TREATMENT OF TAPEWORM INFECTIONS IN MAN

BY

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Remarkably little information is available on the efficacy of different anthelmintic regimes under standard conditions; assessment of their relative merits is therefore difficult or impossible. In an effort to supply this need, detailed observations have been made on all patients treated for tapeworm infections at the Hospital for Tropical Diseases, London, during the past eight years. The series comprises 240 patients distributed into five main treatment groups, the numbers in each of which are now such as to permit an adequate statistical analysis.

Clinical Material and Methods

Of the 240 patients, 238 were infected with *Taenia saginata*, one with *Taenia solium*, and one with *Dibothriocephalus latus*. There were seven children in the series, all infected with *T. saginata*.

Several methods of treatment were used in chronological sequence, and, as a preliminary to each, all food was withheld from the patients for a period which during the earlier years of the study was usually three days, but which later was reduced to two days. During the period of fasting, patients were allowed only bland fluids other than those containing milk, and a small saline purge was administered each morning. If the head of the worm was not immediately recovered, patients were followed up for at least four months before they were regarded as cured.

Treatment Regimes

Oral Administration of Male Fern.—Two mixtures of male fern were used. The first consisted of 8 ml. of extract of male fern, 8 g. of acacia, and cinnamon water to 42 ml.; in the second, to the same constituents 14 ml. of glycerin was added. The dose of male fern was reduced to 6 ml. for adults weighing less than 60 kg., to 4.6 ml. for one child of 12 years, to 4 ml. for two children between 4 and 7 years, and to 2.4 ml. for one child aged 3 years 11 months. "Ribena" was used as a flavouring agent for the young children. In all cases the total dose was divided into three and administered at 15-minute intervals, followed in a further 30 minutes by a saline purge. The mixture containing glycerin was given to 59 patients and that without it to 33. The results of treatment in these two groups have been analysed separately.

Administration of Male Fern by Duodenal Intubation.—The patient lay on the right side after swallowing 65 cm. of Rehfuß tube, and two to three hours later material aspirated through the tube was tested with Congo red. If it was alkaline the tip of the tube was assumed to be in the duodenum, and this assumption was strengthened if, after oral administration of a small quantity of very dilute gentian-violet solution, material immediately aspirated was free from violet colouring. Male fern was administered through the tube either as the plain extract or in the form of a mixture with

glycerin (see above). The results have not been analysed separately. The second method was found to be the simpler of the two, for the viscosity of the plain extract caused it to adhere to the inside of the tube, and this and the internal volume of the tube made it necessary to administer 15 ml. from the syringe in order to deliver 8 ml. from the end of a medium-sized Rehfuß tube. The tube must be swallowed empty if the patient is not to experience the unpleasant flavour of the anthelmintic. It is therefore important to ascertain the amount which must be injected into it in order to fill it and deliver a given amount at its extremity. Failure to attend to this point may well have been responsible for some of the failures ascribed to the drug in the literature. An alternative would be to inject only the amount of the dose and to wash it through the tube with water or other solvent. The undiluted extract, however, is sufficiently viscid to cause an undetermined quantity to remain even after an undesirably large amount of water has been injected into the tube. As with oral treatment, adults weighing less than 60 kg. and also three children aged 12–14 were given 6 ml. of male fern. The tube was removed immediately after delivery of the anthelmintic, and a saline purge was given 30 minutes later. This regime was employed in 52 cases.

Oral Administration of Mepacrine.—A solution of 1 g. of mepacrine in 42 ml. of water was swallowed over the course of an hour by 49 patients, and a saline purge was given 30 minutes later.

Administration of Mepacrine by Duodenal Tube.—To 26 patients 1 g. of mepacrine dissolved in 42 ml. of water was administered by a duodenal tube through which a saline purge was given half an hour later.

Oral Mepacrine and Male Fern.—To 21 patients 0.3 g. of mepacrine dissolved in 20 ml. of water was given in the evening after the usual period of fasting. This was followed by a similar dose early the next morning, and three hours later an emulsion of male fern was given according to the method of administering it outlined above.

All stools on the day of treatment were passed into a bedpan containing a little water. After treatment with male fern it was usually necessary to search for the head of the worm, as in most cases the worm was passed in separate sections; the search was facilitated by the fact that the preliminary starvation had caused the bowel to become empty of faeces. After successful treatment with mepacrine the worm was invariably passed intact a few hours later, and was bright yellow in colour. It is considered important to search for the head of the worm, for when it is not found the patient can be told that a cure can be presumed only if segments do not reappear within three to four months. Without such a follow-up scheme no conclusion can be drawn on the effectiveness of treatment, for in only 60% of the patients under review could the head of the worm be identified after treatment.

Results

Of the 240 patients, 189 (78.7%) were cured by a single course of treatment; 144 (76%) of these passed the head of the worm, and in 45 (24%) it was possible to presume cure as no segments appeared in the stools during the follow-up period. When treatment failed, segments reappeared, on average, 10 weeks later (range 4 to 16 weeks). All seven children in the series were treated with male fern—four orally and three by

duodenal tube—and there were two failures among them. In both these children, aged 12 and 3 years 11 months respectively, male fern was administered orally in dosages which we would now regard as suboptimal. Among the 240 patients two heads were found on four occasions, giving an incidence of double infection with *T. saginata* of 1.6%. The patients infected with *T. solium* and *D. latus* were successfully treated orally with the mixture of male fern containing glycerin. In two patients a concomitant infection with *Giardia lamblia* was found at the time of treatment; mepacrine administered by mouth was successful in eradicating the infection in one and mepacrine by duodenal tube was equally successful in the other.

The results obtained with the five methods of treatment are recorded in the Table. Statistical analysis showed that, with the numbers of patients involved, the differences between them are no more than might easily arise by chance.

Results Obtained With the Various Treatment Regimes

Method	Total	Cured	Doubtful	Failed	Failure Due to Vomiting*
Oral male fern in an emulsion without glycerin	33	24 (73%) H.F. 17 (71%) F.U. 7 (29%)	2 (6%)	7 (21%)	1
Oral male fern in an emulsion with glycerin	59	48 (81%) H.F. 44 (92%) F.U. 4 (8%)	2 (3%)	9 (15%)	2
Male fern by tube	52	42 (80%) H.F. 23 (55%) F.U. 19 (45%)	6 (12%)	4 (8%)	2
Oral mepacrine	49	39 (80%) H.F. 33 (85%) F.U. 6 (15%)	2 (4%)	8 (16%)	5
Mepacrine by tube	26	23 (88%) H.F. 21 (91%) F.U. 2 (9%)	1 (4%)	2 (8%)	1
Oral mepacrine and male fern	21	13 (62%) H.F. 6 (46%) F.U. 7 (54%)	2 (10%)	6 (28%)	2
Total	240	189 (79%)	15	36	13

H.F.=Head found. F.U.=Proof of cure obtained by follow-up. *In patients included in the preceding column.

Discussion and Conclusion

The main conclusion which may be drawn from these studies is that treatment with the different drugs and regimes used has given very similar results. It may thus fairly be stated that under the conditions of this study—namely, the patient being admitted to hospital and denied food for at least 48 hours before treatment—extract of male fern and mepacrine in the dosages used are of equal value as anthelmintics. Adequate fasting is thought to be a valuable preliminary to anthelmintic treatment, for not only does it facilitate contact between the anthelmintic and the worm, but also it renders the head of the worm, if passed, easier to identify than when it must be searched for amid a mass of faecal material. Among those treated by the various methods here employed and who fasted for 72 hours, 84.3% were cured with a single course of treatment, whereas among those who fasted for less than this period 74.5% were cured. The standard error of the difference between these proportions is 5.56 and the actual difference 9.8; thus, although the difference is not strictly statistically significant, it is near the point at which it becomes so, and it seems likely that the additional fasting assisted in improving the therapeutic result.

Failure of the treatment due to vomiting was encountered more often among those treated with mepacrine than with male fern—in 5 out of 144 (3.5%) treated with male fern only, but in 6 out of 75 (8%) treated with mepacrine only. The difference is without

statistical significance, and probably unimportant except in those suffering from an infection with *T. solium*. Such patients, should they vomit, would almost certainly acquire a heavy infection with cysticerci, for mature segments of the parasite would be brought into the stomach and upper small intestine, where they and their contained eggs would be digested by the intestinal ferments, and the larvae thus liberated would gain entrance to the body proper. It is suggested, therefore, that mepacrine should not be employed in patients suffering from *T. solium* infections.

A further point which is thought to be important is the administration of the anthelmintic in a draught or by duodenal tube rather than in capsules. The head of the worm is usually attached high up the small intestine, and if capsules are administered there is some risk that they may not rupture and liberate their contents until they have passed the head. This risk is aggravated by prolonged storage of capsules whereby they become hard and difficult to dissolve. However, provided the anthelmintic is administered in a draught and the patient fasts for 48 hours before treatment, excellent results may be expected after treatment with either mepacrine or male fern in the dosage regimes here employed. The results certainly appear better than those reported from the use of dichlorophen (2:2'-dihydroxy-5:5'dichlorodiphenylmethane). The best of these so far reported are those of Schneider (1959), who obtained cures in 42 of 61 cases (68.5%), and of Mazzotti and Méndez (1956), who cured 34 of their 49 cases—that is, 69.4%. In other reports the results obtained with this drug have been much inferior to these.

Finally, practitioners with fashionable practices may wish to note that among patients who were recently treated for tapeworms at the hospital there have been three who were fashion models. Three fashion models developing tapeworm infections do not make this an occupational disease any more than three swallows make a summer, but the chain of events leading to the infection appears clear. These women are entertained in fashionable restaurants, probably more often than most, and underdone or rare steak is a fashionable meal. Their infection and the common occurrence of the disease in Great Britain underline the desirability of impressing upon restaurateurs and the restaurant-frequenting public the desirability not only of thoroughly cooking beef but also, so far as underdone beef is concerned, of sacrificing gustatory gratification to intestinal integrity.

Summary

Information on the results of treatment of tapeworm infections under standard conditions is scanty, and observations have therefore been made under such conditions in 240 cases.

No statistically significant difference in results was found between five different treatment regimes, including administration of male fern orally or by duodenal tube and of mepacrine by the same routes.

Factors which may give rise to poor results when these regimes are used include inadequate fasting, administration of male fern in capsules instead of in a draught, and, when doses of anthelmintics of small volume are administered through a duodenal tube, failure to take into account the amount required to fill the tube before any is delivered from its distal extremity.

Unfavourably false impressions of the efficacy of a treatment for tapeworms may be obtained unless patients

are followed up for at least four months in cases in which the head of the worm is not recovered after treatment.

Failure of treatment due to vomiting was encountered more often among those treated with mepacrine than with male fern. As vomiting in patients with *T. solium* infections may give rise to cysticercosis, treatment with mepacrine in such cases is best avoided.

Our thanks are due to Sir Neil Hamilton Fairley, Sir George McRobert, and Dr. J. H. Walters for permitting us access to their case records; to Dr. D. S. Ridley and his staff for laboratory help; and to Professor A. Bradford Hill and Dr. W. J. Martin, of the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.

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TOXIC EPIDERMAL NECROLYSIS OCCURRING IN A CHILD

BY

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The term "toxic epidermal necrolysis" was first used by Lyell (1956) to describe a syndrome of toxic origin whereby large areas of epidermolysis preceded peeling, followed by fairly rapid tendency to healing. The skin was extremely tender at the onset. Bullous formation, although common, was only incidental to the process. Lyell had described four cases in adults. Lang and Walker (1956) described a case of an unusual bullous eruption in a Bantu male adult which appears to have been a similar condition, and in 1957 they described four other cases occurring in adults. Rook (1957) added another case to the collection.

So far no cases of this syndrome in children have been reported, although occasional cases are known to have occurred. A case is here reported in a young boy.

Case Report

A boy aged 3 was admitted to hospital with a day's history of blisters, which had been getting progressively bigger and more numerous. Two days previously he had developed what was diagnosed as impetigo. Fourteen days previously he had several attacks of vomiting, which occurred immediately after food and fluids. His small brother, aged 2, had diarrhoea and vomiting at the same time. A diagnosis of cyclical vomiting was made. The vomiting stopped a couple of days later, after "ancoloxin" (pyridoxine hydrochloride and meclozine hydrochloride) had been given.

For the next five days he was anorexic and irritable, after which he felt perfectly fit again. His brother (aged 2) had then been well for some time.

A week before admission another brother, aged 6 years, developed impetigo, and he was given neomycin ointment by his own doctor. Two days prior to admission the patient developed septic spots on his chin, and a diagnosis of impetigo was made. He was also given neomycin ointment. His mother said that he also complained of transient girdle pains, but cursory examination by her revealed nothing. On the day before admission he was noticed to have a few small blisters on the front of his chest. These got bigger and more numerous during the rest

of the time at home. The skin also started to peel. The mother applied neomycin ointment to the affected areas. That night he could not lie down, and cried continuously because of the extreme tenderness of the skin.

There was no relevant family or past history.

On admission he looked extremely ill, but was not moribund, dehydrated, photophobic, or unconscious. His temperature was 100° F. (37.8° C.), pulse 104, and respirations 25.

Physical examination was difficult because of the tender skin over his trunk and upper parts of the limbs. He had impetigo-like lesions around the mouth and chin. There were large areas of peeled and dead skin on the front and back of the trunk. No blisters were seen, but the mother insisted that they had been present the day before. The underlying dermis was raw, moist, pink, and oozing. Between these areas the skin was erythematous and in places wrinkled. Nikolsky's test was positive. Wrinkling and peeling were also noticed on the forehead and in the right retroauricular region. Areas of erythema were also noticed in the flexures of all limbs. Conjunctivitis was not present. In his mouth there was a membranous tonsillitis. The membrane was a dull white colour and very adherent to the tonsil. There were also tender tonsillar lymph nodes. His abdomen was difficult to examine because of the painful areas on its surface. Despite a thorough search no lesions were found in any other system.

Investigations.—A swab of the skin from the impetiginous areas grew mainly *Streptococcus viridans*; a throat swab also grew the same organism. A tonsillar swab did not grow diphtheritic organisms, Vincent's organisms, *Staphylococcus aureus*, or haemolytic streptococcus. On the day of admission a skin biopsy was performed from an erythematous area on the back. It was noticed that the epidermis tended to slither over the dermis during the incision. The histological report of the tissue stated: "The superficial part of the epidermis in the small fragment of the skin has been shed, including the stratum corneum and most of the stratum granulosum (see illustration). There is moderate inflammatory cell infiltration in the dermis consisting of round cells and neutrophil polymorphonuclear leucocytes. The appearances are consistent with the clinical diagnosis of epidermal necrolysis." Estimation of the herpes-virus-neutralizing bodies on admission was negative. A further estimation two months after he had been discharged from hospital also proved to be negative.

Treatment

As the skin was tender and peeling he was covered all over the trunk with "eucerin" (hydrated ointment of wool alcohols) dressings. It was very painful to remove these coverings for the next few days because of the skin tenderness. In an effort to combat the infection and the membranous tonsillitis, he was given oral chloramphenicol palmitate suspension, 250 mg. initially and 125 mg. six-hourly thereafter for six days.

Section of skin removed for histology ($\times 215$), showing the absence of the stratum corneum, and most of the stratum granulosum.