° C.) ...	45	43,710	118	2·5
72°–77° F. (22°–25° C.) ...	33	39,836	466	11·7
Over 77° F. (25° C.) ...	12	9,853	392	39·8
Total	241	198,036	1021	5·1

He further points out that four-fifths of the cases occurred among the hewers, who only constituted one-half of all underground workers, a fact no doubt attributable to the higher temperatures at the working face. The same local distribution was seen in Dolcoath mine. Common opinion among the men associated skin eruptions and breathlessness especially with the main upcast shaft ("New Sump Shaft"); their boils and blains were, indeed, known among the men as "New Sump bunches." This shaft is particularly warm, and, the air at the bottom being saturated with moisture and being decompressed as it ascends, a good deal of moisture is deposited; it is also the main pumping shaft, which makes it all very wet, and was apparently a favourite resort for purposes which, with some imagination, may be described as "sanitary."

The next general group of circumstances which may determine the prevalence of ankylostoma infection by influencing the development of larvæ includes poisons, disinfectants,

[22] Royal Commission on Mines, Cd. 4551, 1909.

and the like. The stout outer sheath of the encapsuled larvæ gives them a considerable power of resisting the action of poisons. Thus Lambinet[23] found that 25 per cent. sulphuric acid took more than half an hour to kill them, while 2 per cent. corrosive sublimate did not kill in six hours. In the same way, but to a less degree, the eggs appear resistant. But this is only because they are protected by a shell.[24] Both eggs and encapsuled larvæ are killed by 0·1 per cent. sublimate, 0·5 per cent. lysol, or any other poison if sufficient time is allowed for the solution to really reach the animal. Recently hatched larvæ are unprotected and are killed very soon. Mixing infected fæces, therefore, with some poisonous substance which will kill neither the eggs nor encapsuled larvæ may prevent the eggs reaching the infective stage by killing off the young larvæ as they hatch out.

That these questions may be of importance in nature is shown by the history of Levant mine in Cornwall. The shafts are on the cliff and most of the workings under the sea; they are badly ventilated, wet, very hot, and were at the time of inquiry extensively soiled with fæces. It was also ascertained that a number of men who were known to be infected had from time to time worked there. We visited the mine, therefore, expecting to find that under these very favourable conditions the disease had become rampant. But no trace of infection could be discovered. Subsequent investigation showed that this immunity was due to the nature of the water in the mine. Some of this comes in on the land side but most of it filters in from the sea, and the water in most of the mine contains between 2 and 3 per cent. of sodium chloride.[25] Experiments in the laboratory proved that this degree of salinity prevents the development of encapsuled larvæ from the eggs, chiefly by its action on the unprotected phase of young larvæ. Encapsuled larvæ placed in salt solutions of different strengths gave the following results at a temperature of 20° C. (68° F.):—

—	3 hours.	18 hours.	2 days.	9 days.	18 days.
0·8% NaCl	Lively.	Lively.	Lively.	Lively.	Lively.
2% ,,	,,	Some dead, some lively.	A few lively.	A few lively.	A few lively.
4% ,,	Motionless.	None moving.	Dead.	—	—
6% ,,	,,	,,	,,	—	—
10% ,,	,,	,,	,,	—	—

[23] Bulletin de l'Académie Royale de Médecine de Belgique, vol. xv., 1901, p. 397.

[24] Ascaris eggs continue to develop in strong formalin (S. Hastings, Archives of the Middlesex Hospital, vol. xix., 1910, p. 233).

[25] Pure Atlantic sea water contains 3·4 per cent. The water in other Cornish mines in which the infection was prevalent contained at most 0·02 per cent. NaCl.

Similar experiments were made with eggs, fresh infected fæces being placed on an island of wet filter paper surrounded by a moat of salt solution at 20° C.

—	After 7 days.	After 12 days.
Tap water.	Lively large larvæ.	Very hearty encapsuled larvæ.
0·8 per cent. NaCl.	Ditto.	Ditto.
2·0 ,, ,,	A few dead first day* larvæ.	Many first day and a few second day larvæ; all dead.
4·0 ,, ,,	Eggs ready to hatch; no larvæ.	No free larvæ; eggs dead.
6·0 ,, ,,	A few embryos in eggs; mostly morulæ.	No larvæ; eggs dead.
Water from Levant mine containing 2·42 per cent. NaCl.	A few first day larvæ; not all dead.	A few dead larvæ; eggs dead.

* That is the stage to which a larva gets one day after hatching at about 35° C. Dead eggs are recognised by the disintegration of their contents.

These laboratory facts are confirmed by the experiments of Bruns and of Calmette and Breton. Epidemiologically it was observed by Schillinger (1885) in Hungary and by Blanchard in Galicia (1885) that the men in the salt mines were not ill and anæmic as they were elsewhere, and Manouvriez [26] has pointed out how the irregular distribution of infection among the coal mines in the Anzin district in the north of France can be explained by the indemnity of those in which the water is salt (1·2 to 4 per cent. NaCl). Monti [27] has also shown that while the disease is causing fearful havoc in most mines in Italy certain workings are quite immune and that the water in these contains 1·85, 2·7, 3·5, 5·6, and even 7·4 per cent. of salt. Chiadini and others have recorded similar observations. Professor Cadman has recorded [28] one coalpit in the North of England where the water contained 13 per cent. salt, but saline waters are exceptional in this country. Other poisons may be present in mine water. In the Transvaal G. A. Turner [29] notes that the water may be acid from the oxidation of pyrites to a degree equivalent to 0·79 per cent. H_2SO_4, and A. May [30] has shown that, while development proceeds normally with 0·05 per cent. H_2SO_4, 0·25 per cent. kills the eggs, while with

[26] Mines de Houille rendues Réfractaires à l'Ankylostome par des Eaux Salées de Filtration, par A. Manouvriez, Valenciennes, 1905.
[27] Second International Congress on Industrial Diseases, Brussels, 1910.
[28] Report on Ventilation of Coal Mines, p. 13 (Cd. 4551), 1909.
[29] Transvaal Medical Journal, vol. iv. 1908, p. 34.
[30] Ibid., p. 40.

0·1 per cent. the eggs hatch, but the young larvæ are soon killed. Slightly acid water is common in mines, but I do not know whether such a degree as this is at all frequent. Belger [31] found iron sulphate very effective as a disinfectant.

Influence of Fæcal Contamination.

The prevalence of ankylostoma is, under natural circumstances, determined by the physical agents which condition the development of infective larvæ from the egg. But it is important to note that the course of nature may be interfered with in a way which, in this immediate connexion, has been singularly effective. Modern methods of sewage disposal are so obviously contrary to the general scheme which nature has devised for the circulation of nitrogen among living organisms that it hardly needed the advocacy of Dr. Poore to produce an abstract conviction that fæces should rightly return to us in the form of cabbages. Sanitary science in this country has fortunately been directed by notions of practical convenience rather than by conceptions of fundamental biological truth, and if the care with which fæces are carried away from us and broken up has somewhat diminished the return of vegetables, it has at any rate had a far greater effect in diminishing the return of parasites. If, indeed, all contact between man and his excretions could be prevented all the world over as thoroughly as is done in this country at the present day, it would be no matter of surprise if before very long ankylostoma, ascaris, and trichocephalus became as extinct as the dodo—a convincing proof of the biological iniquity of our arrangements. The prevalence of these parasites in man is probably the best test we have of the efficacy of the disposal of fæces in any place. The chief drawback to the test is that the duration of life of the adult worm in man is indefinite and may be considerable, so that evidence is obtained of the cumulative effect of conditions which have prevailed during the preceding few years rather than in the immediate past. I have already referred to the fact that in an examination of the stools of 500 in-patients in Guy's Hospital taken at random French and I found trichocephalus dispar [32] in 39 cases, or 8 per cent., and in the age-period 5 to 40 as many as 33 out of 282, or 12 per cent., were infected. No other worms were found in unselected cases. Post-mortem experience shows that ascaris is not now found in more than one body in about 300 or 400 in Guy's Hospital. Forty years ago Cobbold recorded trichocephalus in 70 per cent. at Greenwich and in 90 per cent. in

[31] The Lancet, Feb. 5th, 1910, p. 359.

[32] There was one case of ascaris infection, but the lad had been admitted to have the worms expelled, so that it was not an unselected case.

Dublin,[33] and ascaris was evidently a common-place occurrence. Among recent data relating to the prevalence of intestinal worms among reasonably civilised people we may note those of Stiles, Garrison, Ransome, and Stevenson,[34] who in 3457 persons in two asylums for the insane and in an orphanage in the United States found trichocephalus in 7·7 per cent., ascaris in only 0·5 per cent. Among 200 consecutive children between 2 and 12 years in the United States Schloss[35] found 11 per cent. with trichocephalus and 2 per cent. with ascaris. Chantemesse and Rodriguez[36] (1908) found trichocephalus eggs in the stools of 91 out of 134 (67 per cent.) of patients suffering from typhoid and in 45 out of 62 (72 per cent.) of other hospital patients. In 1891 Drivon[37] found trichocephalus in 76 per cent. of hospital patients at Lyons. The remarkable thing about these figures seems to be that infections are so numerous. In people of less complicated habits these nematodes may be extraordinarily prevalent. Thus in fæces found by the roadside near Lausanne Galli Valerio[38] found ascaris in 48 per cent. and trichocephalus in 68 per cent., which shows clearly how common infection may be in temperate climates among those who have no use for sanitary conveniences. The following table summarises some modern results of systematic examination in tropical countries.

—	Number examined.	Percentage infected with—		
		Ankylostoma.	Ascaris.	Trichocephalus.
Djerid oasis: Tunis[39]	107	21	68	12
St. Vincent, W.I.[40]	414	82	56	53
China[41]	—	—	92	—
Filipino prisoners[42]	4106	52	26	59
Natal: Indian coolies[43]	709	44	83	19
Panama[44]	232	49	8	17
Transvaal: natives in mines[45]	692	48	20	0·3(?)
India: gaol prisoners[46]	—	72	36	12
French Guiana: prisoners[47] ...	639	72	2	6
Tonkin[48]	1000	51	71	78

[33] In 1835 (*circa*).

[34] Bulletin No. 28, Hygiene Laboratory, U.S. Public Health and Marine Hospital Service, Washington, 1906. Literature.

[35] American Journal of the Medical Sciences, vol. cxxxix., 1910, p. 675.

[36] Bulletin de l'Académie de Médecine, vol. lix., 1908, p. 407.

[37] Journal de Physiologie et de Pathologie Générales, vol. x., 1908, p. 127.

[38] Centralblatt für Bakteriologie, Orig., vol. xliv., 1907, p. 531.

Such conditions are, however, not confined to the tropics nor to other countries than our own. In Cornish miners these worms are very common. The majority of examinations of stools there were made for the diagnosis of ankylostoma infection; in heavily infested cases these are found in the first few microscopic fields examined and the specimens were, as a rule, not searched further. Even from such cursory examinations one formed the impression that trichocephalus was very common and ascaris pretty frequent. In mines, however, which were either altogether free from ankylostoma or only slightly infected the specimens were searched more thoroughly and in them we found trichocephalus in 79 per cent. and ascaris in 25 per cent. In one series of 23 samples 8 were free from worms, 4 had trichocephalus only, 1 had ascaris only, 6 had trichocephalus and ascaris, 2 had trichocephalus and ankylostoma, and 2 had trichocephalus, ascaris, and ankylostoma. In all, 15 people had 27 worm infections between them, not counting oxyuris.[49] The prevalence of these worms in the Cornish miners[50] may to some extent be associated with the tropical temperatures which obtain underground; the eggs of both ascaris and trichocephalus are not infective when swallowed unless they contain a developed larva, and this development is accelerated by warmth. Their prevalence in the ordinary population of England and North-Western Europe in times past, and under suitable circumstances at the present day, shows, however, that no great warmth is necessary, and there can be no hesitation in ascribing their abundance in Cornish miners to the filthy conditions which prevailed underground. Nine years ago there was very inadequate privy accommodation at the mines on the surface, and underground no provision was made at all. The men worked in three eight-hour shifts, and, apart from the cases of necessity which must arise under these circumstances, they had developed a

[39] Gobert and Catouillard: Bulletin de la Société de Pathologie Exotique, vol. i., 1908, p. 229.

[40] C. W. Branch: Journal of Tropical Medicine, vol. viii., 1905, p. 261.

[41] J. J. Matignon: Bulletin de l'Académie de Médecine, vol. xlv., 1901, p. 366. Only 25 per cent. of Europeans infected.

[42] Garrison: Philippine Journal of Science, vol. iii., 1908, p. 191.

[43] B. Nicol: Transvaal Medical Journal, vol. v., 1910, p. 228.

[44] G. H. Whipple: American Journal of the Medical Sciences, vol. cxxxviii., 1909, p. 40.

[45] G. A. Turner: Transvaal Medical Journal, vol. iv., 1908, p. 34.

[46] C. F. Fearnside: Brit. Med. Jour., vol. ii., 1900, p. 541.

[47] Brimont: Bulletin de la Société de Pathologie Exotique, vol. ii., 1909, p. 423.

[48] Mathis and Leger: Ibid., p. 488.

[49] Oxyuris is common, but neither eggs nor worms are often found in the examination of ordinary samples of fæces. After anthelmintics the worms are easily seen.

[50] Bréhon (Archives de Parasitologie, vol. ix., 1905, p. 540) found tricho cephalus in 50 per cent. and ascaris in 10 per cent. of 1708 miners in the Pas de Calais; ankylostoma two cases only.

regular habit of defæcating underground. The sanitary accommodation at their homes was excellent, though often separated from the house, and I suppose that the warmth and quiet rendered the underground workings more attractive, combined with the fact that once the men had gone down there might be no need for immediate hurry—an obvious consideration for the shifts due underground at 10 P.M. and 6 A.M. For the most part use was made of blind ends and odd corners, but the whole of the mines were more or less offensive, and fæces were trodden about everywhere. Particularly significant perhaps was the fact that a great deal of travelling up and down is effected by climbing ladders, the cage which accommodates men ("gig") being substituted for that used for hauling mineral ("skip") only at the times of changing shift. In this climbing the hands and arms become covered with mud and filth which has been carried on to the ladders on the men's boots. Some of these ladders are in the same shaft with the cage and pumping apparatus. The latter requires constant attention, and for examination and repair the men climb about on the ladders and cross-timbers. These beams were, we were informed, a favourite resort, which made the lot of the repairing gang particularly beastly.

These horrid conditions have now been much improved. In 1904 sanitary appliances were introduced into Dolcoath mine in the form of loose pails which can easily be brought to surface, emptied, and cleaned. After some turbulence on the part of the less responsible workmen their use became habitual, and it is now the exception to find fæces loose in the mine. In 1905 the provision of such conveniences was made compulsory by the Home Secretary.

In coal-mines the fæcal contamination is, for various reasons, much less serious. In some places in South Wales there is, as I am informed by Professor Cadman, a strong local feeling on the subject which has a most beneficial effect. The actual stink and nuisance is much diminished by the deodorising effect of the coal, and in searching for fæcal deposits in coal-pits one has to rely mostly on sight. In any case the bulk of fæces subsisting in exposed situations in a coal-pit at any moment will always be less than in a metalliferous mine owing to the relatively transitory nature of the exposed surface. At the working face the coal is excavated and removed very much more quickly in tons per man than is the granite or other hard rock which forms the matrix of most metalliferous deposits. As the coal is taken out, the roof is allowed to fall in and fill up the gap, and the men seem to make it a habit to defæcate in the "goaf" or "gob" in which the waste débris is stowed, and which will very shortly be shut off for ever from any further contact with human beings. Even the main roads which lead from the shafts to the working face are constantly being renewed; the floor tends to rise and the

roof to fall, so that the surface has to be frequently cleaned up. In the hard rock of metalliferous mines, on the other hand, progress is much slower at the site of actual excavation, and the roads are practically permanent.[51] Hence fæces tend to accumulate as they do in communities of fixed abode; coal-miners enjoy some of the advantages of a nomadic people.

Insanitary Conditions and Spread of Ankylostoma Infection.

One of the most striking examples of the influence of neglect of sanitary precautions on the spread of ankylostoma infection is afforded by the prevalence of the disease in the Southern United States. It is clear from the comprehensive observations of Stiles and many others[52] that ankylostomiasis is one of the most potent causes of chronic ill-health and inefficiency among the agricultural population in these parts. In the large cities it is limited to imported cases and those infected away from home. What is surprising to us is that the farming class should be so grossly filthy in their habits. Dock and Bass[53] state that in the country there are few privies, and such as there are are only used for shelter and convenience. The safe disposal of fæces is not considered and, owing to defective construction, pigs and fowls can root and scratch about among them and so scatter eggs around. They show by direct experiment that ankylostoma eggs can be fed to chickens and larvæ readily hatched from the eggs when they are subsequently p ssed by the fowls. In this way infection might be disseminated very widely.[54] During wet weather fæces are liable to be washed out of the primitive shelters, which are, if possible, placed on a slope to keep them as dry as may be. About three-quarters of the rural population have not got a privy even of this inefficient sort. Any more or less retired place near the house is used by the adults, while of the rest of the family they say, "It is often possible to determine the number of children in a family by the number of piles of fæces in the backyard. ..... In small towns, where many country people come to market, there is often some near-by thicket, or gully, or barnyard to which the country people go when they get 'in a tight,' in preference to privies, to which they are unaccustomed even if they are available. The country people are more or less infected, and they thus convert these resorts into veritable hotbeds of hookworm larvæ. We remember

[51] Dolcoath mine, for example, has been working continuously since 1799.

[52] The bibliography of American literature on "Uncinariasis" during the last three or four years has assumed gigantic proportions.

[53] Hookworm Disease, by G. Dock and C. C. Bass, 1910.

[54] Possibly also by flies. Galli-Valerio, Centralblatt für Bakteriologie, Orig., vol. liv., 1910, p. 194.

such a 'gully' near a country town, and with our present knowledge we now see ample explanation of the ground itch and anæmia among many of the town boys, who often went barefoot in warm weather. The most favoured parts of the 'gully' were so much used for this purpose that there often seemed to be no more room. Many of the country schools are not provided with any sort of a privy." A lurid picture of the habits of a white population which is said to represent the purest breed of English that still survives. In Georgia, Wells[55] found about 24 per cent. of the total white population outside towns infected; of 280 school children 137, or 49 per cent., had the worm. Among university students from the Southern States 37, 42, and 37 per cent. have been found infected in different inquiries; among army recruits 60 and 88 per cent.; half the white population of Mississippi are infected, and in the cotton-mills 13 per cent. are ill enough to hinder their work.

Conditions Favouring Infection by the Skin.

Besides the physical circumstances which prevail and the efficacy with which the disposal of fæces is carried out, a third group of circumstances which may materially influence the prevalence of ankylostoma infection is found in the degree to which the human skin is immediately accessible to the larvæ. Wearing boots is in many circumstances obviously a pretty complete protection, and to this no doubt Europeans owe their almost complete immunity when living in places in the tropics where the barefooted natives are infected to a man. Infection on the feet is doubtless the commonest mode of attack, and it is on the feet that "ground itch" and "mazamorra" characteristically occur. Boots are, of course, no great protection when the nature of the occupation brings the hands and arms into intimate contact with infected earth. Hence the special prevalence of infection among agriculturists in the tropics, and among brickmakers and miners in North-Western Europe. Cornish miners wear boots which are often leaky, thin canvas trousers, and some sort of vest or shirt, together with a hard hat. In the hotter places they usually work stripped to the waist. "Bunches" are somewhat rare on the feet, occurring most commonly on the arms and legs. It is obvious from looking at the men that they are liable to be smeared with mud all over their bodies while doing their work in the cramped quarters which they have underground. Hence one is not surprised at the occurrence of the skin lesions in any part. "Sat down on muddy stone last Thursday, and has bunches on left buttock which came out the same night," is a representative note.

[55] Journal of the American Medical Association, vol. liv., 1910, p. 1852.

Such are the conditions which determine the prevalence of ankylostoma infection. Three are of outstanding importance—moisture, temperature, and fæcal contamination of the soil, and to ensure the existence of the parasite in any place all three must be simultaneously favourable. In the tropics this coincidence is commonly found. In mines in North-Western Europe, on the other hand, infection is often rendered impossible because one of these three conditions is unfavourable. Fæcal contamination is, or at any rate has been, everywhere pretty extensive, and most mines of any size are in parts either hot enough *or* wet enough. But relatively few underground works are at the same time and place hot enough *and* wet enough to give the parasite a reasonably good opportunity. If conditions are not unfavourable, the intensity of prevalence, as measured by the proportion of persons exposed who are infected and the proportion of those who have a large enough infection to make them ill, will vary as the product, rather than as the sum, of the degree to which moisture, temperature, and fæcal contamination are coincidently suitable for the development of the increasing number of eggs which the soil receives as infection becomes more widespread and more intense among the human population. Thus, one may have every grade of prevalence, from the scattered cases which, as Iberer [56] has shown, occur among the general population in the south of Hungary to the universal infection subsisting in Porto Rico, just as in Cornish mines, which are rather cool and dry, only 10 per cent. of underground workers are infected and none are sick, while at least 95 per cent. harbour the worm in hot, wet workings and 5 per cent. are too ill to work.

[56] Münchener Medicinische Wochenschrift, June 9th, 1903.

LECTURE III.

Delivered on March 9th.

THE TREATMENT AND PROPHYLAXIS OF ANKYLOSTOMA INFECTION.

MR. PRESIDENT AND GENTLEMEN,—Ankylostoma may be attacked either in the parasitic or the saprophytic phase, and treatment of infection includes the treatment both of persons and of places.

With regard to personal treatment, two different objects may be aimed at, first to make the individual physically well and able to work, and secondly to render him incapable of laying down infection for others. It is important to realise that curing a man of ankylostomiasis is by no means equivalent to curing him of ankylostoma infection: the former is generally easy, the latter may be extraordinarily difficult.

Many cases of ankylostomiasis may be cured by removing them to a place where no further infection is possible. Under these circumstances the worms become less numerous and the poisonous effects of those which remain diminish. Thus in Cornwall a number of men who had given up underground work because of dyspnœa and faintness and had remained on surface had all much improved without any further treatment. This, however, does not always occur. In an exceptional case, undiagnosed and untreated, the patient was still very ill four years after the last exposure to infection and had only 30 per cent. of hæmoglobin. In Porto Rico it had been observed, before the cause of the anæmia there prevalent had been discovered, that anæmic agricultural labourers nearly always improved if they went to live in a town; this was attributed to better food and lodging, but was, of course, due to the avoidance of the constant reinfections associated with country life. Ashford[2] gives the following details regarding 28 inmates of the Girls' Christian Orphanage at Porto Rico who were noted as being anæmic on admission and had been in residence two years or more; 26 were still infected. The average hæmoglobin percentage was 81; only one had under 60 per cent. and six less than 70 per cent.

There do not appear to be any extensive statistics on this point; it would, indeed, be rather scandalous if there were. But some light is thrown on the matter by the following data

[2] Anæmia in Porto Rico, 1904, p. 50.

given by Nicol,[3] showing how infection dies out in Indian coolies working in Natal. The figures are the more remarkable since the conditions prevailing in Natal cannot possibly be taken as excluding the possibility of reinfection.

	Number examined.	Percentage infected.
On arrival	223	81
,, ...	215	86
On estates	614	61
,, ...	709	45
After 5 years in Natal	184	53
,, ,, ,, ...	80	43

But doing nothing is, as has been already pointed out, a fearfully slow way of getting rid of infection; the original worms live on for years. For this purpose definite anthelmintic treatment is required.

Drug Treatment.

Four drugs have found favour with different practitioners —thymol, β-naphthol, eucalyptus oil, and male fern. Many others have, of course, been tried and recommended. In most tropical countries thymol is generally used; in Germany and Belgium eucalyptus and male fern are preferred. The most valuable experience in this respect is that of the Porto Rico Commission. During ten years 300,000 cases have been carefully examined, treated, and the effects ascertained. Moreover, all four drugs have had a good trial. Male fern was found uniformly useless, eucalyptus was so horribly nauseating that its administration became impracticable, while thymol and β-naphthol were about equally efficacious in expelling the worms, one dosing (i.e., two half-drachm doses) of either killing on the average about 75 per cent. Thymol has the disadvantage that it costs about five times as much as β-naphthol, but after a lengthy trial the latter drug was eventually discarded in favour of thymol owing to the discovery that β-naphthol may set up a fatal acute nephritis in persons whose kidneys are already somewhat diseased. Nicol [4] has observed the same thing in Natal. All the drugs in question are, of course, poisonous enough if they are absorbed from the bowel into the economy; permanent blindness has been caused by male fern in a few cases in Westphalia, and both thymol and β-naphthol have been the immediate cause of death in a few persons who were already very ill.[5] But the not uncommon impression that thymol is very dangerous is certainly untrue so long as no active

[3] Transvaal Medical Journal, vol. v., 1910, p. 228.
[4] Loc. cit.
[5] Sandwith: The Lancet, June 2nd, 1894, p. 1365.

measures such as drinking alcohol are taken to promote its absorption. It is also desirable that it should be clearly recognised that small doses (e.g., 5 grains) are quite useless.[6] Two or three half-drachm doses at hourly or two-hourly intervals are necessary if any considerable proportion of the worms present are to be killed. Taking all the evidence into consideration, one comes to the conclusion that there is no drug better than thymol, and that β-naphthol and male fern should be avoided. It is possible, however, that the most efficacious remedy is not the same for *A. duodenale* as for *A. americanum*, though at present there is no definite evidence to this effect.

It is not usual to find that one dosing is sufficient to expel all the worms. The following figures from Porto Rico show the number of weekly doses which had to be given till no eggs could be found in the fæces:—

Number of doses of thymol.	Number of persons.	Per cent.
1	1518	42
2	1166	32
3	518	14
4	247	6
5	104	3
6	47	1
7	19	2
8	6	
9	3	
10	1	
11	1	
Total	3630	100

Of the 184 cases recorded by Sandwith[7] in Egypt only 23 per cent. were cured by one dosage with thymol, and 23 per cent. required more than three dosings; the largest number necessary was eight and the average number two and a half.

Number of doses.	Number of persons.	Per cent.
1	42	23
2	58	31
3	42	23
4	25	14
5	9	5
6	4	4
7	2	
8	2	
Total	184	100

[6] Fearnside (Brit. Med. Jour., vol. ii., 1900, p. 541) records several cases who took 20 or 30 grains thymol for 10 to 30 days, and still had plenty of eggs at the end. Evidently what is wanted is a high concentration of thymol lasting for only a short time, such as is produced by three 30 grain doses at intervals of two hours instead of 24 hours.

[7] THE LANCET, June 2nd, 1894, p. 1365.

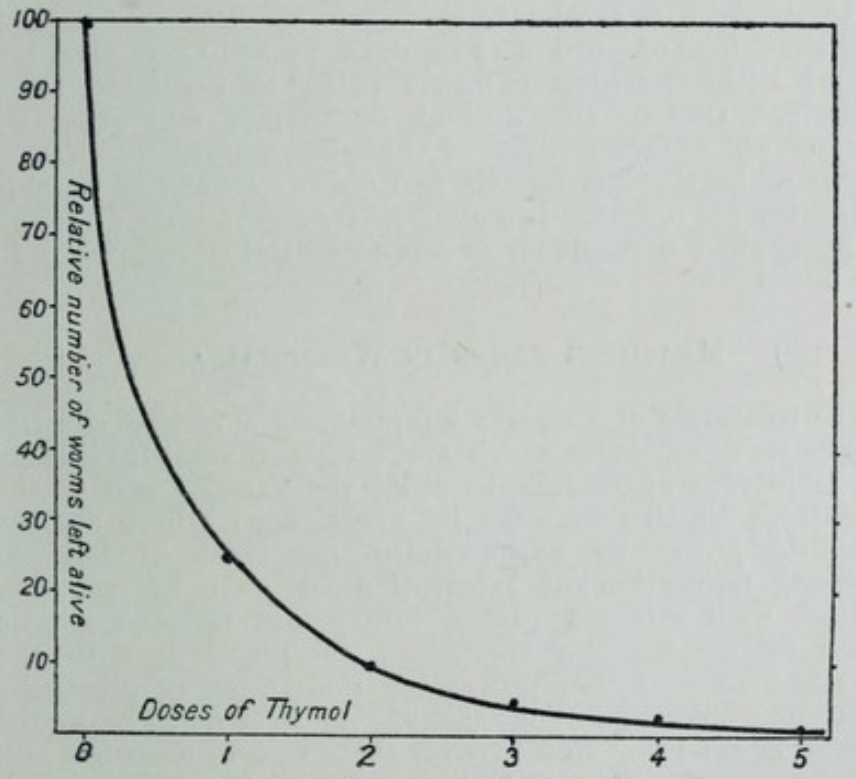
The first dose kills about three-quarters of the worms present, the second and succeeding doses smaller and smaller numbers, as shown by the following data obtained by Ashford by careful enumeration of the worms expelled. The figures are averages from 40 patients treated with thymol and 30 with β-naphthol.

Percentage of Total Number of Worms Expelled by Each Dose.

	Thymol.	β-naphthol.
First dose...	76·8	72·2
Second ,, ...	16·0	15·9
Third ,, ...	4·7	5·6
Fourth ,, ...	1·5	2·9
Fifth ,, ...	0·7	2·1
Total	99·7	98·7

In other words, after one dose on the average 255 per 1000 of the worms still remain, after two doses 95 per 1000, after three doses 44 per 1000, after four doses 22 per 1000, and after five

FIG. 1.



Results of treatment with thymol.

doses 7 per 1000 (Fig. 1). Each successive dose, therefore, kills 74, 63, 54, 50, and 68 per cent. of the worms present when it is given. Is this due to a natural variation in the

original resistance of the worms or to an acquired tolerance? Since small doses will generally kill a few worms, there are reasons for thinking that some individuals are specially susceptible as a few others are specially resistant.

All these data refer to persons who have been exposed to constant reinfection. In the case of the Porto Rico patients, who were for the most part treated at home, the possibility of reinfection during the course of treatment cannot be altogether excluded. With hospital patients in Egypt it is possible that a batch of larvæ had entered the body shortly before treatment was begun, and thymol is relatively ineffective in killing young worms.[8] Hence these results may not be strictly applicable to cases suffering from only a single invasion of some standing. But it is quite clear from the experience gained in Cornwall and in Westphalia that more than one dose is generally required before the eggs disappear from the stools.

As to how far the failure to find eggs in the stools can be taken as definitely proving that the individual is entirely free from worms is an open question. Bruns's observation that about twice as many treated cases are found to be still infected if their stools are tested by culture instead of by direct microscopical examination requires serious attention, and renders it necessary to accept many data as to the effect of treatment with some reserve.

A great deal of good may be done by killing most of the worms without taking immense pains to eradicate them entirely. One or two dosings of thymol will generally restore an ordinary case of ankylostomiasis to such a degree of health that he will feel quite well and be capable of leading the ordinary life of an active working man, though in many such a residuum of worms will still be present in the bowel.

Measures taken in Westphalia.

The treatment of endemic ankylostoma infection consists of a series of measures which are indicated unmistakably by our knowledge of the life-history of the parasite and of the conditions which determine its prevalence: killing out the parasitic phase by anthelmintic treatment of infected persons, prevention of reinfection of men by avoiding contact with infected places, killing out the saprophytic phase by making the conditions incompatible with the development of larvæ, preventing reinfection of places by regulating the disposal of fæces. As Perroncito says, the matter is settled. But how far these various measures are, on the one hand, practicable and, on the other hand, efficacious requires a good deal of further consideration.

The history of the progress and persistence of the infection

[8] Porto Rico Commission Report, 1904, p. 109.

in the Westphalian coalfield [9] furnishes probably one of the most complete accounts of the effect of measures taken against a parasite with a full knowledge of its life-history and of the circumstances which condition its existence. The first cases of ankylostomiasis among Westphalian colliers were observed in 1892, and up to the end of 1895 23 cases (two of them fatal) were recorded. In consequence of official regulations, after 1895 all colliers who showed any signs of anæmia were periodically examined for ankylostomiasis, and in this way Tenholt showed that the disease was scattered about among a number of collieries. The total number of collieries was 290, with about 190,000 underground workers in 1902.

Years.	Number of cases.	Number of collieries affected.
1896	107	16
1897	113	32
1898	99	24
1899	94	27
1900	275	42
1901	1030	65
1902	1974	108

Few of these men were seriously ill, though all of them were more or less anæmic; only five deaths in all from ankylostomiasis are known to have occurred. The marked increase in the number of cases beginning in 1900 coincided with the introduction of a system which made compulsory the watering of the roads in dry collieries in order to lay the dust and so reduce the risk of explosions. This produced conditions favourable to the development of infective larvæ, and the disease, which had smouldered for many years, flared up into a considerable epidemic. The number of cases of anæmia increased proportionately much more than the number of infected pits. This would be expected, since watering would only tend to spread the infection by putting into circulation, so to speak, a large number of heavily infected men. The increase in the number of mines producing cases of anæmia is, no doubt, partly due to this, but probably in greater part to declaration by "Wurmkranken" of an infection which had previously, under less favourable circumstances, been intense enough to give only "Wurmträger." The conditions, as far as wetness and warmth, were apparently as favourable in 1901 as in 1902; the considerable extension of severity in the latter year illustrates the progressive effect of the infection of an increasing number of men with increasing doses of worms. The increase was much the same in all the pits. The following table

[9] Report on Ankylostomiasis in Westphalian Collieries, by J. S. Haldane, Cd. 1843 (1903). Bruns: International Congress on Industrial Diseases, Brussels, 1910.

gives the figures for some of the larger and more heavily infected collieries:—

Number of Cases of Ankylostoma Anæmia.

—	1896.	1897.	1898.	1899.	1900.	1901	1902.
Lothringen	2	2	7	5	38	50	137
Erin	15	12	25	19	68	285	367
Hannibal	—	—	—	2	3	6	27
Julie	—	—	—	—	1	4	36
Graf Schwerin	9	12	11	9	33	378	427
Steingatt	21	6	0	6	7	12	84
Schamrock	—	4	4	17	41	199	402

At the end of 1902 the managements of nine of the larger collieries made arrangements whereby the whole of their men were examined. Though only 958 men were anæmic, eggs of the worm were found in the stools of as many as 6190. This discovery excited considerable attention, and vigorous measures were taken in hand and a series of official regulations were made, of which the more important were as follows. No new hands were to be allowed to work underground until on microscopical examination the fæces had proved to be free from ankylostoma eggs. In each colliery at least 20 per cent. of the men employed underground were to have their fæces examined microscopically on three different occasions in order to ascertain the extent to which the various pits were infected. If a pit was known to be infected or was discovered to be infected by this preliminary investigation, the whole of the men were to be examined at the rate of at least 200 per week. Any man found to be infected was not allowed to return to underground work until he had been treated, if necessary on two or more occasions, and his fæces found by microscopical examination on three separate days to be free from eggs. The treatment was carried out in special hospitals erected for the purpose, the funds for this being provided by the Knappschafts-Verein, a wealthy union for sickness and invalidity insurance maintained under Government supervision partly by the men and partly by the colliery owners. People who felt quite well naturally did not like to be subjected to the prescribed process for eradicating their parasite, especially as it involved the very real hardship of losing at least three-quarters of their wages. After some trouble, however, the difficulty was to some extent surmounted by the collieries making up the allowance to all men under treatment to full half-pay. At the same time general sanitary improvements were effected. More, and more attractive, privies were provided on the surface, with an

adequate supply of pails throughout the underground workings; shower baths were fitted up for the men on coming out of the pit in place of the common baths in which it was supposed that infection might spread.[10] Efforts were also made, though only in a few places, to disinfect the mud and water in the mines.[11] Finally, the whole process of holding an inquisition for ankylostoma in all the men and treating those infected was repeated periodically.

Such arrangements constitute a comprehensive attempt to stamp out the infection altogether. If none but men free from infection are allowed to work underground, the infection subsisting cannot at any rate increase, and must in course of time diminish owing to the natural death of the larvæ. The regulation of the disposal of fæces underground helps to prevent any infected men who have escaped detection transmitting their infection to others. The point which is obviously a weak link is the absence of any vigorous and united attempt to kill the larvæ underground. Their possible duration of life is such that, all addition to their numbers being prevented, the mine may remain infective for many months at least, and men from whom all worms have been expelled will be liable to reinfection on returning to work. As regards the prevalence of infection in 1903 the results of this campaign are as follows :—

District.	Number of workers.	Number infected.	Per cent.
Hamm	812	30	3·7
Dortmund I.	12,398	195	1·6
Dortmund II.	13,976	435	3·1
Dortmund III.	13,874	3,882	28·0
Recklinghausen East	11,223	1,126	10·0
Recklinghausen West	11,780	275	2·3
Witten	9,240	372	4·0
Hattingen	8,207	512	6·2
Bochum South	9,411	874	9·3
Bochum North	10,711	2,359	22·0
Herne	12,785	2,373	18·6
Gelsenkirchen	10,603	516	4·9
Wattenscheid	12,987	1,301	10·0
Essen East	10,917	157	1·4
Essen West	11,098	256	2·3
Essen South	8,378	1,197	14·3
Werden	1,316	210	16·0
Oberhausen	19,014	1,091	5·7
Total	188,730	17,161	9·1

[10] It is very doubtful if washing is of much use as a prophylactic measure. The larvæ appear to penetrate the skin very quickly. French opinion, however, supports the efficacy of washing (Colliery Guardian, May 15th, 1908).

[11] Bruns: Münchener Medicinische Wochenschrift, Nos. 2, 3, and 4, 1905.

With regard to the effect of treatment, Bruns (1910) gives the following summary, a good many men having been cured at the point where accurate figures begin to be available.

	Number of infected men.	Per cent.
May–October, 1903	14,548	100·0
February, 1904	3,663	25·3
November, 1904	3,288	22·6
October, 1905	2,352	16·2
December, 1905	2,103	14·5
January, 1907	1,366	9·4
August, 1907	1,111	7·6
April, 1908	895	6·2
March, 1909	749	5·2

The history of a single colliery—the Schamrock pits of the Hibernia Company—may also be given in detail, showing the rapid diminution which may be effected in 18 months,[12] though the pits were still infected in 1910.

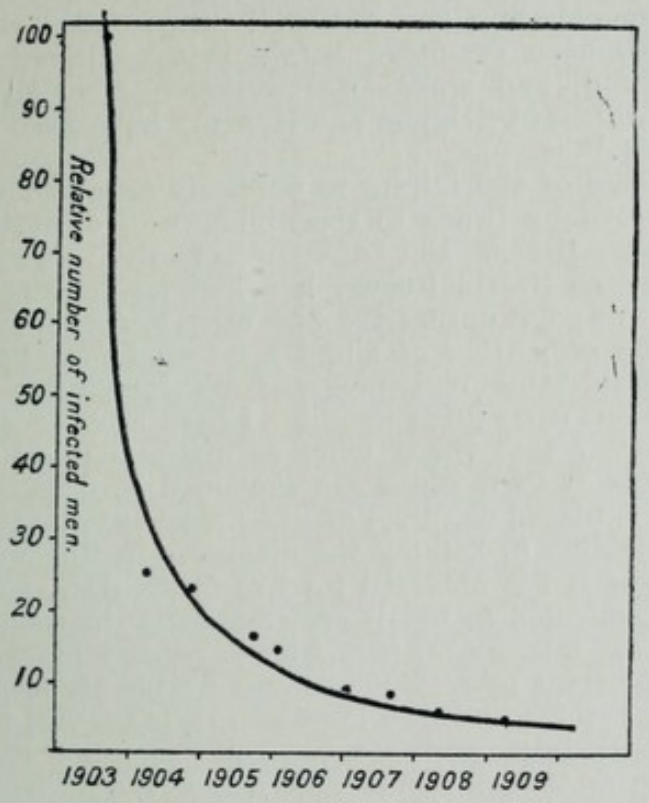
Schamrock pits.	Date.	Number of men examined.	Percentage found infected.
First inquisition.	Dec., 1902–May, 1903.	2126	34
Second ,,	May–July, 1903.	2110	28
Third ,,	Aug.–Oct., 1903.	2045	17
Fourth ,,	Nov.–Dec., 1903.	2126	10
Fifth ,,	Jan.–Feb., 1904.	2205	8
Sixth ,,	March–April, 1904.	2215	6
Seventh ,,	April–May, 1904.	2086	4
Eighth ,,	July–Aug., 1904.	2000	3
Ninth ,,	Sept.–Oct., 1904.	2130	1½

In other words, after one year's work the number of infected men had been reduced by 75 per cent., after six years by 95 per cent. (Fig. 2). Cases of anæmia have not now been seen for a long time, and the disease itself, apart from the procedures taken to cure it, causes no industrial inconvenience. In mines which were at first particularly severely infected, the reduction has been especially well marked: at Schamrock from 37 per cent. of all underground workers to 0·5 per cent., at Erin from 80 per cent. to 4 per cent., at Graf Schwerin from 80 per cent. to 4 per cent., at Julia from 20 per cent. to 0·8 per cent. At the beginning about 1 man

[12] Bruns: Münchener Medizinische Wochenschrift, 1905, No. 22.

in 10 in the whole district was infected, now only 1 man in about 200.

FIG. 2.



Showing reduction in infected men.

RESULTS IN WESTPHALIA.

I am not in a position to state even approximately [13] how much has been expended in producing this result, but it is evident that the examination of fæces, provision of hospitals and staff, sick pay for workmen, and the various sanitary improvements must have consumed a great deal of money. The results which have been obtained at the present time are these: (1) that sickness has been abolished, and (2) that the infectivity of the mine has been considerably reduced. But it is important to note that the infection has not been eradicated and as far as this is concerned the campaign has failed in its main object. For so long as a few infected men remain, and any chance of their depositing infected stools underground continues, it would be possible to relax the periodical hunts for "Wurmträger" only at the risk of a repetition of the disaster of 1900–01. The history of these

[13] The examination and treatment of each miner is said to cost about £4, which alone accounts for about £150,000. In the first nine months of 1903 £60,000 were spent in all, plus about an equal sum spent by the mine-owners.

very mines shows that when the conditions became favourable infection spread rapidly. These favourable underground conditions still remain. If, therefore, precautions were withdrawn, the improved habits of the men are the only obstacle to another widespread outbreak. Re-importation of infection from outside seems unlikely. Since 1897 all foreign men have been examined before being allowed to work underground, and since 1900 workmen from the heavily infected mines of Belgium and Hungary have been excluded altogether.[14]

The cause of the failure to eradicate infection altogether is attributed by Bruns to the difficulty of detecting slight infections. Bruns, the director of the bacteriological laboratory at Gelsenkirchen, has had an immense experience on this point during the last eight years in Westphalia, where the proportion of slightly infected men has always been considerable and progressively increasing, and his opinion must carry great weight. I have referred already to his discovery that about twice as many men are found to be infected if their stools are examined by culture as when reliance is placed on direct microscopical examination. The chief objection to making the diagnosis in this way is that the answer is not obtained for five or six days, but if it is found practicable to use it systematically the results should be of great interest. Apart from a paucity of eggs, other sources of error may be introduced by the absence of eggs for about two months after infection, their absence for a time after anthelmintic treatment and the production of supposititious fæces, though this last fraud has been prevented. The examination of the leucocytes is, of course, of no value in these cases.

Measures in Belgium.

In the Belgian coalfield, with its centre at Liége, a campaign has been carried on along much the same lines and with the same idea that the infection might be stamped out altogether. The difficulties, as Malvoz points out, were more considerable in Belgium than in Westphalia. When the campaign was started in earnest, 26 per cent. of the underground workers were infected—i.e., twice as many proportionately as in Westphalia, and it was necessary to undertake the hygienic education of a population 20 per cent. of whom were illiterate and whose independent spirit, traditional in the Walloons, rendered them rather fretful against official regulations. Above all, in Belgium there was no wealthy Knappschafts-verein. However, the periodical

[14] Bréhon (Archives de Parasitologie, vol. ix., 1905, p. 540), among 118 men from Belgium applying for work in the coal mines in Pas de Calais, found 11 infected. Only about 1 per 1000 of the local miners were infected.

examination of men and treatment of those found infected have led to much the same sort of result as in Westphalia.

	Number of men working in each group of mines.	
	1902	1909
Mines with 0- 5% of men infected	6,830	16,170
,, 5-10% ,, ...	3,380	5,740
,, 10-20% ,, ...	5,150	4,410
,, 20-50% ,, ...	6,060	300
,, 50% and over ,, ...	5,680	0

In all, then, from 26 per cent. in 1902 the percentage of infected workmen fell to 11 per cent. in 1906 and to 4 per cent. in 1910, and along with this considerable reduction in "ankylostomés" there has been a disappearance of "ankylostomiasiques." The failure to eradicate infection altogether or even reduce it to the level reached in Westphalia is no doubt largely due to inaccurate diagnosis of slightly infected men. The Belgian authorities attribute it also to the difficulty of introducing a proper system of underground privies, the ill-will of the men in using such conveniences as have been provided, and the difficulty of expelling the worms quite completely from some individuals. As in Westphalia, reliance has been placed almost entirely on male fern, and thymol has never been given a proper trial. The available evidence, as has been mentioned above, is strongly in favour of thymol being the better anthelmintic of the two, and, curiously enough, it is in the continental coal-fields that the most conclusive proof has been obtained that a moderate excess in the dose of male fern is not a little dangerous either to sight or life.

The main conclusion which may be drawn from the history of these two campaigns against ankylostoma infection is that it is impossible to completely stamp out infection from heavily infected mines by methods at present available which do not include any practicable and efficacious means of destroying the saprophytic phase in the mine itself. The enthusiastic prophecy of Calmette and Breton [15] has not been fulfilled. Writing in 1905 they say: "In Westphalia the number of infected miners has been reduced from about 18,000 at the beginning of 1903 to 2500 or 3000 at the present time, and the district will be totally freed from the epidemic before the end of 1905."

By energetic treatment and provisions for preventing fæcal contamination of the underground workings a great deal may be done without the elaborate apparatus which has been used in Westphalia. Thus at Brennberg in Hungary Goldman found 85 per cent. of the men infected in 1896, many of them being seriously ill. By 1898 the number had

[15] L'Ankylostomiase, Paris, 1905, p. 101.

fallen to 47 per cent., in 1900 to 23 per cent., and in 1902 to 8 per cent. The problem here was somewhat more complicated, since a few cases occur among the general population as well as in the miners.

Ankylostoma Infection in Cornwall.

In Cornwall ankylostoma infection was first definitely identified in October, 1902, in underground workers in Dolcoath Mine at Camborne. It is impossible now to ascertain how and when infection was first introduced, but it seems probable that it came from tropical countries rather than from the infected continental mines. There is not much interchange of men between metalliferous mines and coal-pits. On the other hand, Cornwall is one of the chief centres of metalliferous mining and the manufacture of mining machinery in the world, and men are constantly going and coming from various parts of Asia, Africa, North and South America, and Australia. One meets, indeed, with men who have worked in mines, chiefly as experts in rock-drilling, in five continents. In many of these places ankylostoma is prevalent on the surface as well as underground, and it is easy to see how infection may have been brought. At Dolcoath the disease began to attract attention about 1895–96, and in 1897–98 the cases of severe anæmia were so numerous as to cause considerable trouble. Most of the cases seem to have arisen in men working in the main engine shaft ("New Sump shaft"), an upcast, warm and wet. At the beginning of 1900 artificial ventilation was introduced, by which means the temperatures in and round the New Sump shaft were somewhat reduced. Most of the bad cases gave up underground work; it is, indeed, extremely dangerous if not impossible for an anæmic man liable to fits of dizziness and faintness to climb about on the ladders and stages underground. Being removed from any chance of reinfection[16] by taking to work on the surface or away from the mine altogether, the great majority progressed more or less rapidly towards recovery, so that, for one reason and another, the disease had passed its worst when its nature was discovered in 1902 by Haldane.

Number of Cases admitted for Anæmia to the West Cornwall Hospital, Redruth.

1893	1	1898	23
1894	3	1899	12
1895	9	1900	11
1896	13	1901	7
1897	29	1902	8

[16] As in Westphalia, Belgium, and Northern France, there has been no extension of infection to the general population in Cornwall, or even to those working on the surface at dressing ore, &c.

At this time, however, cases of anæmia were still numerous enough. The general pallor of the men was very striking on looking at a shift as a whole, and complaints of shortness of breath on climbing the ladders were very frequent. Without anything like an exhaustive search among the 750 underground workers at Dolcoath, we found 14 men with less than 50 per cent. hæmoglobin, and 19 more with less than 75 per cent. The disease, in short, was at that time a material hindrance in carrying on the work of the mine. Examination of men who had no symptoms of ankylostomiasis beyond "bunches" showed that practically every underground worker was infected. In the winter of 1903–04, of 65 men taken at random, 61, or 94 per cent., proved to be worm-carriers. Roughly speaking, therefore, 95 per cent. were infected and 5 per cent. were definitely ill—a severe infection. In the worst Westphalian mines 70–75 per cent. were infected, and at the most about 6 per cent. of those infected showed any clinical signs of anæmia.

Steps taken in Cornwall.

Among Cornish miners there is no trades union organisation or other provision for sickness and invalidity; wages are low, and till the rise in price of tin in 1906 the tin mining industry had for many years been greatly depressed; most of the mines did well if they paid expenses. It seemed, therefore, quite out of the question to undertake anything like the campaign initiated in Westphalia, though the total number of workmen concerned was only about 5000 instead of 190,000. The steps taken to combat the disease were therefore of the simplest kind. Once the nature of the disease was recognised it was, in the great majority of cases, very easy to cure those actually sick by the repeated administration of thymol. The effect of treatment has been almost entirely gauged by the obvious results; no serious attempt has been made to ascertain whether all the worms have been destroyed. Having been restored to a condition of efficiency, therefore, the men returned to work in a place which was still infected. They were, of course, reinfected again and again; any return of symptoms was noted at once and corrected by a dose of thymol. In this way actual sickness from ankylostomiasis has been practically abolished. At the same time steps were taken to introduce sanitary reforms underground. In 1905 a special rule was established by the Home Secretary for metalliferous mines in Devon and Cornwall that—

> The owner, agent, or manager shall cause a sufficient number of suitable sanitary conveniences to be provided above and below ground, in suitable and convenient places, for the use of the persons employed, and to be constantly kept in a clean and sanitary condition, and no person shall relieve his bowels below ground elsewhere than in those conveniences.

In 1904 such sanitary appliances were actually in use in Dolcoath in the form of loose pails which could easily be brought to surface, emptied, and cleaned. On the occasion of an inquiry in 1908 it was found that these pails were properly used, and there was an immense improvement in the conditions underground, it being almost impossible to discover loose fæces anywhere. The general appearance of the men was quite different, and there was none of the general anæmia which had been so noticeable five years before. On carefully going through two-thirds of the underground hands, we could only find one case of anæmia, in the person of a boy who said he felt quite well. A special investigation was made of persons who had come to work in Dolcoath since the introduction of underground pails, and who had not previously worked underground anywhere, or only in mines which were known to be free from ankylostoma. Of 89 persons, mostly boys, who came in this category, 68 (76 per cent.) were found to be infected, and most of them gave a history of having had "bunches" on one or more occasions. This shows that, though now there is no material illness, there has been relatively little reduction in the probability of a fresh worker becoming infected. Larvæ must therefore still be pretty widely spread in the mine, but their abundance has evidently been a good deal diminished. "Bunches" have become less frequent and less severe, and the diminution of illness is not altogether attributable to early diagnosis and treatment, since there has been a great reduction in the number of cases requiring treatment. This confirms the view that severe illness is generally due to massive and repeated infections.[17]

From the point of view of industrial efficiency the same result has been obtained in Cornwall as in Westphalia, and at a small fraction of the cost and trouble. In neither place does the disease now interfere in any way with work, except for the loss of time during compulsory treatment under the German system. But the German system has this great advantage—that it has within a few years very largely reduced the number of men who are capable of carrying the infection to fresh places. This result could not be obtained under the Cornish system except after a very long time. Except in so far as their habits of defæcation may have been educated, any dozen men from Dolcoath are at the present time not much less likely to infect any suitable mine to which they may go than they were eight years ago.

Most of the other important Cornish tin-mines are grouped with Dolcoath in the neighbourhood of Camborne and Redruth. There has always been a free interchange of workmen between Dolcoath and these other mines. But

[17] In consequence of the sinking of a new shaft and some rearrangement of the ventilation the deeper part of the main shaft has lately become a down-cast and the temperatures have been correspondingly reduced.

even before the nature of the disease was recognised, there was much less illness in them and no trouble was caused by the presence of infection. At the height of the epidemic, indeed, Dolcoath obtained such an evil notoriety among the men that many of them left to work in the neighbouring mines which general experience showed to be healthy. No systematic examination has been made of all the mines, but as regards the larger workings it has been ascertained that infection is present and that it has failed to spread because they are on the whole not so deep, cooler, and in some instances drier than Dolcoath. The number of infected men found is as follows :—

Mine.	Percentage of underground hands infected.		
	All men.	Men who had worked in Dolcoath.	Men who had not worked elsewhere.
East Pool	—	—	47
South Crofty ...	—	—	18
Grenville	24	47	15
Tincroft	25	50	9

In West Kitty mine at St. Agnes, a shallow, cold, and dry mine, we found only one man infected; he had recently returned from the gold mines in Mysore. In Levant mine at St. Just, a deep, hot, and wet mine, infection is prevented by the salinity of the water.

Ankylostoma in the Tropics.

It remains to consider what can be done to combat the disease in the tropics, where the severity of its incidence is in many places far beyond anything met with in Westphalian or Cornish mines. Though the importance of ankylostomiasis as a factor in tropical industrial life has been well known for many years, the extent of its ravages does not appear to have been sufficiently recognised. Professor J. Cadman, who is familiar with the disease in Cornwall, tells me, for example, that the workmen in the pitch diggings in Trinidad are for the most part in a wretched state of ankylostoma anæmia, and it is hardly to be expected that efficient manual labour can be done under these circumstances. But the only serious attempt which has been made to combat the disease is the campaign started in Porto Rico after its occupation by the United States in 1898.[18] In 1899 Ashford found that

[18] Reports on Anæmia in Porto Rico, San Juan, 1904, 1905, 1907: Journal of the American Medical Association, vol. liv., 1910, p. 1757.

the prevalent anæmia was due to ankylostoma and not to malaria and bad food as had been commonly supposed. From 1890 to 1899 about 15 per cent. of all deaths were attributed to "anæmia," and following the hurricane of 1899, with its destruction of houses and excessive rainfall, out of 35,781 deaths 11,885 (33 per cent.) were from anæmia. In 1904 a commission was appointed to deal with ankylostomiasis, consisting of P. G. Igaravidez, W. W. King, and B. K. Ashford. On inquiry it was found that at least 90 per cent. of the peasants were infected, and generally so heavily that they were markedly anæmic. About half the agricultural population (i.e., some 300,000 persons) appear to have had 50 per cent. or less hæmoglobin. Thus in one series of 343 cases blood examination showed:—

Hæmoglobin.	Persons.	Hæmoglobin.	Persons.
Below 20%	17	60–69 %	32
20–29	64	70–79	20
30–39	78	80–89	8
40–49	75	90–100	3
50–59	46		

This is in marked contrast to the degree of anæmia found among Belgian coal-miners. Of 200 cases recorded by Herman and Dascotte [19] only two had less than 60 per cent. hæmoglobin.

Hæmoglobin.	Persons.	Hæmoglobin.	Persons.
Under 50 %	1	70–79 %	71
50–59	1	80–89	103
60–69	7	90–100	17

The peasants worked mostly on coffee plantations and were strangers alike to latrines and boots. The moist, warm soil was saturated with fæces in the neighbourhood of their houses. Having established the overwhelming importance of ankylostoma, the commission in 1904 treated 5490 cases with thymol, partly in hospital, but mostly as dispensary out-patients. Of these, 48 per cent. were cured, 31 per cent. improved, and 0·5 per cent died, while 19 per cent. were lost sight of. With such encouraging results the treatment was in subsequent years carried out on a larger scale. Thus in the year ending June 30th, 1907, there was a central station with 34 dispensaries in different parts of the island. Patients attended at these stations, had their stools examined, and received appropriate anthelmintic drugs, which were in nearly all cases taken away and consumed at home. A week later the stools were re-examined, and so on till eggs were no longer found or the patient ceased to return. In this way 89,233 patients—i.e., 11 per cent. of the whole

[19] Bulletin de l'Académie Royale de Médecine de Belgique, vol. xxii. 1908, p. 75.

population—paid 425,131 visits to the dispensaries: in 30 per cent. the clinical type of disease was slight, in 43 per cent. moderate, and in 27 per cent. severe. The results were as follows:—

Cured	22,936 = 25·7%
Practically cured...	15,507 = 17·4
Under treatment	36,132 = 40·5
Ceased to return	14,451 = 16·2
Died	193 = 0·2

Under the heading "cured" are included only those cases whose fæces failed to show eggs and whose blood was restored to a normal condition as judged by the hæmoglobinometer. The "practically cured" group comprises those who had had four doses, a treatment found by previous experiments to expel 96 per cent. of worms. Those who "ceased to return" were doubtless also benefited by such treatment as they had.

Treatment consisted of 60 grains of thymol in two doses with sodium sulphate as a purgative. Each patient received with the medicine a card with the following instructions:—

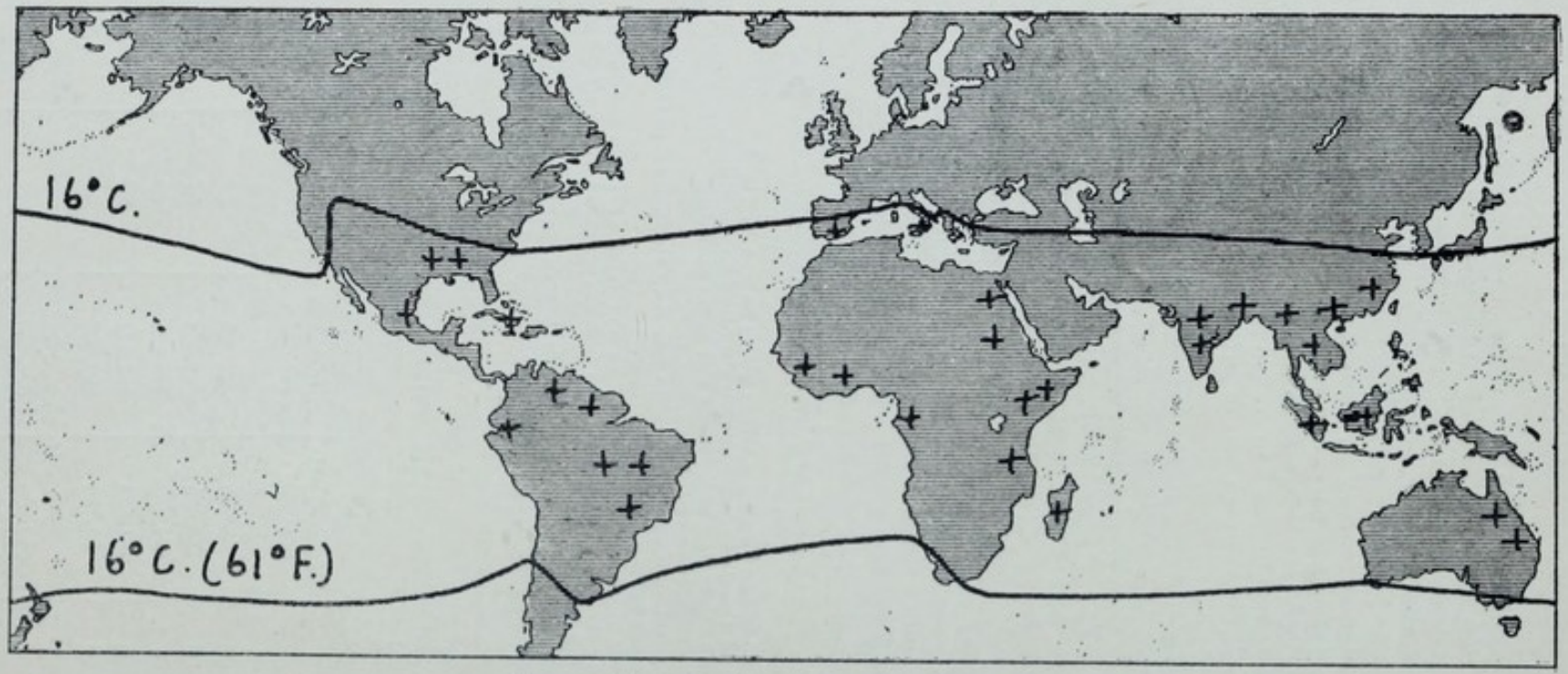
Anæmia Commission of Porto Rico.

Take one of the two purgatives given to you to-night.
Take at 6 o'clock to-morrow morning half the capsules.
Take the other half at 8 o'clock the same morning.
Take a purgative at 10 o'clock.
You should neither drink wine nor any alcoholic liquor during the time you are taking these medicines.
Come for more medicines until the physician says you are cured.
Have a privy in your house. Do not defecate on the surface of the ground, but in the privy.
Do not walk barefooted so that you may avoid contracting mazamorra in your feet. Wear shoes, and you will never suffer from anæmia.

The following table summarises the work done in 1904–09:—

—	New patients treated.	Number of visits.	Number of deaths.	Amount spent.
1904–05	5,490	22,000	27	£991
1905–06	18,865	76,896	67	2,162
1906–07	89,233	425,131	193	9,823
1907–08	81,375	472,407	93	11,390
1908–09	54,725	305,698	46	6,472
Total ...	249,688	1,302,032	426	£30,838

FIG. 3.



Geographical distribution of ankylostoma.

Since 1909 Dr. Ashford tells me that the total number treated has reached just about 300,000, of whom the great majority (over 90 per cent.) have been turned from sick into well persons at a cost of about 2*s.* 6*d.* apiece.

It is, of course, hopeless under these conditions to attempt directly to kill off the worm altogether either in men or in the soil. But Dr. Ashford and his colleagues, besides contributing a great number of valuable observations on the pathological and medical aspects of the disease, have given a convincing demonstration of the possibility of minimising the ill-effects of infection. By reducing the number and intensity of infections and by regulating the disposal of fæces the infectivity of the soil will in course of time become very much less; the introduction of the habit of wearing boots should to a large extent prevent the access to man of what larvæ still persist (Fig. 3). It is much to be regretted that similar operations have not been undertaken in other places where, as in Trinidad, British Guiana, or Assam, the conditions are much the same.