

Original Articles.

THE TREATMENT OF ANKYLOSTOMIASIS,
OR HOOKWORM DISEASE.

BY CLAYTON LANE, M.D.,

MAJOR, I.M.S.,

Civil Surgeon, Darjeeling.

THIS paper has been written at the request of the Committee of the Darjeeling Planters' Association, and its point of view is that which it is hoped will prove most useful in obtaining a healthy and efficient labour force. The loss of efficiency caused by a moderate degree of infection with hookworms is a fact which is possibly not widely realised, and it would probably be of commercial advantage in many cases to treat the whole labour force for hookworms at regularly recurring intervals of from 6 to 12 months. It may, however, be again pointed out that the prevention of infection by the proper disposal of faeces is the ideal at which one has to aim, both medically and economically.

The treatment of ankylostomiasis resolves itself into two parts, the expulsion of the parasites, and the removal of any ill-effects which these may have produced, of which the chief is anæmia. It is not necessary to go into any detail regarding the treatment of the anæmia with iron and other drugs, except to say that improvement will not occur until the parasites have been removed. This paper will then deal entirely with the question of the best method for securing the expulsion of the parasites.

Before entering into details regarding the different possible lines of treatment, it will be wise to consider a few important points, equally applicable to them all. The first of these is that no single course of treatment by any known drug or combination of drugs can be relied upon to expel all the ankylostomes which are present. This means, of course, that one cannot expect to get rid of all the worms with less than two courses of treatment, and that more even than these may be required. How many courses must actually be given may be determined in one of two ways—either by actual observation, or by inference.

Actual observation can be carried out, by a medical man with many duties, only if an occasional case has to be treated and if the patient is in a hospital. It may be done in one of two ways. If a microscope be available it will be possible to determine after each course of treatment whether ankylostome ova are still present in the stools. In relying on this test it is essential to remember that there is a fallacy underlying it, namely, that any course of anthelmintic treatment interferes

with the egg-laying power of such ankylostomes as are left behind that no eggs are found in the stools for some days after the course is finished. This effect often lasts for nearly a week, and rarely may last apparently as long as a fortnight. It is therefore useless to examine the stools for ova until nearly a week has passed since the last anthelmintic course. It is well too to remember another better known fallacy, namely, that it is not possible to say by the examination of one microscope slide only that there are no ankylostomes left in the bowel, but that at least 15 slides must be looked through before it can be said, with any approach to certainty, that this is the case.

If no microscope be available it is possible to ensure a complete cure by repeating the courses of treatment till no more ankylostomes are passed. Apart from the difficulty of being certain that the person to whom the disagreeable duty of washing and searching the stools is entrusted carries it out properly, it is well to remember that after a course of treatment ankylostomes may continue to be passed for about a week, so that if absolute accuracy is wanted all stools passed within that period must be examined. This also is one of the reasons for not following one course of treatment by another at an interval of less than a week. Absolute accuracy too entails the giving of an unnecessary course of treatment; that is to say the last treatment, which results in the passage of no worms, is unnecessary.

In view of the large amount of labour and time required to ensure accuracy it is obvious that the number of courses of treatment required will in most cases have to be a matter of inference, that is to say, will be merely the number which actual experience has shown to be *usually* sufficient. This number varies for different drugs and will not be correct in every case; but it is sufficiently accurate for practical purposes, and is usually the only method available for the use of those for whom this paper is intended. It will be shown presently how this method can be used with a reasonable degree of accuracy.

Passing now to the drugs to be actually employed it is convenient to note first that the essential character of an anthelmintic is that it should be a drug which will poison the worms without poisoning their host; and so it comes about that anthelmintic drugs are almost insoluble in water and cannot readily pass through the intestinal wall into the circulation and poison the host. The sole exception to this rule is chloroform, and the measure of safety associated with this drug lies evidently in the fact that it is very rapidly excreted from the blood by the lungs, the excretion being practically as rapid as the absorption. Since the whole essence of anthelmintic treatment is that the drug used should poison the

worms without poisoning their host, it is obvious that the less of the drug which can be used for this purpose the less chance is there of the host being poisoned. It is equally obvious that the emptier the bowel the more concentrated will be the drug, and the less of it will be required to kill the parasites. Accordingly it will always be of great advantage to empty the bowel as far as possible before any anthelmintic is given. This will be greatly assisted by a light diet on the day before treatment is begun, particularly in the case of natives of India whose ordinary food is very bulky and contains a large amount of indigestible matter. It is not however always easy to arrange this, and in any case the contents of the bowel can be greatly lessened in amount, and the concentration of the anthelmintic drug correspondingly increased, by a sharp purgative taken the evening before the vermifuge is administered. A tablespoonful of Epsom salts forms a satisfactory purge.

Although many drugs have been used from time to time for the expulsion of ankylostomes, there are only four lines of treatment which have hitherto proved useful. They are as follows:—

THE EUCALYPTOL TREATMENT.—After the usual preliminary treatment on the previous evening, and as soon as the bowels have been opened next morning, a dose of fifteen minims of oil of eucalyptus, twenty-five minims of chloroform, and five drachms of castor oil is given, and is repeated in half an hour.

THE BETANAPHTHOL TREATMENT.—After the usual preliminary treatment on the previous evening three doses, each consisting of ten grains of betanaphthol, are given at 6, 7, and 8 A.M., and a dose of Epsom salts at 10 A.M.

THE THYMOL TREATMENT.—This is precisely the same as the betanaphthol treatment except that each of the three doses consists of twenty grains. In this case, as in the last, the drug can be given in cachets or in emulsion.

THE CHENOPODIOL TREATMENT.—After the usual preliminary treatment fifteen minims of oil of chenopodium are given on sugar at 6, 8, and 10 A.M., and at noon an ounce of castor oil.

The next matter to be considered is the relative advantages and disadvantages of these different treatments from four different points of view:—

1. THE CLINICAL POINT OF VIEW.

(a) **THE EUCALYPTOL TREATMENT.**—Major B. K. Ashford, Medical Corps, U. S. Army, of the Porto Rico Anæmia Commission, says:—“The use of eucalyptol is absolutely unjustifiable; it is very dangerous and well nigh impossible to repeat on account of the resistance of the patient, the chief symptoms being extreme debility, dizziness, dyspnoea, and syncope. In our short experience with the drug it was generally

necessary to administer stimulants to prevent a fatal result.”

On the other hand Manson says of it:—“It is a very efficient vermifuge much less unpleasant and much less dangerous than thymol or betanaphthol.”

I have personally used it in some hundreds of administrations, and have very rarely had any untoward symptoms arising. I possess also intimation as to its gratifying success in out-patients. The treatment paralyses rather than kills the ankylostomes, and the castor oil is an essential part of it; for the ankylostomes must be expelled before they recover from the stupifying effect of the drugs and attach themselves again to the wall of the gut.

(b) **THE BETANAPHTHOL TREATMENT.**—Such of the drug as is absorbed from the bowel into the circulation is excreted by the kidneys, and in its passage through these organs is apt to produce a dangerous or fatal acute inflammation, if the kidneys are not previously sound. In severe ankylostomiasis the kidneys are frequently in a state of fatty degeneration, and very susceptible to damage, so that, before giving the drug in these extreme cases, it is important to be certain that there is no albumen in the urine. The drug is a direct poison to the worms.

(c) **THE THYMOL TREATMENT** may cause a good deal of burning in the stomach, irritation of the bowel, dizziness and depression, and in this case also such of it as is absorbed is excreted by the kidneys and may irritate these organs if they are not sound. It is therefore not a good drug to use in gastritis, dysentery, heart-disease, old age, great debility, or where there is albumen in the urine. It is a direct poison to the worms.

(d) **THE CHENOPODIOL TREATMENT** has hitherto not been extensively used for any medical purpose, so that what is said about its safety must be accepted with some reservation. The plant from which the oil is obtained is a common weed over large tracts of America, but in spite of this only 12 cases of poisoning have been reported over a period of more than 50 years. Of these cases 8 proved fatal. It appears to act on the central nervous system, and in all the fatal cases the doses appear to have been excessive. It merely paralyses the worms, and does not immediately kill them, and in itself is rather constipating; so that, as in the case of the eucalyptol treatment, an aperient must accompany the drug.

In severe cases of ankylostomiasis all these drugs require to be used with caution, that is to say the doses should be smaller, and the number of courses of treatment should be correspondingly increased. It is probable that Ashford's cases treated with eucalyptol were of this nature; otherwise it is difficult to account for his anxieties. In giving thymol it is very important

to remember that it is very soluble in alcohol and in oils, and that when dissolved it will be rapidly absorbed and will become poisonous to the host of the parasites. It is true that some physicians, particularly Bozzolo, the originator of the treatment, deliberately give enormous doses of thymol and then give alcohol in order to increase its effect. On the other hand the American experience, the largest in the world, lays great stress on the importance of care in this direction. Deaths do undoubtedly occur if care is not taken, and the Americans are so convinced of the need for this that they even exclude milk from the preliminary diet, in case an excess of thymol might be dissolved by the fat of the milk, be absorbed, and produce poisoning. For a similar reason castor oil ought not to be used as the purgative accompanying this treatment. It is also with a view to preventing poisoning that certain Americans have recently advised the practice, advocated above, of giving the thymol in three doses of twenty grains each instead of in two doses of thirty grains each; for if serious symptoms should show themselves the rest of the treatment can be stopped and the total amount taken will be less. In cases with great weakness the preliminary purging should be omitted, and the doses reduced, as mentioned above, to a half or a third of the standard dose. The remarks regarding thymol apply equally to betanaphthol. Chenopodiol appears likely to prove a safe vermifuge, when reasonable care is taken over its dosage. In spite of practice by some to the contrary it is strongly advised that the standard doses given above be never exceeded; and that in cases where the kidneys are unsound either the eucalyptol or chenopodiol treatment be used in decidedly reduced doses. It is also urged that for safety's sake the rule of not following one treatment by another with an interval of less than one week be never broken. With attention to those points none of the treatments can be considered as unsafe.

2. THE HELMINTHOLOGICAL POINT OF VIEW.—By this term is meant the readiness with which the species of ankylostome passed can be identified. If ankylostomes, while still alive, be dropped into hot seventy per cent. spirit they take up characteristic attitudes at the moment of death, and the different kinds can be readily differentiated from one another without the microscope. In determining the relative distribution of the different ankylostomes it is a great advantage to have the ankylostomes passed while still alive, and in these cases the use of either eucalyptol or chenopodiol is strongly to be recommended.

3. THE POINT OF VIEW OF EFFICIENCY.—It has been noted above that one course of treatment will not usually expel all the hookworms present in any particular person. This fact has been used in the following way to ascertain the

relative efficiency of different drugs. In a number of cases two different courses of treatment have been given to each patient one after the other. The first course has varied and the second has consisted of thymol. The worms in every case were counted separately for the two sets of treatments, and the relative numbers ascertained. Reduced to percentages these figures were as follows:—

Eucalyptol	removed in the first treatment	38%	} of the whole number recovered.
Betanaphthol	" " "	68%	
Thymol	" " "	83%	
Chenopodiol	" " "	91%	

These are average figures and they show the truth of the statement made above that no single course of treatment by any known drug or combination of drugs can be relied upon to expel all the hookworms present. The percentage of worms left behind after two courses of treatment by chenopodiol or thymol is so small that for practical purposes one may look upon two courses as all that are necessary. Regarding betanaphthol one course of treatment will remove 68% of the worms, and leave behind 32%. The second course will remove 68% of those that were left behind after the first treatment, but even then there will remain a fairly large percentage, requiring a third course of treatment to effect a practical cure. Similar reasoning gives five courses of eucalyptol as necessary to effect the same purpose. For a reason which will be plain presently we will call these figures "the Units of Inverse Efficiency" and tabulate them thus for convenience:—

	Unit of Inverse Efficiency.
Eucalyptol treatment	5
Betanaphthol treatment	3
Thymol treatment	2
Chenopodiol treatment	2

4. FROM THE POINT OF VIEW OF EXPENSE.—The expense of effecting a cure may be looked upon as a combination of three factors, namely, efficiency, dose, and cost per pound of the drug or drugs used. These factors can be reduced to a formula by means of which the relative expense involved in the use of the different anthelmintic courses at any particular time can be immediately ascertained. The formula consists of three sets which we will call the Unit of Inverse Efficiency, the Unit of Dose, and the Unit of Cost.

The Unit of Inverse Efficiency has Just been considered.

The Unit of Dose is the weight of the dose of betanaphthol required for a full treatment, that is thirty grains. Taking this as 1, the unit for eucalyptol treatment will be 2.6, that is to say thirty minims of oil of eucalyptus equivalent to 1 unit, and fifty minims of chloroform equivalent to 1.6 units. The dose of thymol, being sixty grains for the treatment, is equivalent to 2 units; and the dose of chenopodiol being

forty-five minims represents 1.5 units. These may be tabulated as follows:—

Eucalyptol.	Dose in grains or minims.	Unit of dose.
—Oil of eucalyptus ...	{ 30	{ 1
—Chloroform ...	{ 50	{ 1.6
Betanaphthol ...	30	1
Thymol ...	60	2
Chenopodiol ...	45	1.5

The Unit of Cost is merely the expression in decimals of the cost per lb. of the drugs which are used. These of course vary from time to time, and are doing so enormously now as the result of the war. The figures given immediately below represent the present cost of the drugs in India, with the exception of Chenopodiol, which is practically unobtainable here, but which is quoted in England at 1s. 6d. per oz., and could presumably be landed in India at the price given in the table:—

Eucalyptol.	Cost per lb.	Unit of cost.
—Eucalyptus, oil of, ...	Rs. A. { 2 0	{ 2
—Chloroform ...	{ 2 12	{ 2.75
Betanaphthol ...	3 8	3.5
Thymol ...	16 0	16
Chenopodiol ...	24 0	24

Whether the reader has or has not followed the preceding argument is immaterial for my present purpose, so long as he realises that, in order to ascertain the relative cost of these different lines of treatment all that is necessary is that he should multiply together the three different units given above, having first satisfied himself as to the correctness of the unit of cost which he is using. The only point which is not quite straightforward is in the case of the eucalyptol treatment, where there are two different drugs to be considered. In this case the unit of dose and the unit of cost for chloroform must be multiplied together, and the unit of dose and the unit of cost for oil of eucalyptus must be multiplied together separately, the two results added together, and the total so formed multiplied by the unit of inverse efficiency for the treatment; which is of course the result of the effect of the two drugs taken together. This sounds rather complicated, but the actual example will show clearly what is meant.

Treatment.	Unit of dose.	Unit of cost.	Unit of inverse efficiency.	Relative cost of treatment.
Eucalyptol—				
Oil of Eucalyptus ...	1	× 2	= 2	
Chloroform ...	1.6	× 2.75	= 4.4	
		6.4 ×	5	= 32
Betanaphthol ...	1	× 3.5	× 3	= 10.5
Thymol ...	2	× 16	× 2	= 64
Chenopodiol ...	1.5	× 24	× 2	= 72

In order to make clear how rapidly the unit of cost is varying at present, there is inserted

here for comparison a similar table showing the relative cost of different treatments as they stood before the war began:—

Treatment.	Unit of dose.	Unit of cost.	Unit of inverse efficiency.	Relative cost of treatment.
Eucalyptol—				
Oil of Eucalyptus ...	1	× 4.7	= 4.75	
Chloroform ...	1.6	× 2	= 3.3	
		8.05 ×	5	= 40.25
Betanaphthol ...	1	× 2.5	× 3	= 7.5
Thymol ...	2	× 7	× 2	= 28
Chenopodiol ...	1.5	× 48	× 2	= 144

In this last table the figures for the first three treatments are taken from the price list of a well known Calcutta firm, and that of chenopodium is the actual price paid for the drug to another Calcutta firm, a price which was no doubt a fancy one.

The way in which the price of thymol has risen since war was declared is very striking. It will rise higher almost certainly, for it has hitherto been made practically entirely in Germany, and is now unobtainable in some parts of the world. It is already quoted in London at 25 shillings a pound.

Oil of chenopodium is obtained from the seeds of *Chenopodium anthelminticum*, a plant which grows as a most pestiferous weed across the southern parts of the United States from Florida to California. It is cultivated in increasing quantity in Maryland, and the manufacture of the oil is almost entirely limited to that part. Since the plant grows so profusely it is at least possible that the difficulties of obtaining thymol, and to a lesser extent of betanaphthol, will stimulate the production of the oil to a degree sufficient to produce a material reduction in its price, and it will be wise for medical officers of tea gardens and other concerns employing large numbers of coolies to keep an eye on its price in the future, bearing in mind that the relative cost of treatment by it is even now little more than that by thymol. At the same time, since the United States requires about 100,000 treatments a year, there does not seem much likelihood of their allowing of much export of the oil for the use of other countries. They will be too hard put to it in the carrying on of their own immense campaign against hookworms to be likely to spare the material they can produce and use in their own country.

It is very plain that the treatment of severe cases of ankylostomiasis requires care and judgment and can only be safely undertaken by a medical man. In these cases expense cannot be the main consideration; but that drug must be used which is the most suitable under the circumstances. On the other hand in mild cases the conditions are quite different. The only

symptoms exhibited may be a certain slight degree of anæmia possibly not noticeable except by special means, with slackness and inefficiency as a worker. With a labour force limited in number and to which further addition is difficult, and which is also relatively inefficient on account of a moderate degree of infection with hookworms, it is proper from the medical point of view, and essential from the commercial one, to use that anthelmintic whose relative cost, obtained by the method explained above, is the least.

So far as the writer is aware the different lines of treatment have not hitherto been presented to practitioners in such a way that they can without difficulty determine immediately (provided they have accurate information as to unit of cost) their relative cost; and it is hoped that the simple formula here put forward may prove of real value to medical officers of tea gardens and other large commercial concerns whose money-earning capacity is interfered with by hookworm infection of moderate degree among their workers.

SHRAPNEL WOUNDS OF THE KNEE-JOINT.

BY C. NEWTON-DAVIS, M.B., B.S. (Lond.),
CAPT., I.M.S.

THE two following cases have many features in common and are not without interest:—

CASE I.

Sepoy Abdullah was admitted to Hospital on November 4th with a history that one week previously while lying under cover he had been struck by a shrapnel bullet in the back of the right thigh.

On admission patient was in some pain and looked worn out after his experiences. His temperature was normal. The right leg was flexed at the knee at an angle of 135°. The joint was rather hot and there was a small amount of fluid in it. Any attempt to move the joint caused great pain. Behind in the middle line 3½ inches above the mid point of the joint was a small punctured wound. Through this a small amount of pus escaped.

The X-ray photograph showed a shrapnel bullet imbedded in the outer and posterior aspect of the inner condyle of the femur (*i. e.*, in the inter condylar notch). The patient was anæsthetised and the limb gently straightened. There was a good deal of resistance felt in the joint. A back splint was applied. This was removed daily, the limb massaged, and the wound dressed. In a fortnight the wound in the popliteal space had completely healed. By this time the swelling in the joint had disappeared. There was

now no evidence whatever of inflammation in the joint or around it.

Up till this time it had been thought inadvisable to passively move the joint and so possibly infect it from the obviously septic channel made by the bullet.

Now, however, daily passive movement of the knee-joint were commenced. Under chloroform, some adhesions were broken down, but full flexion of the joint was not possible.

The removal of the bullet was decided on. Chloroform was administered. The patient was turned on to his left side in the semi-prone position. A vertical incision 5" long was made in the popliteal space ½" to the inner side of the middle line. The track made by the bullet in entering was carefully avoided. The vessels and nerves were retracted to the outer side. All bleeding was stopped and the edges of the wound well retracted. On opening the joint a small amount of clear synovial fluid escaped. The limb was slightly flexed and the posterior part of the capsule opened for 1½". Exploration of the joint with the finger at first revealed no foreign body. A head light was not available and working, as we were, in an improvised theatre, it was not possible to get a good view of the structures inside the joint. Systematic search revealed a chip of bone hidden by a fold of synovial membrane. This fragment had been scooped out of the upper part of the internal condyle by the bullet in its course. Renewed search failed to reveal the bullet, and further operation was postponed and a telephone bullet probe sent for. This instrument in a very short time gave unmistakable evidence of the presence of a metallic foreign body. Following the probe with the finger the rounded surface of a bullet was felt slightly raised above the level of the bone.

The posterior three-quarter of the bullet was firmly imbedded in the bone. It was removed with some difficulty being finally levered out with a gouge. The adjacent bone and joint surfaces were cleared of *débris* and the capsule closed with catgut. The wound was closed, no drain being left. The limb was placed on a back splint. The patient and joint were watched very carefully but no complications arose.

The stitches were removed on the eighth day when the wound was healed.

Massage and passive movements were commenced at once. Movements rapidly returned, and a month after the operation active extreme flexion was painless and the man able to walk without difficulty.

CASE II.

Sepoy Narjit Ali was admitted to hospital on December 2nd with the history that 8 days previously he had been struck in the back of the left knee by a bullet from a bursting shell.