Clinical Trichuriasis in hospitalised Kuala Lumpur children [1]

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IN MALAYSIA, as throughout much of the world, infection with **Trichuris trichiura** (whipworm or **chaching halus**) is common. A 1962 survey revealed **Trichuris** eggs in the faeces of 88.7% of some 1,359 persons studied in seven states (ICNND, 1964), while Lie Kian Joe (1964) found that 62% of 1,031 Kuala Lumpur General Hospital paediatric patients, aged 2-7 years, were infected. Stoll in 1947 estimated that 227 million Asians, and 355 million people worldwide, were infected with **Trichuris.**

The commonness of the worm and the apparent uncommonness of symptoms attributable to it have caused this parasite's pathologic potential to be neglected. Yet, when large numbers of worms are present in children, a distinctive and important clinical syndrome results. Such children suffer from a refractory and often debilitating diarrhoea or dysentery and frequently develop iron deficiency anaemia.

To better characterise this disorder as it occurs in children in Kuala Lumpur, we studied 26 children with chronic or recurrent diarrhoea and high **Trichuris** egg counts who were admitted to the gastrointestinal ward of the Kuala Lumpur General Hospital over a 4-month period. This paper reports our findings.

Materials and Methods

From mid-January through mid-May, 1968, stool specimens were collected from children admitted to hospital with a chief complaint of chronic or recurrent diarrhoea or dysentery. Specimens were placed in a thiomersal-iodine-formalin (TIF) solution in the ward and examined later in the Division of Rural Health Research of the Institute for Medical Research. Worm eggs were counted using the Dunn (1968) modification of the Beaver (1950) direct smear method, and the smears were carefully examined for amoeba trophozoites or cysts. Children with more than 50 eggs per smear of approximately 3 mg. (about 1/300 ml.) of faeces were included in the study. Duplicate counts were made on each of two specimens obtained before treatment. The hospital

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laboratory performed white cell counts, haemoglobin measurements and stool cultures for bacterial pathogens on each patient at the time of admission. The child's mother (or other responsible family member) was questioned concerning the nature and duration of symptoms, including frequency of bowel movements, the presence of blood or mucus in stools, and of rectal prolapse, pica and previous diarrhoeal episodes; the sibling rank of the child; and the family's sanitary facilities and sources of water and milk.

After these preliminaries, the children were randomly allocated to one of four treatment programs consisting of:

(1) a single retention enema of approximately 400 ml. of a 0.2% solution of hexylresorcinol;

(2) this same kind of enema accompanied by orally administered thiabendazole (Mintezol (R) chewable tablets) in a twice daily dosage of 25 mg./kg. of body weight for 3 days;

(3) the same kind of enema with the same dosage of thiabendazole extended to 5 days; or

(4) the same dosage of thiabendazole for 5 days without the enema.

In children with co-existing amoeba infections, the initiation of therapy with emetine followed by Embequine (R), or with one of the assigned trichuriasis regimens was similarly determined by random assignment. All patients were hospitalised for at least six days, with discharge and later therapy ordered as clinically indicated. Most children were seen again as outpatients 1-2 weeks and 3-4 weeks after discharge, with later follow-ups whenever possible.

Results

The 26 children studied (14 males, 12 females) ranged in age from two to seven years (median age, four years). In terms of ethnic classification, there was a strikingly disproportionate number of Sikh and Pakistani children in the study group. Of 346 children aged 2-7 years admitted to the paediatric gastrointestinal unit from January 12 – May 12, 1968, only 6% were Sikhs and 1% were Pakistanis, with 35% Chinese, 34% Indians other than Sikhs, and 24% Malays. In contrast, the 26 children with severe trichuriasis included eight Sikhs (31%), two Pakistanis, four Chinese, eight Indians other than Sikhs, and four Malays. Subjects tended to be young children in large families; fifth was the median family position, with six the median number of children per family. By history, the median number of daily bowel movements was four, with a median duration of one month. A history of blood in the stools was given for 22 of the 26 children, with mucus reported in 16 of 23 and rectal prolapse in nine of 23 (for whom that information was available). Recent diarrhoea in another child in the family was reported for ten of 25 children.

Regarding sanitary facilities, 13 families said they had latrines (usually pit or bucket); nine said they had none. Water supply was from municipal pipes for 15; nine said they used wells. Five families reported the use of unprocessed cow's milk; 14 said they used only commercial milk. We observed no notable geographical grouping of cases, other than the fact that most came from settlements on the fringe of Kuala Lumpur, which were neither clearly urban nor rural.

On admission to the hospital, all but two of the 26 children (92%) were anaemic by World Health Organisation standards (haemoglobin less than 11.5 gm/100ml) (Jelliffe, 1966). The median haemoglobin was 7.3 gm/100 ml and 21 had values less than 10 gm/100 ml. Most children had a mild leukocytosis, with a median white blood cell (WBC) count of 13,000. Eosinophilia (greater than 300 eosinophils/mm. (3)) was found in 18 (78%) of 23 children, with a median value of 1200 eosinophils/mm.(3)

Concomitant **Entamoeba histolytica** infection was detected in eight of the 26 children, with a pathogenic strain of **Escherichia coli** in two of 22 and **Shigella sonnei** in one of 22 children cultured. However, these figures may be below true incidence because of difficulties in obtaining reliably fresh stools for laboratory procedures. **Ascaris** eggs were found in the stools of 11 and hookworm in five of the 26 children. **Trichuris** egg counts on admission (based on the individual mean of duplicate counts on two specimens per patient) gave a median of 134 with a range of 64-660 eggs per smear.

None of the therapeutic regimens used emerged as distinctly superior. Most children improved gradually during hospitalisation without dramatic response to any specific therapy. Egg counts were usually lower at time of discharge than when the children were admitted, but the infection was rarely eradicated. Later counts were sometimes higher, suggesting that therapy might suppress egg production without eliminating the parasite. Children receiving thiabendazole for five days, along with a hexylresorcinol enema, appeared to experience a more pronounced reduction in egg count and more prompt and sustained clinical improvement than those receiving the other regimens. However, some children on each regimen did well and some poorly, and the numbers involved were too

small to permit any rigorous comparison of therapeutic efficacy.

Case Report

J.K. was a 6-year-old Sikh girl with a 4-year history of recurrent episodes of bloody diarrhoea, which had thrice previously led to hospitalisation. She was the sixth of eight children, and a younger sibling had also been admitted to hospital with similar complaints. Her mother reported she often saw the child eating sand and dirt. When admitted, J.K. was pale but otherwise normal. Her haemoglobin was 6 gm/100 ml, WBC 19,500 with 12% eosinophils. Faecal examination revealed many **Trichuris** eggs, a few **E. histolytica** cysts, and a light **Ascaris** infection. **Trichuris** egg counts in duplicate on three different pre-treatment specimens were 63 and 59*, 263 and 240, and 108 and 95 per smear. Results of stool culture for bacterial pathogens were negative.

The child was treated for five days with 375 mg. of thiabendazole twice daily and 1 cc. of Imferon (R) daily; folic acid and vitamin B complex were also given. No anti-amoebic agent was used. Her condition improved and she was discharged a week after beginning therapy, at which time the **Trichuris** egg count was reduced to eight and ten eggs per smear, and the **Ascaris** had disappeared. She was seen in follow-up at ten days and again at three weeks after discharge and was subjectively much better, with normal bowel movements. However, **Trichuris** egg counts had risen to 231 and 168 at three weeks and **E. histolytica** cysts were again found. Ten weeks after treatment, she had again developed bloody diarrhoea and was given a week's course of tetracycline for the amoebae noted previously. **Trichuris** egg counts were 2 and 24, and 22 and 19. She again became asymptomatic and remained so during three more months of follow-up.

Discussion

The clinical syndrome observed in these 26 children corresponds closely to that noted in various parts of the world by Getz (1945), Whittier **et al.** (1945), Jung and Beaver (1952), and Jung and Jelliffe (1952). The diarrhoea is distinctive for frequent passage of small amounts of stool commonly mixed with blood and mucus. The faecal volume is usually small, and straining at defecation often produces rectal prolapse. Although the worms are found throughout the large bowel in post-mortem studies, symptoms in heavy infections seem primarily due to a concentration of worms embedded in the mucosa of the rectum and lower colon, where they can easily be seen on proctoscopic examination.

This location of the parasite makes the use of egg counts to estimate parasite burden relatively unreliable. Dunn (1968) developed his "preserved direct smear" method (used in this study) expressly for field surveys but showed it to be directly comparable in precision to the Beaver (1950) saline direct smear method, which was used in clinical studies of trichuriasis by Jung and Beaver (1952). The utility of both these methods rests on the assumption that mixing of faecal material (including worm eggs) in the bowel is sufficient to make the egg count in a 1-to-5-mg. sample from a single stool an estimate of total egg production and thus of total worm burden. In clinical trichuriasis, not only are most symptom-producing worms so low in the bowel as to minimise mixing, but eggs tend to cluster in bits of mucus adhering to the bowel wall. A child with many worms in his rectum may thus pass several soft stools containing few eggs, then with additional straining (due to rectal irritation) expel large numbers of eggs mixed with mucus. Layrisse **et al.** (1967) compared egg counts from 3-day faecal collections with numbers of worms expelled after administration of stilbazium iodine and found a significant correlation of number of worms passed with total eggs passed in three days, but none with eggs per gram of faeces. However, 3-day stool collections are rarely practicable, and, as Jung and Beaver (1950) demonstrated, even in trichuriasis, direct smear egg counts provide a useful semiquantitative approximation of the intensity of infection.

In contrast to bacterial or viral infections, where the mere detection of a known pathogen is considered sufficient for clinical diagnosis, the presence of small numbers of intestinal nematodes rarely causes disease. The exceptions are the occasional wanderers, such as an **Ascaris** in the common duct, whose chance location does damage (Warren, 1970). The clinician therefore needs to have some idea of the intensity of the infection before he can judge whether the worm is, in fact, causing his patient's symptoms.

A World Health Organisation Expert Committee (1964) has suggested that anaemia only results from infection with **Necator** americanus (the hookworm commonly found in West Malaysia) when the egg count is greater than 6,600 eggs per gram of faeces for men, or 10,200 for women. With trichuriasis, estimates for the egg-count threshold associated with diarrhoea vary from 2,000 to 30,000 eggs per gram of faeces. Our arbitrary cut-off value for inclusion in this study (50 eggs per smear or approximately 15,000 eggs per gram) was based largely on the fact that

*This designates the count of each of two separate smears from a single specimen.

heavier counts are rarely found in asymptomatic children during field surveys. In our series and that of Jung and Beaver (1952), however, 70% of the children with diarrhoea or dysentery had egg counts greater than 100 eggs per smear (approximately 30,000 eggs per gram of faeces). Jung and Beaver estimated that this may represent as many as 1,000 mature worms (male and female), which is interestingly the same figure as the average derived by Layrisse **et al.** (1967) from egg and worm counts on 3-day fecal collections.

Layrisse **et al.** (1967) also studied the relationship of the **Trichuris** burden to anaemia and reported an average blood loss of about 0.005 ml. per worm per day, or approximately 0.25 ml./1,000 eggs per gram of faeces. They estimated that infections of more than 800 parasites (equivalent to approximately 24,000 eggs per gram of faeces or 80 eggs per 3-mg. direct smear) induce anaemia in children by unbalancing iron metabolism. But since egg counts give only a rough (though useful) approximation of worm burden, the counts on any given faecal specimen may be well below this level in an individual whose anaemia (or diarrhoea) is caused by a heavy **Trichuris** infection.

The most striking epidemiologic feature of trichuriasis in our series is its frequency in Sikh children. Probably the outstanding environmental difference between Sikhs and other Malaysians is their keeping of dairy cattle and use of milk products, often home-processed without pasteurisation. However, there is no apparent reason why this should influence the development of **Trichuris** infections, which occur by ingestion of faecally-contaminated soil where the eggs must have incubated for at least several weeks. Perhaps the keeping of cattle is associated with the shaded, moist soil conditions in which **Trichuris** eggs develop best. One of us (H.K.V.) has been particularly impressed with the prevalence of pica amongst Sikh children, and this may well be the major mode of infection.

Concomitant infections with **E. histolytica** occured in about 30-40% of cases in both our series and that of Jung and Beaver (1952). The possible interrelationship of helminth-amoeba-bacteria in producing diarrhoea and dysentery is poorly understood and deserves further study. We should stress, however, as do Jung and Beaver, that heavy **Trichuris** infections alone may produce dysentery and, when both amoebae and **Trichuris** are present, the worm may be at least as important a pathogen as the amoeba.

There is no widespread consensus on the best method of treating trichuriasis. Most drug trials (such as those of Huang and Brown, 1964; Franz **et al.**, 1965), are conducted with older children and adults with light infections, using "cure" (absence of eggs after therapy) as the criterion of efficacy. It is often not clear how to apply such results to treating symptomatic children in an endemic area, where the important goal is to reduce a heavy parasite burden to a level that is innocuous to the host. But its achievement is still more difficult to evaluate, because of the influence of nonspecific host factors and supportive measures (for example, correcting the anaemia or improving nutrition), the limited correspondence between egg counts and worm load, and wide variations in clinical response.

Jung and Beaver (1952) used 0.2% hexylresorcinol enemas (already described) and reported that, while no infections were "cured", all subjects became asymptomatic within 1-10 days. The difficulties with this method are that the buttocks must be protected with petroleum jelly to prevent chemical burn, the solution should be retained for 15-30 minutes (usually requiring attendance of a nurse or competent assistant), and repeat administration may be needed for full effect.

The most promising results reported for treating paediatric trichuriasis are for stilbazium (Monopar (R)) (Layrisse **et al.**, 1967), but reportedly there have been difficulties in achieving a commercially satisfactory formulation of this drug and it is not currently available. Dithiazinine (Telmid (R)) (Frye **et al.**, 1957) is still sometimes cited as the most effective trichuricide, but the high incidence of severe gastrointestinal side effects and the reports of a number of drug-induced deaths (Abadie and Samuels, 1965; Goodman and Gilman, 1965) make its routine use unjustified.

Several textbooks of medicine (Beeson and McDermott, 1967; Wintrobe **et al.**, 1970) now recommend thiabendazole (Mintezol (R)) as the drug of choice in a dosage of 25 mg./kg. twice daily for 2-5 days, but no studies evaluating its use in symptomatic paediatric cases seem to be available. Our efforts in this regard suggest that treatment for 2-5 days with thiabendazole alone is usually not adequate for children with heavy worm burdens that produce clinical illness. Although differences in outcome were not significant and each of several regimens of hexylresorcinol by enema and thiabendazole by mouth gave a spectrum of success and failure, the longer (5-day) course of thiabendazole along with a hexylresorcinol enema distinctly tended to give more impressive re-

sults than the other methods used. Whalen and colleagues (1970) report that prolonged courses of thiabendazole (3-4 weeks instead of the usual 3-5 days), which they found necessary to prevent relapses in infections with **Capillaria philippinensis**, also produced superior results in eradicating **Trichuris** infections. The mode of transmission of capillariasis, including the possibility of auto-infection, is presently uncertain and "eradication of infection" may therefore be therapeutically important. But with trichuriasis in an endemic area (where re-infection is likely soon after leaving the hospital), prolonging therapy to remove "every last worm" is of dubious merit. However, since thiabendazole is nontoxic and at the dosage prescribed (25 mg./kg. of body weight) appears to be well tolerated by children, it would seem reasonable to try longer courses of the drug, with or without hexylresorcinol by enema, in treating refractory cases.

The correction of the frequently concomitant iron-deficiency anaemia and malnutrition and the specific treatment for any co-existing amoebiasis or bacterial enteritis are also important in the management of the trichuriasis syndrome.

Summary

Twenty-six children, aged 2-7 years, admitted to the Kuala Lumpur General Hospital in early 1968 with chronic or recurrent diarrhoea and heavy **Trichuris trichiura** infections were studied. Epidemiologically, the group was notable for the disproportionate number of infections in the Sikh ethnic group. The illness was characterised by frequent bloody, mucoid stools and moderate to severe anaemia. About a third of the cases had co-existing amoebiasis, but amoebae did not appear to be more important than the **Trichuris** in producing symptoms.

Pending further trials and commercial availability of stilbazium, a combination of hexylresorcinol enemas and oral thiabendazole seems to be the most useful therapy available. However, the clinical course of the infection is highly variable, and treatment may need to be prolonged or repeated.

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