

## A TRIAL OF OXANTEL IN TRICHURIASIS

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### SYNOPSIS

In this study we are reporting on the efficacy of Oxantel in eight Trichuriasis children admitted into the Paediatric Unit, Singapore General Hospital with gastrointestinal symptoms, protein caloric malnutrition and nutritional anaemia. Detailed case history is given of each of these cases to show their socio-economic background. Oxantel was administered in the form of a suspension given in a dose of 10 mgm per kilogram body weight twice a day usually for four days. Stool examination was conducted once before treatment and for consecutive days after treatment. This was followed whenever possible by one stool examination two weeks later and another after 3 months.

The response to Oxantel was judged by its ability to relieve gastrointestinal symptoms such as diarrhoea, and decrease the ova count in the faeces. Oxantel was well tolerated by all patients and none of them showed any adverse reaction to the drug, which did not alter the morphology of the ova that was passed in the faeces. In one of the patients parasites re-appeared after a complete cure. This was certainly a case of re-infection, and indicates the importance of environmental sanitation in keeping the population free of intestinal helminthiasis.

### INTRODUCTION

The most common intestinal helminth found in Singapore and Malaysia is *Trichuris trichiura* (Desowitz *et al*, 1961; Lie, 1964). In a survey done in the Singapore General Hospital 38% of the children were found to be infected with *Trichuris* with the highest prevalence rates amongst Malays, followed by Indians and the Chinese (Kan *et al*, 1971).

Chemotherapy of trichuriasis has been unsatisfactory until recently. Dithiazanine iodide which is an effective trichuricide is no longer used because of its serious side effects.

Recently, two anti-*Trichuris* drugs have been introduced; they are Mebendazole and Oxantel (Trans-1, 4, 5, 6 tetrahydro-2- (trans-3-hydroxystyryl)-1-methyl pyrimidine (CP-14-445). In a previous study Mebendazole was shown by us to be an effective drug against this parasite (Paul and Zaman, 1975). In the present study we are reporting on the efficacy of Oxantel in 8 trichuriasis cases admitted into the Paediatric Unit, Singapore General Hospital with gastro intestinal symptoms, protein-caloric malnutrition and nutritional anaemia. Detailed case history is given of each of these cases to show their socio-economic background.

### MATERIAL AND METHODS

Oxantel was administered in the form of a suspension given in a dose of 10 mg/kg body weight twice a day, usually for four days. Stool examination was conducted once before treatment and for four consecutive days after treatment. This was followed whenever possible by one stool examination 2 weeks later and another after 3 months. The technique of examination was that of an ordinary direct smear using 2 mgm of faeces, according to Beaver's method (1950).

#### Case 1

Z.B.M.Y. was a 5-year old Malay girl and admitted because of fever and reproductive cough of 8 days duration and was referred from a rural infant welfare clinic at Bedok. There was a past history of diarrhoea for which the child had been treated symptomatically at the infant welfare clinic. The child was the youngest of 10 children, the eldest being 20 years. The father earned only \$100/- a month, as an odd job labourer, and he belonged to the lower income group. This child had been followed up regularly at the maternal and child welfare clinic and although the initial weight at birth was normal, the weight gain was slow and she was at most times along the 25th percentile in weight. Physical examination revealed a height of 101 cm and a weight of 13.4 kg, being 10th and 25th percentile respectively, using Singapore standards. She was malnourished and febrile with an injected throat and tonsils. There were also signs of pneumonitis on the left side with diminished air entry and adventitious sounds. Blood examination

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showed a haemoglobin of 8.2 gm%, a total white cell count of 15,700 cmm with polymorphs 67%, lymphocytes 17%, monocytes 3% and eosinophils 13%. Platelet count was 690,000 cmm. Serum protein showed a normal albumin globulin ratio 4.0 gm% to 3.6 gm% respectively. Serum iron was 35 micrograms % and folic acid 25.0 ng/ml. The culture of the throat swab grew coliform organisms with candida species. A radiograph of the chest showed the presence of consolidation of the left lung. Examination of the faeces showed the presence of *Trichuris* ova. The child was given a course of Ampicillin and Cloxacillin for the chest infection and Oxantel for trichuriasis. The results of treatment with Oxantel were as follows:—

Date	Ova Count	Dosage of Oxantel
6.3.75	248 per 2 mgm	10 mg/kg bd
7.3.75	189 per 2 mgm	10 mg/kg bd
8.3.75	68 per 2 mgm	10 mg/kg bd
9.3.75	Not done	10 mg/kg bd
10.3.75	21 per 2 mgm	Nil
11.3.75	2 per 2 mgm	Nil
13.3.75	0 per 2 mgm	Nil

The child was sent to a convalescent home at Changi on 13.3.75 and she put on 2 kg in 3½ months at the home. The stools were examined at the end of November 1975 and they showed no evidence of any ova. In November 1975 the child was 17.5 kg (75th percentile) and measured 108 cm (50th percentile), using Singapore standards. This showed that the child was cleared of trichuriasis infestation and had improved nutritionally.

## Case 2

N.S.H. was an 8-year old girl living in Jurong in a rural area hut, admitted because of postmeasles bronchopneumonia. In addition, there was a history of vomiting roundworms about 2-3 ascarids for the past two days and a history of mild diarrhoea. The child had a cough with nonproductive sputum and there was marked anorexia with loss of appetite. The patient was the second in a family of 4 children and belonged to the lower income group, the father earning \$300/- per month.

Physical examination revealed a child who was severely wasted. She weighed 11.7 kg (3rd percentile) and measured 99.6 cm (3rd percentile), using Singapore standards. There was a postmeasles staining of the skin and the pharynx was congested. The chest was full of bilateral crepitations. The liver was 5 cm below the right costal margin. No abnormality could be detected in the other systems. Blood examination showed a haemoglobin of 9.8 gm%, with total white cell count of 11,200 cmm and a platelet count of 590,000 cmm. The serum iron was normal being 125 micrograms% but the bone-marrow showed depletion of iron stores, and there

were giant myelocytes and megoloblasts as well. The serum albumin was low being only 2.9 gm% while the serum folic acid was also low being 2.0 ngm%. The culture of the stools did not reveal any *Salmonella*, *Mycelia* or pathogenic *E. coli* but a direct smear showed the presence of *Ascaris* and *Trichuris* ova.

The child was put on a course of Ampicillin and Cloxacillin to clear the chest infection and she did well. Examination of the stools revealed 60 *Ascaris* ova per 2 mgm and 7 *Trichuris* ova per 2 mgm of stool. The results of treatment with Oxantel were as follows:—

Date	Ova Count	Dosage of Oxantel
21.3.75	7 per 2 mgm	Nil
22.3.75	7 per 2 mgm	10 mg/kg bd
23.3.75	4 per 2 mgm	10 mg/kg bd
26.3.75	0 per 2 mgm	10 mg/kg bd
27.3.75	0 per 2 mgm	10 mg/kg bd

In addition Piperazine was given for the roundworm infestation.

Examination of the stool on 2.12.75 did not show evidence of any ova. On her last check-up date on 30.3.75 she had grown by 7 cm and measured 107 cm, which was at the 10th percentile and weighed 15.6 kg which was at the 10th percentile, using Singapore standards. The haemoglobin had risen to 11.7 gm%. The *Trichuris* infestation in this child was light and cleared within 2 days of treatment.

## Case 3

P.E.T. was a 9-year old Chinese child admitted for an established rheumatic carditis with subcutaneous nodules. The history dated 15 days ago when the child had fever with prominent nodules over bony prominences, proximal interphalangeal joints, and vertebral column, malleolus and fibula. There was no past history of sore throat or involuntary movements. In this particular case, there was no past history of diarrhoea but because the child came from a rural area of Singapore, a routine examination of the stools was done for *Trichuris* ova. Physical examination revealed a height of 1.7 metres and a weight of 15 kg, both were below the 3rd percentile, using Singapore standards. He had visible nodules over the occiput, vertebral column, proximal interphalangeal joints, palmar surface, head of fibula and malleolus. The apex beat was in the fourth left intercostal space three inches from the mid-sternal line, and there was a systolic thrill and bruit with a mid diastolic bruit due to mitral incompetence and stenosis. The pulmonary second sound was loud and fixed. The other systems were essentially normal. Blood examination showed a haemoglobin of 10.4 gm%, a total white cell count of 15,000 cmm with polymorphs 44%, lymphocytes 32%, monocytes 0% and eosinophils 24%. The

platelet count was 310,000 cmm. The ESR was 51 mm per hour. Examination of the stools revealed 28 *Trichuris* ova per 2 mgm.

The patient was treated as a case of rheumatic carditis and was given injection of Benzathine Penicillin. We did a detailed social investigation into this family and they had an extended family system, a total of 32 members living in a one-hall attap hut in a rubber estate. There was no modern sanitation and the toilet was some distance from the home. Both physical and social over-crowding were present. The results of treatment with Oxantel were as follows:—

Date	Ova Count	Dosage of Oxantel
17.3.75	28 per 2 mgm	Nil
18.3.75	28 per 2 mgm	10 mg/kg bd
19.3.75	22 per 2 mgm	10 mg/kg bd
20.3.75	1 per 2 mgm	10 mg/kg bd
21.3.75	0 per 2 mgm	10 mg/kg bd

As soon as the stools were cleared of *Trichuris* he was sent to the convalescent home where he made remarkable progress. He put on 5 kg and on 27.9.75 weighed 20 kg (30th percentile) and measured 116½ cm (10th percentile), using Singapore standards. The last examination of the stools on 18.5.76 showed no evidence of any ova.

#### Case 4

M.R.B.M.B. was a 13-month old Malay boy who was admitted because of fever and cough of eight days duration. The child was noted to be breathless on the day of admission. There has been a history of past diarrhoea which was treated symptomatically by the infant welfare clinic. The child also lived in the rural area of Singapore and was the fourth child in a family of five children. The family income was \$200/- per month which belongs to the lower income group.

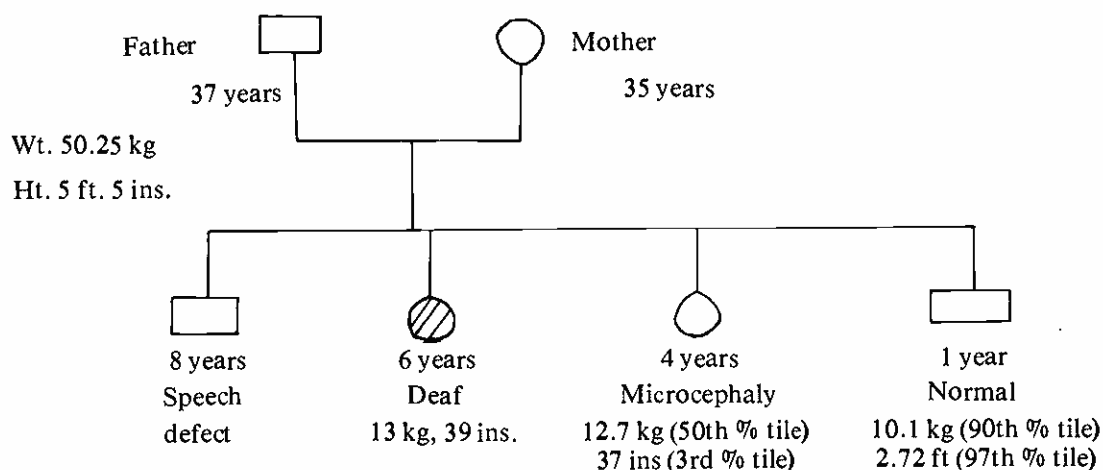
Physical examination revealed a height of 77 cm and a weight of 9.5 kg being 20th percentile and 25th percentile respectively, using Singapore standards. The percussion note was dull over the right lower chest and the air entry was diminished. The liver was enlarged one cm below the right costal margin.

The haemoglobin was 7.5 gm% and the platelet count was 170,000 cmm with an ESR of 80 mm per hour. The total white cell count was 11,800 cmm with a differential count of polymorphs 70%, lymphocytes 15%, monocytes 2% and eosinophils 4%. The serum iron was 34 micrograms% and serum folate was 1.6 ugm%. The patient was treated as a case of lobar pneumonia and was given injection of Ampicillin to control the infection and was later changed to Co-trimoxazole. A blood transfusion was also necessary in addition to the iron mixture and folic acid was given for the megaloblastic anaemia.

A detailed social history revealed that the family of five children had to depend on the income of the father who earned \$260/- per month. They lived in a one-room home, and this was shared by the 7 other family members. The results of treatment with Oxantel were as follows:—

Date	Ova Count	Dosage of Oxantel
13.5.75	107 per 2 mgm	Nil
14.5.75	185 per 2 mgm	10 mg/kg bd
16.5.75	27 per 2 mgm	10 mg/kg bd
17.5.75	12 per 2 mgm	10 mg/kg bd
18.5.75	11 per 2 mgm	10 mg/kg bd
19.5.75	0 per 2 mgm	Nil
7.8.75	22 per 2 mgm	Nil

The child was sent to the Convalescent Home at Changi for convalescence and he put on 3 kg, weighing 12 kg on discharge making him at the 90th percentile, using Singapore standards, and grew 5



cm making him 85 cm which was at the 75th percentile, using Singapore standards.

### Case 5

L.B.L. was a 6-year old female referred from the infant welfare clinic because of failure to thrive and for delayed milestones; she was also a deaf child. There was a history of passing worms.

Physical examination revealed a child with a height of 1 metre and a weight of 13 kg both of which are at the 3rd percentile, using Singapore standards. She was proportionately dwarfed and had a small head. No abnormality could be detected in the heart, lungs or abdomen. The central nervous system was normal. She was three other siblings of which the elder brother had speech disorder and the youngest sister was a microcephalic. The following was the genetic tree:

The father was the only bread earner of the family. His income was \$400/- per month which was inadequate for the family. The diet was poor and lacked iron and protein. Blood examination showed that the haemoglobin was 6.7 gm% while the white cell count was 8,800 cmm with polymorphs 50%, lymphocytes 20%, monocytes 1% and eosinophils 29%. The reticulocyte count was 5% and the platelet count was 350,000 cmm. The serum iron was low being 40 micrograms% and the bone-marrow showed no evidence of iron stores. The serum folate was 13.5 ngm%.

She was treated as a case of iron deficiency anaemia, and given 200 cc of blood with Mist Ferrous Sulphate and a high protein diet as well. The child showed a heavy infestation of *Trichuris*, the ova count being 217 ova per 2 mgm of stool. The results of treatment with Oxantel were as follows:—

Date	Ova Count	Dosage of Oxantel
12.7.75	217 per 2 mgm	10 mg/kg bd
13.7.75	—	10 mg/kg bd
15.7.75	18 per 2 mgm	10 mg/kg bd
16.7.75	0 per 2 mgm	10 mg/kg bd

There was a sharp drop in the *Trichuris* egg counts after treatment with Oxantel and the hookworm infestation was later cleared with Bephenium.

### Case 6

L.P.P. was the youngest sister of Case 5, and she was referred by the infant welfare clinic as being malnourished and was severely anaemic and mentally retarded. This child was a normal baby at birth but had delayed developmental milestones. Physical examination revealed a child with a height of 89 cm and a weight of 10.7 kg, both were at the

3rd percentile, using Singapore standards. There was a soft systolic murmur to the left of the sternum and the liver was 2 cm below the right costal margin. Blood examination showed low haemoglobin of 4.8 gm% while the total white count was 5,400 cmm, polymorphs 44%, lymphocytes 41%, monocytes 2% and eosinophils 13%. The serum folic acid was low being 5.4 ng/ml. The serum iron was also low being 45 mgm% and the serum albumin was 4.3 gm%. Examination of the stool revealed a heavy infestation of *Trichuris*, ova count being 80 per 2 mgm of faeces. This child also had hookworm infection. The results of treatment with Oxantel were as follows:—

Date	Ova Count	Dosage of Oxantel
28.5.75	280 per 2 mgm	10 mg/kg bd
29.5.75	67 per 2 mgm	10 mg/kg bd
30.5.75	16 per 2 mgm	10 mg/kg bd
31.5.75	13 per 2 mgm	10 mg/kg bd
12.6.75	4 per 2 mgm	Nil
18.6.76	0 per 2 mgm	Nil

In addition the child was given Bephenium to clear the hookworm infestation. This child has been followed up as an outpatient for one year and now his weight is 15.7 kg i.e. a weight gain of 5 kg, reaching the 50th percentile in weight, using Singapore standards.

### Case 7

H.B.H. was a 2-year old Malay female admitted because of diarrhoea for more than twenty times a day prior to admission. The stools were watery and yellow with no blood or mucus, and the child had vomiting with inability to retain feeds. Physical examination revealed a child with a height of 79 cm and a weight of 8.7 kg, both were at the 3rd percentile, using Singapore standards. She was malnourished, and was about 7% dehydrated and breathless and lethargic. The other systems were normal, except for the crepitations heard at the left lower zone in the lung.

Blood examination showed a haemoglobin of 10.1 gm%, and a total white cell count of 6,100 cmm, with polymorphs 57%, lymphocytes 27%, monocytes 3%, and eosinophils 13%. The chest X-ray showed pneumonic changes in the lung fields. While examination of the stools revealed a heavy infestation of *Trichuris* with 274 ova per 2 mg of faeces and *Ascaris* 108 ova per 2 mgm of stool.

The patient was given parenteral fluid and plasma for the dehydration and Ampicillin and Cloxacillin for the treatment of the broncho-

pneumonia. The results of treatment with Oxantel were as follows:—

Date	Ova Count	Dosage of Oxantel
18. 9.75	274 per 2 mgm	Nil
21. 9.75	Not done	10 mg/kg bd
22. 9.75	44 per 2 mgm	10 mg/kg bd
23. 9.75	24 per 2 mgm	10 mg/kg bd
24. 9.75	13 per 2 mgm	10 mg/kg bd
19.12.75	0 per 2 mgm	10 mg/kg bd

We looked into the physical environment of the child and found that the family lived in a two-room zinc house with poor sanitary facilities and a dirty environment. The child was sent to the convalescent home after treatment, where her weight increased by 2 kg. The last examination of the stool on 19.12.75 showed no ova on direct smear.

#### Case 8

S.B.A. was a 5-year old Malay boy who came from a family of 4 children. Both parents were working and had a total income of \$500/- per month, while the home was furnished with a television set and a refrigerator, it lacked proper sanitation.

This child was admitted in September 1975 for colicky abdominal pain localised mainly to the epigastrium for three days. Three days prior to admission he vomited two roundworms and the parents remarked that he has had previous episodes of diarrhoea and vomiting.

On physical examination the patient was thin and undernourished, and he weighed 12.2 kg and measured 1.0 metre which was below the 3rd percentile in weight and height, using Singapore standards. The heart and lungs were clear. The

abdomen was not tender and the liver was palpable below the right costal margin. Suprapubic masses was felt at both flanks. Blood examination showed a haemoglobin of 11 gm%. The total white cell count was 8,400 cmm with polymorphs 68%, lymphocytes 21%, monocytes 2% and eosinophils 8%.

Examination of the stool showed *Trichuris* and *Ascaris* ova. The results of treatment with Oxantel were as follows:—

Date	Ova Count	Dosage of Oxantel
22. 9.75	48 per 2 mgm	Nil
23. 9.75	175 per 2 mgm	10 mg/kg bd
24. 9.75	145 per 2 mgm	10 mg/kg bd
25. 9.75	26 per 2 mgm	10 mg/kg bd
26. 9.75	1 per 2 mgm	10 mg/kg bd
27. 9.75	0 per 2 mgm	Nil
29.12.75	0 per 2 mgm	Nil

The patient was given Piperazine for ascariasis. The child had put on one kg weight in a subsequent examination at the outpatient clinic.

#### RESULTS

As seen from table and clinical profile of the above eight patients, all were from underprivileged homes with poor sanitary facilities. There were 3 males and 5 females in this series and their ages ranged from 2 years to 9 years. Their weights and heights were in the majority of children below the third percentile, using Singapore standards. Compared to the series described by Lee *et al* from Malaysia (1975) the duration of diarrhoea was not long and sometimes not present. Pica and rectal prolapse were also absent from this series as the worm loads were not very high. Anaemia and malnutrition was, however, present in all the cases, to a variable degree. In Cases 5 and 6 where the *Trichuris* egg count was high, diarrhoea and anaemia were also severe.

TABLE  
OXANTEL TRIAL ON EIGHT CHILDREN WITH WHIPWORM INFESTATION

Case	Age	Sex	Race	Haemoglobin Grams %	Drug Oxantel	Pre ova treatment count per 2 mgm stool	Post-ova treatment count								% Reduction
							1 day	2 day	3 day	4 day	5 day	6 day	7 day	3 mths	
1.	5½ yrs	F	Malay	8.9 gm %	Oxantel	248 Trichuris	189	68	—	2	21	2	0	0	100%
2.	8 yrs	F	Chinese	9.8 gm %	Oxantel	7 Trichuris	7	—	4	—	0	0	—	—	100%
3.	9 yrs	M	Chinese	10.4 gm %	Oxantel	28 Trichuris	—	22	3	—	1	0	—	0	100%
4.	13 mths	M	Malay	7.6 gm %	Oxantel	107 Trichuris	185	—	27	11	12	—	—	22	88%
5.	6 yrs	F	Chinese	3.8 gm %	Oxantel	217 Trichuris	217	—	—	—	18	8	—	0	100%
6.	4 yrs	F	Chinese	4.8 gm %	Oxantel	280 Trichuris	67	16	13	—	4	—	—	0	100%
7.	2 yrs	F	Malay	10.2 gm %	Oxantel	274 Trichuris	—	44	24	—	13	—	—	—	100%
8.	5½ yrs	M	Malay	11.8 gm %	Oxantel	48 Trichuris	175	145	26	—	1	0	—	—	100%

### Anthelmintic efficiency

This response to Oxantel therapy was judged by its ability to relieve gastro-intestinal symptoms such as diarrhoea and decrease the ova count in the faeces. Oxantel was well tolerated by all patients and none of them showed any adverse reaction to the drug. Oxantel, unlike Mebendazole, did not alter the morphology of the ova that were passed in the faeces.

### DISCUSSION

*Trichuris trichiura* is cosmopolitan in distribution but occurs mostly in the tropics. The adult worms are located in the caecum and the upper parts of the colon. However, in heavy infestation the whole large intestine may be involved. They attach themselves into the intestinal tissues by embedding their anterior end into the mucous membrane. Infection occurs by ingestion of eggs containing larvae which hatch in the lumen of the intestine and mature in about 12 weeks without migrating through the lungs. In this respect they differ from hookworm and *Ascaris*, both of which migrate through the lungs to complete their life-cycle. The clinical aspects of trichuriasis has been described previously by Wong (1962) in Singapore and Kamath (1973) in Malaysia. The symptoms vary from diarrhoea and prolapse of the rectum to malaise and lassitude.

At present there are two drugs available for the treatment of trichuriasis. These are Mebendazole and Oxantel, the last one being reported in this paper. The mode of action of these drugs is, however, different. Mebendazole acts by interfering with the exogenous glucose uptake by the parasites. The consequent increased utilization of endogenous carbohydrates reserve leads to inadequate energy supply and death of the nematodes. As Oxantel is an analogue of Pyrantel it probably acts by paralysing the neuro-muscular apparatus of the worm leading to its paralysis and expulsion. The drug is administered as pamoate salt which prevents its systemic absorption and, therefore, is a safe preparation when given orally.

Oxantel administered in a dose of 10 mg/kg b.d. for four days proved to be very effective in the series of patients investigated. Satisfactory results with this drug were also obtained by Lee *et al* (1975) in a clinical trial in Malaysia. Lee *et al* (1975) had

monitored their cases by sigmoidoscopic examination in addition to the ova counts. They found that after the end of the treatment the mucous membrane was free of parasites and appeared normal.

In the series reported here patients also had other pathological lesions particularly respiratory tract infection. We do not know how far the presence of worms contributed to the morbidity of these patients by adversely affecting their nutritional status and lowering their immunological defences. As *Trichuris* is embedded in the mucous membrane of the large intestine it is possible that it provides a portal of entry for the bacteria from the large bowel to enter the circulation resulting in infections of other organs of the body.

In one of the patients (Case 4) parasites reappeared 3 months after a complete cure. This was certainly a case of re-infection and indicates the importance of environmental sanitation in keeping the population free of intestinal helminthiasis.

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