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HOOKWORM INFECTION

HOOKWORM disease is an essentially preventible disease; it is easy to diagnose, easy to cure, and easy to prevent. Yet in India, as well as in many other parts of the world, millions are allowed to suffer from it. One reason for this is that it is not a dramatic and deadly infection like cholera, nor an insidious and deadly one like tuberculosis, but it is none the less a serious debilitating infection that affects whole populations decreasing their working capacity and increasing their susceptibility to other infections over many years. Again, it is not a disease in which a chance infection, by possibly a single organism, sets in train a series of pathological processes that eventually culminate in a serious disturbance in health of short or long duration, but in that the infection—or 'infestation' as some writers prefer to call it to distinguish it from 'infection' where multiplication of the parasite occurs within the host—acts quantitatively and cumulatively, it is more like a slow chemical poison to which the victim must be subjected over a long period of time before the full effect is apparent.

A single pair of hookworms finding their way into the intestine will settle down in the intestinal mucosa, take their negligible ration of blood, and produce a negligible amount of 'toxic' substance; they will live their allotted span of, say, five years, and die, and then their bodies will pass out harmlessly, leaving the host no worse off than when they entered his body. However, what they will have done during their sojourn that is not negligible is to have passed some millions of ova, which, though incapable of harming the host himself at the time, given suitable conditions will develop into an army of larva which, to borrow the technique of the realistic writer, placed end to end would reach from the tea garden in Assam to the company's head office in Leadenhall Street. In actual fact, they will not of course reach anywhere but will remain where they are in the warm damp soil ready to infect the next passer-by.

The individual thus infected with a single pair of worms, or even up to as many as 50 worms, is, in the vast majority of cases, not a medical problem at all, but he *is* a public health one; he can carry his light load of hookworms without detrimental effect to himself, and, if he is not subjected to further infection, the hookworm load will not increase, but as long as he defæcates indiscriminately in the fields around his house, or where he works, he is scattering infection that will remain a continuous source of danger to which he and his bare-footed companions will be continually subjected.

Pathogenicity is ultimately a matter of load. It must be granted that there are some subjects who will carry with complete impunity a heavy load of hookworms that would cause serious symptoms in others, and that even a light load may upset a particularly suspectible individual; nevertheless in the long run, where large numbers are concerned—and the hookworm problem only becomes a problem where large numbers are concerned—environmental conditions being equal, the individual with heaviest hookworm load will suffer the worst disabilities, attributable to hookworm infection. Thus, chance infection (using the word to refer to the process of becoming 'infested'), unless this chance infection happens to be a massive one as it has been in rare instances reported in the literature, is unimportant; it is the continuity of the infection and the summation of the infestation that matters.

The hookworm egg develops in the damp soil into a larva and that larva, awaiting its chance (which incidentally is in most circumstances rather less than that the holder of a single ticket has of winning the Derby sweep), settles on and eventually penetrates the skin of a prospective host; after a six-weeks journey through his tissues the larva finds its way into the intestinal canal and becomes a mature worm. There, lying attached to the mucous membrane of her host and sucking his blood, not only to meet her nutritional needs but, wantonly, the female worm passes her eggs, which mixed with the fæces are placed back on the soil wherever the host defæcates; the cycle is thus complete.

This cycle has a number of vulnerable points. The most vulnerable of all is during the egg and larval stages in the soil. In a dry soil, in either a hot or a cold climate, they will not survive for more than a few days, but in a hot damp one they will live for some weeks. It is this fact that determines the varying distribution of hookworm infection in different parts of the country where the habits of the populations are similar. The next two weak points in the cycle are where the ova leave the host and where the larvæ enter again; in the first case, if the eggs are not passed into the soil but into a septic tank they will be destroyed, and, in the second, as larvæ do not migrate any considerable distance, if nobody passes over the spot where the larvæ are waiting, or if feet are protected properly by shoes—ordinarily shoes do not present an impassable barrier—again the cycle will be broken.

The Indian villager usually defæcates in the open ground near his home, in the process he welds both weak points in this cycle, for he scatters the infection on a suitable medium and at the same time becomes further infected himself. On tea estates matters are worse, for

it is common practice for the coolie to defæcate amongst the tea bushes where he or she and the other bare-footed labourers stand for many hours during the day.

At the same time this is a point at which a complete break in the cycle could be effected by the introduction of efficient sanitation, by the provision and the exclusive use of latrines suitable for the particular locality. Once the ova have reached the soil, if nature does not destroy them, man has little chance of doing so; no really successful method of soil sterilization has ever been put into practice. Nor is it a practical measure to attempt to stop infection by the use of shoes. Shoes or boots naturally form some protection, especially in moderately dry weather, but during the rainy season the larvæ will penetrate a comparatively sound pair of boots, even if larvæ-infected mud does not find its way through lace holes.

The last weak point is in the intestinal tracts where the worm can be subjected to the effect of drugs taken by the patient. Attack at this point will only reduce the worm load of the patient temporarily, for, meanwhile, if he is still following his ordinary habits, he will be re-infecting himself all the time. Treatment can only effect a break in the cycle if it is associated with a change of defæcating ground, and if it includes the whole population; even then it would have to be repeated in order to catch the larvæ migrating through the tissues, unless it were done at a time of year when no reinfection was taking place.

It must be apparent that the only really efficient measure for the permanent reduction of hookworm disease is the introduction of a system of satisfactory latrines, and this fact should never be lost sight of by sanitarians and employers of labour. The latrine problem is a difficult one, but a beginning must be made and medical officers responsible for the labour in industrial concerns should do everything to make their employers realize the vital importance of making some sort of beginning in the matter of latrine provision. The Factories Act of 1934 has made it compulsory to supply latrines in factories and this has focussed attention on the subject. The form the latrine should take will be dictated by circumstances. The bored-hole latrine (*I. M. G.*, **70,** 391) has the advantage of low cost so that individual or household latrines can be installed, with their obvious advantages over communal latrines which one does not need to be fastidious to appreciate. The bored-hole latrine is not, however, suitable in all circumstances nor for all terrains (*I. M. G.*, **76,** 126) and in a recent number another useful form of latrine was described (*I. M. G.*, **75,** 677).

The whole crux of the matter is the maintenance of the latrines in a cleanly state. If they are not kept clean they will not be used habitually and further they will attract flies and in themselves become an actual danger. On the other hand, a clean and efficient sanitary system will solve other more serious medical problems, as well as that of hookworm disease.

Anthelminthic drugs.—Millenia-old customs cannot be changed in a day, or even in a year or two, and therefore other methods of controlling hookworm disease must be considered. The alternative is wholesale anthelminthic treatment. As we have indicated above, this deworming has to be very thorough and very complete to effect control of the disease in the whole population, but even with this limitation it is worth attempting, for it will reduce the source of infection which in turn will reduce the chances of re-infection, even if it falls short of achieving a complete disinfestation of the whole population. Further than this, it will confer a considerable benefit on the individuals treated, at the time and for a year or so, until they have again become heavily reinfected.

Twenty-five years ago, the treatment of hookworm infection presented a serious problem; chloroform and thymol, the only specifics, were not very efficient and were extremely expensive. Beta-naphthol was useless in small and dangerous in effective doses. Then oil of chenopodium appeared; it was a more efficient drug and less discriminating, in that it destroyed other helminths, *e.g.*, ascaris, as well as hookworms, but it was variable in its ascaridol content for which constituent it depended both for its efficacy and its toxicity. Oil of chenopodium is now a pharmacopœial drug, its ascaridol content is standardized, and it has taken its place as a useful anthelminthic. Next carbon tetrachloride ($C Cl_4$) was introduced (1921); this is a drug of undoubted efficacy as an anthelminthic and was used by the Rockefeller workers in extensive hookworm campaigns in the American continent. It was given in hundreds of thousands of cases by some workers without causing any ill-effects, but in the hands of others fatalities were reported. Given in large doses it damages both the liver and the kidneys; on rare occasions the same thing occurs when it is given in therapeutic doses. With a drug of this kind absolute safety is essential, as a few fatalities will ruin a treatment campaign. If out of a thousand coolies receiving carbon tetrachloride one fairly healthy man dies during the night following his treatment, which was intended to cure him of an infection he didn't even know that he was suffering from, it is useless to explain to his friends that at least ten of the 999 other coolies would probably have died of some disease acquired through the debility of hookworm infection, had they not been treated, nor is it any consolation to his relatives to know that the man himself would not have died had he not had a drinking bout the night before. This sort of things happened far too frequently on tea gardens and elsewhere in this country for carbon tetrachloride to be received with any enthusiasm for wholesale treatment, and its use

was limited to conditions where the patient could be treated in hospital and kept under observation for at least 24 hours, or could otherwise be trusted not to take any alcohol.

Then, in 1925, came the closely related drug tetrachlorethylene (C_2Cl_4); no great publicity was given to its début, for meanwhile the attention of the Rockefeller Foundation had been deflected into other channels and the same extensive hookworm campaigns were not being undertaken. It was found that tetrachlorethylene caused no damage to the livers of cats and dogs when administered in large doses even with alcohol (*I. M. G.*, **68,** 554). The first clinical trials with this drug did not indicate that it had any special advantages over carbon tetrachloride, but in India the fact that it was a safe drug attracted attention and it has been used very extensively during the last decade (*I. M. G.*, **64,** 424; **68,** 617; **69,** 500; **72,** 650; **74,** 198; **75,** 652).

Meanwhile, further reports have come from America where, though it has been used in hundreds of thousands of cases, only one case of temporary ill-effect has been reported. All these reports indicate that it is at least as good as carbon tetrachloride in its anthelminthic action.

Thymol.—A quarter of a century ago thymol held an important place as an anthelminthic, but its numerous disadvantages, the high cost, the difficulty of administration, its toxicity, a subject to which C. A. Lane devotes over seven pages in his book *Hookworm Infection,* and its relative inefficacy necessitated further research for a better anthelminthic. Thymol was first introduced by Bozzolo in 1879, but its principal advocate was Ashford, a geat American helminthologist, so great that when other more efficient anthelminthics were introduced he acknowledged the fact; before his death some eight years ago Ashford came into line with nearly all other American helminthologists and admitted the anthelminthic inferiority of thymol compared with oil of chenopodium, carbon tetrachloride and tetrachlorethylene. In this country, thymol was used extensively, particularly by C. A. Lane, up to twenty years ago, but since then it has been displaced by other, more efficient anthelminthics. To all intents and purposes, as a practical anthelminthic for extensive administration to hookworm-infested populations, thymol died twenty years ago, since when from time to time its ghost has flitted, often rather aggressively, through the pages of our invaluable contemporaries the *Lancet* and the *Tropical Diseases Bulletin.* In order to exorcize this ghost, Maplestone and Mukerji undertook an investigation on the comparative anthelminthic properties of thymol and tetrachlorethylene (*I. M. G.*, **75,** 193). The results of this trial were entirely convincing; they showed that a single treatment with thymol left behind 38.1 per cent of *Ancylostoma duodenale* and that after a second treatment with thymol 22.1 per cent of worms still remained to be removed by other drugs. After a single treatment with tetrachlorethylene only 3.8 per cent of worms were left and after a second treatment none. In the case of *Necator americanus,* both drugs were more successful; the first treatment with thymol left 6.8 per cent of the worms and that with tetrachlorethylene less than one per cent. In a single treatment with thymol only one patient in a series of 25 was cured, and in three others the infestation was reduced to a negligible figure; this left 21 requiring further treatment. With a single treatment with tetrachlorethylene, nine were cured and in 13 others the infestation was reduced to a negligible figure; this left only three requiring further treatment.

Perhaps more significant is the fact that 12 patients received three courses of thymol; the first course removed 679 *A. duodenale,* the second 183, and the third 43; as these patients still showed a significant infestation, thymol was superseded with the result that of 108 worms that had survived three courses of thymol 105 were removed in a single treatment with tetrachlorethylene.

The evidence as it stands to-day seems to indicate that tetrachlorethylene, with its copybook unblotted over a period of more than ten years, is a safer drug than thymol, with its doubtful past record, but we will not press this point; tetrachlorethylene is at least as safe, it is infinitely more efficacious, it is far cheaper, and it is easier to administer. It seems, therefore, to us that it is quite time that the thymol wraith was finally laid.

Thus, if the control of hookworm disease by disinfestation of the population is to be attempted, tetrachlorethylene is the most satisfactory single drug. This should be given in doses of 4 c.cm. for adults, with correspondingly small doses for children. It is best administered shaken up in two ounces of saturated solution of sodium sulphate, in a single dose; individual doses must be shaken up separately and taken quickly, as the tetrachlorethylene tends to settle very rapidly. A single treatment will effect the removal of 99 per cent of necators and 96 per cent of ancylostomes; a second treatment, say a month later, is obviously indicated where complete disinfestation is the aim, especially if ancylostomes predominate.

Hookworm anæmia.—From the public health point of view, that is all that need be done, but from the point of view of the individual the matter should not be left here. The main disabilities that the individual with hookworm infection suffers are a direct result of the anæmia. This anæmia is produced mainly by the slow but steady draining of the blood of the host by the hookworms attached to the intestinal mucosa, with the resulting exhaustion of iron reserves. The anæmia produced is microcytic and hypochromic, and is a true secondary

anæmia; the toxic action of the hookworm metabolites on the hæmopoietic organs is of secondary importance.

On the important subject of the treatment of this anæmia, C. A. Lane in his book *Hookworm Infection* has but two paragraphs, he writes :— 'Anæmia is the main secondary feature requiring treatment and iron is the standby'. So far so good, but he goes on 'Nevertheless so long as infection persists the giving of iron is in general useless; and even after disinfestation the hæmopoietic organs, *particularly the bone marrow,* may be in no position to use the iron which is placed at their disposal until arsenic, organic or inorganic, has been added to the medication'. In our opinion there is not the slightest evidence to support such a statement; it is possible by iron administration alone to bring the hæmoglobin up to a level well within the normal range of the patient's class, even in a very heavily infected patient (*I. M. G.*, **76,** 1), and there is no foundation for the suggestion that after the removal of the worms there is any depression of hæmopoietic function, or that if there were arsenic would remove it.

The remaining paragraph is given, without comment, to complete the quotation. 'There is evidence that traces of copper are necessary. It is unknown whether the carbon tetrachloride which accumulates in the bone marrow after treatment by that drug produces lesions which hinder subsequent recovery from anæmia. The occasional likeness of the blood picture of ankylostomiasis to that of pernicious anæmia indicates on general principles the giving of liver or red marrow; which might perhaps also prove useful in anxiety after carbon tetrachloride administration'! Elsewhere, Lane has severely criticized writers who have laid special emphasis on iron administration in hookworm infection. It is no more irrational to treat the anæmia before removing the worms than it is to give symptomatic treatment in any other disease; frequently such treatment is definitely indicated first, to be followed later by the removal of the cause. This is sometimes the case in severe hookworm anæmia, when, for the comfort of the patient, it may be better to give a course of ferrous sulphate before administering the anthelminthic, though the natural sequence is to remove the majority of the worms by one treatment and then to treat the anæmia.

It is, on the other hand, utterly absurd to remove the worms only and allow the patient to linger on for many months in an anæmic state. Indian dietaries are usually poor, if not actually deficient, in available iron and therefore many people live on the border-line of iron starvation. On such a diet, it will be months, possibly even years, before an individual can make good his iron deficiency and build up a reserve, whereas by suitable treatment this can be achieved within a few weeks. In many cases, the disappointments with the immediate results of a hookworm campaign that have been experienced are due to this simple fact. The propaganda value of curing the anæmia should not be underrated; the immediate improvement in well-being experienced by the patient and the immediate increase in his working capacity will impress the patient and his employer far more than a post-dated promise of such improvement.

The most convenient and cheapest way to administer iron is in the form of ferrous sulphate tablets, nine grains twice daily. Ferrous iron in the form of a mixture is probably more efficacious; ferrous ammonium sulphate made up with glucose will 'keep' for some weeks, and of this mixture a dose containing twenty grains of the iron salt (equivalent to a little under three grains of metallic iron) should be given twice daily.

We will conclude by saying that no hookworm campaign is complete unless a three-point attack is made, the spread of infection curtailed by provision and habitual use of suitable latrines, the disinfestation of the individuals affected by a suitable anthelminthic, preferably tetrachlorethylene, and the anæmia cured by the administration of iron in large doses. The provision of latrines alone, even if they are used exclusively, will only effect appreciable improvement in the course of a few years but the improvement will be permanent. Deworming alone is often disappointing, unless very thoroughly carried out in the whole population, as it takes many months for the blood to improve sufficiently to be reflected in the clinical picture and meanwhile reinfection will be taking place all the time. Administration of iron alone will produce a marked and immediate improvement in health, but this improvement will disappear within a year or so. Thus, the most permanent results will be obtained by the first measure, the most spectacular by the last, whereas in practice the second is the one that is most frequently put into operation.

L. E. N.

Special Articles

HÆMATOLOGICAL TECHNIQUE

PART IX

By L. EVERARD NAPIER, F.R.C.P. (Lond.)
and
C. R. DAS GUPTA, M.B. (Cal.), D.T.M.
(*From the School of Tropical Medicine, Calcutta*)

(15) *Gastric analysis*

Introduction.—The gastric juice in the normal individual contains hydrochloric acid, free and in the combined state, the enzymes pepsin and rennin, and the 'intrinsic factor of Castle'. Examination of the aspirated gastric juice, primarily for acidity, but also for the presence of the enzymes, and for other normal and abnormal characters, is known as gastric analysis.