REGULAR DEWORMING: TO BE OR NOT TO BE?

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Human Intestine is a hub of millions of microbes some are useful while some are pathogenic. The relationship between children and worms is well known since ages. For all these pathological worms both clinically important and essential micro and macro nutrients are lost. Worms were also crucified for inability to gain weight, poor haemoglobin ,Gi blood loss, anaemia and even mental and behavioural changes. Hence regular de-worming was suggested in various national programs. Few of recent meta-reviews, meta-analysis and RCTS have interesting feedback on the issue. Let's discuss important few original articles influencing anti-helimenthic therapy or de-worming in pediatric practice in year wise fashion. Commonly observed precautions and drug dosages are included in the end for easy reference.

Major To be trials(proponents of regular deworming):

1. Stephenson LS, Latham MC, Adams EJ, Kinoti SN, Pertet A. Weight gain of Kenyan school children infected with hookworm, *Trichuris trichiura* and *Ascaris lumbricoides* is improved following once- or twice-yearly treatment with albendazole. *J Nutr* 1993; **123:** 656–65.
2. Stephenson LS, Latham MC, Kurz KM, Kinoti SN, Brigham H.Treatment with a single dose of albendazole improves growth of Kenyan schoolchildren with hookworm, *Trichuris trichiura*, and *Ascaris lumbricoides* infections. *Am J Trop Med Hyg* 1989; **41:** 78–87.
3. Stoltzfus RJ, Savioli L, Chwaya HM, Albonico M, Tielsch JM.School-based deworming program yields small improvement in growth of Zanzibari school children after one year. *J Nutr* 1997; **127:** 2187–93.
4. Alderman H, Konde-Lule J, Sebuliba I, Bundy D, Hall A. Eff ect on weight gain of routinely giving albendazole to preschool children during "Child Health Days" in Uganda: a cluster randomized controlled trial. *BMJ* 2001; **333:** 122–24

Major not to be trials (opponents of regular deworming):

1. Dossa RA, Ategbo EA, de Koning FL, van Raaij JM, Hautvast JG. Impact of iron supplementation and deworming on growth performance in preschool Beninese children. *Eur J Clin Nutr* 2001; **55:** 223–28.
2. Greenberg BL, Gilman JB, Khatoon H, et al. Single dose piperazine therapy for *Ascaris lumbricoides*: an unsuccessful method of promoting growth. *Am J Clin Nutr* 1981; **34:** 2508–16.
3. Rousham EK, Mascie-Taylor CG. An 18-month study of the eff ect of periodic anthelminthic treatment on the growth and nutritional status of pre-school children in Bangladesh. *Ann Hum Biol* 1994;**21:** 315–24.

Reasons for discrepancies:

Hall A, Anwar KS, Tomkins A, Rahman L. The distribution of *Ascaris lumbricoides* in human hosts: a study of 1765 people in Bangladesh. *Trans R Soc Trop Med Hyg* 1999; **93:** 503–10.

Soil-transmitted helminths and schistosomes tend to be unevenly distributed between hosts so that 80% of all worms may be found in 40% of people or fewer.

Important articles reviewing regular de-worming :

2013:

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http://dx.doi.org/10.1016/S0140-6736(12)62126-6

Population deworming every 6 months with albendazole in 1 million pre-school children in north India: DEVTA, a cluster-randomised trial

Shally Awasthi, Richard Peto, Simon Read, Susan M Richards, Vinod Pande, Donald Bundy, and the DEVTA (Deworming and Enhanced Vitamin A) team

INCLUSION:

Participants in this cluster-randomised study were children in catchment areas of 8338 ICDS-staffed village child-care centres (under-5 population 1 million) in 72 administrative blocks

RESULTS:

1. Estimated compliance with 6-monthly albendazole was 86%
2. . After at least 2 years of treatment, weight at ages 3·0–6·0 years (standardised to age 4·0 years, 50% male) was 12·72 kg albendazole versus 12·68 kg control (difference 0·04 kg, 95% CI −0·14 to 0·21, p=0·66).

3. Comparing the 36 albendazole-allocated versus 36 control blocks in analyses of the primary outcome, deaths per child-care centre at ages 1·0–6·0 years during the 5-year study were 3·00 (SE 0·07) albendazole versus 3·16 (SE 0·09) control, difference 0·16 (SE 0·11, mortality ratio 0·95, 95% CI 0·89 to 1·02, p=0·16), suggesting absolute risks of dying between ages 1·0 and 6·0 years of roughly 2·5% albendazole versus 2·6% control. No specific cause of death was significantly affected.
4. **despite halving the prevalence of worm infection, the randomised comparison did not provide significant evidence of an effect of deworming on survival** (mortality RR 0·95, 95% CI 0·89–1·02).
5. in this lightly infected rural population routine deworming of pre-school children had little effect on mortality

2012:

Deworming drugs for soil-transmitted intestinal worms in children: effects on nutritional indicators, haemoglobin and school performance.

Taylor-Robinson DC, Maayan N, Soares-Weiser K, Donegan S, Garner P - Cochrane Database Syst Rev - 2012; 11(); CD000371

Inclusion : 42 trials, including eight cluster trials, 65,168 participants

Results:

1. treating For children **known to be infected with worms (by screening),** a single dose of deworming drugs may increase weight (0.58 kg, 95% CI 0.40 to 0.76, three trials, 139 participants; low quality evidence) and may increase haemoglobin (0.37 g/dL, 95% CI 0.1 to 0.64, two trials, 108 participants; low quality evidence), but we do not know if there is an effect on cognitive functioning (two trials, very low quality evidence).
2. **Single dose deworming for all children In trials treating all children**, a single dose of deworming drugs gave *mixed effects* on weight, with no effects evident in seven trials, but large effects in two (nine trials, 3058 participants, very low quality evidence). The two trials with a positive effect were from the same very high prevalence setting and may not be easily generalised elsewhere. Single dose deworming probably made little or no effect on haemoglobin (mean difference (MD) 0.06 g/dL, 95% CI -0.06 to 0.17, three trials, 1005 participants; moderate evidence), and may have little or no effect on cognition (two trials, low quality evidence)
3. **Mulitple dose deworming for all childrenOver the first year of follow up, multiple doses of deworming drugs given to all children** may have little or no effect on weight (MD 0.06 kg, 95% CI -0.17 to 0.30; seven trials, 2460 participants; low quality evidence); haemoglobin, (mean 0.01 g/dL lower; 95% CI 0.14 lower to 0.13 higher; four trials, 807 participants; low quality evidence);

cognition (three trials, 30,571 participants, low quality evidence); or school attendance (4% higher attendance; 95% CI -6 to 14; two trials, 30,243 participants; low quality evidence);

4. For height, we are uncertain whether there is an effect of deworming (-0.26 cm; 95% CI -0.84 to 0.31, three trials, 6652 participants; very low quality evidence)
5. Deworming may have little or no effect on haemoglobin (0.00 g/dL, 95%CI -0.08 to 0.08, two trials, 1365 participants, low quality evidence); cognition (two trials, 3720 participants; moderate quality evidence).
6. For school attendance, we are uncertain if there is an effect (mean attendance 5% higher, 95% CI -0.5 to 10.5, approximately 20,000 participants, very low quality evidence).

7. **Screening children for intestinal helminths and then treating infected children appears promising, but the evidence base is small. *Routine deworming drugs given to school children has been more extensively investigated, and has not shown benefit on weight in most studies***, except for substantial weight changes in three trials conducted 15 years ago or more. Two of these trials were carried out in the same high prevalence setting.

8. **For haemoglobin and cognition, community deworming seems to have little or no effect, and the evidence in relation to school attendance, and school performance is generally poor**, with no obvious or consistent effect.

Conclusion: Our interpretation of this data is that it is probably misleading to justify contemporary deworming programmes based on evidence of consistent benefit on nutrition, haemoglobin, school attendance or school performance as there is simply insufficient reliable information to know whether this is so.

2000:

Effectiveness and costeffectiveness of albendazole in improving nutritional status of pre -school children inurban slums.

Awasthi S, Pande VK, Fletcher RH. Indian Pediatr. 2000 Jan;37(1):19-29.

Conclusions:
Six monthly albendazole reduces the risk of stunting with a small increase in the expenditure on health care from the payer's perspective. Larger trials are needed to study the effect of albendazole on prevention of stunting, cognitive functions and all-cause childhood mortality.

2001:

Six-monthly de-worming in infants to study effects on growth.

Awasthi S, Pande VK. Indian J Pediatr. 2001 Sep;68(9):823-7.

It was concluded that there was an improvement in weight with six monthly ABZ over 1.5 years. However, a much larger trial would be needed to determine whether there is any net effect of improvement in weight on under five mortality rate.

Bull World Health Organ. 2001;79(8):695-703. Epub 2001 Oct 24.

Evaluation of efficacy of school-based anthelmintic treatments against anaemia in children in the United Republic of Tanzania.

The results suggested that deworming programmes should be included in public health strategies for the control of anaemia in schoolchildren where there are high prevalences of hookworm and schistosomiasis.

2003

Food Nutr Bull. 2003 Dec;24(4):332-42.

Anthelmintic treatment improves the hemoglobin and serum ferritin concentrations of Tanzanian schoolchildren.anthelmintic treatment is a useful tool for reducing anemia in areas with high hookworm and schistosomiasis endemicity.

Author Interpretation and analysis: to be or not to be?

1. Intermittent de-worming of school-age children can improve weight gain in some high-prevalence areas only based on analysis of recently available RCTS.AND REVIEWS.
2. First screen followed by treatment sos if necessary can be valid approach with due practical/microbial behavior limitations in low prevalence regions.
3. None of the previous trial is large enough to assess effects on mortality.
4. In preschool children regular de-worming agents had little effect on weight gain or in mortality.
5. It is premature to introduce routine de-worming mass programmes based on available evidence of consistent benefit on nutrition, hemoglobin, school attendance or school performance due to insufficient reliable information.
6. Anthelmintic drugs need to be integrated with nutritional interventions such as micronutrient supplements to promote recovery and have a rapid effect in diagnosed infected cases or in high prevalence regions.
7. Some earlier studies have shown positive effects on weight gain by use of deworming agents while some refuted the evidence which has created some confusion. This variability in the results may be because of unevenly distributed worms in hosts. But Cochrane meta-analysis and recent large trials in 2013 and 2012 have well studied the issue.

DRUGS TO BE USED FOR DEWORMING:

Albendazole:

1. Following oral administration, albendazole is poorly absorbed from the GI tract. To increase bioavailability it is recommended to give albendazole with a fat-containing meal; the absorption of albendazole increases between 5 to 6.5-fold compared to when given with a non-fatty meal.

2. Grapefruit juice also increases albendazole's oral bioavailability. The clinical consequence of the interaction is not clear, but it is possible that patients taking albendazole with grapefruit juice may experience increased adverse effects.

3. Albendazole plasma concentrations increase significantly in patients with hepatic disease.

4. Since renal elimination of Albendazole and its primary metabolite is negligible, it is unlikely that renal impairment alters the clearance of these agents.

5. Experience with albendazole use in children < 6 years of age is limited; data are even more rare for infants. Safe and effective use of albendazole has not been established in neonates, infants, or children < 24 months of age.

6. Theophylline serum concentrations and the patient's clinical status should be monitored carefully when albendazole is prescribed and on discontinuation of albendazole therapy.

7. Concomitant administration of albendazole with dexamethasone increases the plasma concentration of albendazole sulfoxide, presumably via reduction in albendazole sulfoxide clearance.

8. praziquantel increases albendazole bioavailability. Use albendazole cautiously in combination with praziquantel.

9. Elevated hepatic enzymes (15.6%, < 1 %), nausea/vomiting (3.7%, 6.2%), diarrhea, dizziness/vertigo (1.2%, < 1%), headache (1.3%, 11%), and abdominal pain (6%, 0%) are most significant sideeffects. LFTs should be performed prior to start of therapy and every 2 weeks during treatment. Hepatic abnormalities requiring drug discontinuation occur in roughly 3.8% of patients with hydatid cyst disease. In most cases, liver toxicity is reversible upon drug discontinuation.

10. Albendazole may cause a reduction in total white blood cell counts due to bone marrow suppression; these effects are usually reversible. Leukopenia occurs in < 1% of patients, and results in discontinuation of therapy in 0.7% of patients.

11. Initial therapy for patients with inflammed parenchymal cysticercosis should focus on symptomatic treatment with anti-seizure medication. Treatment of parenchymal cysticerci with albendazole or praziquantel is controversial (Maguire JM: *N Engl J Med*350:215, 2004). Patients with live parenchymal cysts who have seizures should be treated with albendazole together with steroids (6 mg dexamethasone or 40-60 mg prednisone daily) and an antiseizure medication (Garcia HH, et al: *N Engl J Med*350:249, 2004). Patients with subarachnoid cysts or giant cysts in the fissures should be treated for at least 30 days (Proaño JV, et al: *N Engl J Med* 345:879, 2001). Surgical intervention or CSF diversion is indicated for obstructive hydocephalus; prednisone 40 mg/day may be given with surgery. Arachnoiditis, vasculitis, or cerebral edema is treated with prednisone 60 mg/day or dexamethasone 4-6 mg/day together with albendazole or praziquantel (White Jr AC: *Annu Rev Med* 51:187, 2000). Any cysticercocidal drug may cause irreparable damage when used to treat ocular or spinal cysts, even when corticosteroids are used. An ophthalmic exam should always precede treatment to rule out intraocular cysts.

Bibliography:

https://www.clinicalkey.com/#!/ContentPlayerCtrl/doPlayContent/6-s2.0
1180/{"scope":"all","query":"albendazole"}

NITAZOXANIDE:

1. Food and Drug Administration (FDA) approved the use of nitazoxanide for the treatment of diarrhea caused by*Cryptosporidium* species in children 1-11 yr of age and by *Giardia intestinalis* in children ≥1 yr of age.
2. The bioavailability is doubled with food. The drug is well absorbed from the gastrointestinal tract.
3. no pharmacokinetic studies have been performed yet in patients with compromised renal or hepatic function
4. Common adverse effects include abdominal pain, diarrhea, and nausea. Rare side effects include anorexia, flatulence, increased appetite, fever, pruritus, and dizziness.
5. Experimentally demonstrated to have activity against both hepatitis C and rotavirus,

Cryptosporidiosis *(Cryptosporidium)*

Drug of choice:	Nitazoxanide		1-3 yr: 100 mg bid × 3 days
			4-11 yr: 200 mg bid × 3 days
Giardiasis *(Giardia duodenalis)*			
Drug of choice:	Metronidazole		15 mg/kg/day in 3 doses × 5 days
	Nitazoxanide		1-3 yr: 100 mg every 12 hr × 3 days
			4-11 yr: 200 mg every 12 hr × 3 day
	Tinidazole		50 mg/kg once (max 2 g)

Bibliography: Nelson current edition.

PRAZIQUANTEL:

1. Praziquantel is rapidly absorbed with peak levels in 1-2 hr and plasma half-life of about 1-3 hr.
2. Adverse effects can be seen in 30-60% of patients, although most are mild and disappear within 24 hr. Common adverse effects include headache, abdominal pain, dizziness, and malaise.

TINIDAZOLE:

1. FDA approved for treatment of trichomoniasis and for giardiasis and amebiasis in children ≥3 yr of age.
2. After oral administration, tinidazole is rapidly and completely absorbed and distributes into almost all tissues and body fluids, including crossing the blood-brain barrier and placental barrier. It is excreted via urine and feces. Hemodialysis increases clearance of drug

INFECTION	DRUG	ADULT DOSAGE	PEDIATRIC DOSAGE
Ascariasis (*Ascaris lumbricoides,* roundworm)			
DOC	Albendazole	400 mg once	400 mg once
OR	Mebendazole	100 mg bid × 3 days or 500 mg once	100 mg bid × 3 days or 500 mg once
Capillariasis *(Capillaria philippinensis)*			
Drug of choice:	Mebendazole	200 mg bid × 20 days	200 mg bid × 20 days
Alternatives:	Albendazole	400 mg daily × 10 days	400 mg daily × 10 days
Enterobius vermicularis (pinworm) infection			
Drug of choice:	Pyrantel	11 mg/kg base once (max 1 g);	11 mg/kg base once (max 1 g);

	pamoate	repeat in 2 wk	repeat in 2 wk
OR	Mebendazole	100 mg once; repeat in 2 wk	100 mg once; repeat in 2 wk
OR	Albendazole	400 mg once; repeat in 2 wk	400 mg once; repeat in 2 wk
Clonorchis sinensis(Chinese liver fluke)			
Drug of choice:	Praziquantel	75 mg/kg/day in 3 doses × 1 day	75 mg/kg/day in 3 doses × 1 day
OR	Albendazole	10 mg/kg × 7 days	10 mg/kg × 7 days
Hookworm infection *(Ancylostoma duodenale, Necator americanus)*			
Drug of choice:	Albendazole[7]	400 mg once	400 mg once
OR	Mebendazole	100 mg bid × 3 days or 500 mg once	100 mg bid × 3 days or 500 mg once
OR	Pyrantel pamoate[7]	11 mg/kg (max 1 g) × 3 days	11 mg/kg (max 1 g) × 3 days
Echinococcus granulosus (hydatid cyst)			

Drug of choice	Albendazole	400 mg bid × 1-6 mo	15 mg/kg/day (max 800 mg) × 1-6 mo
Strongyloidiasis *(Strongyloides stercoralis)*			
Drug of choice	Ivermectin	200 µg/kg/day × 2 days	200 µg/kg/day × 2 days
Alternative:	Albendazole	400 mg bid × 7 days	400 mg bid × 7 days
Taenia solium (cysticercosis)			
Treatment of choice		See f**ootnote**	
Alternative:	Albendazole	400 mg bid × 8-30 days; can be repeated as necessary	15 mg/kg/day (max 800 mg) in 2 doses × 8-30 days; can be repeated as necessary
OR	Praziquantel[7]	50-100 mg/kg/day in 3 doses × 30 days	50-100 mg/kg/day in 3 doses × 30 days
Trichuriasis (*Trichuris trichiura,* whipworm)			
Drug of choice:	Mebendazole	100 mg bid × 3 days or 500 mg	100 mg bid × 3 days or 500 mg

		once	once
Alternative:	Albendazole[7]	400 mg × 3 days	400 mg × 3 days
	Ivermectin[7]	200 µg/kg daily × 3 days	200 µg/kg daily × 3 days

Schistosomiasis *(Bilharziasis)*			
Schistosoma haematobium			
Drug of choice:	Praziquantel	40 mg/kg/day in 2 doses × 1 day	40 mg/kg/day in 2 doses × 1 day
Schistosoma japonicum			
Drug of choice:	Praziquantel	60 mg/kg/day in 3 doses × 1 day	60 mg/kg/day in 3 doses × 1 day
Schistosoma mansoni			
Drug of choice:	Praziquantel	40 mg/kg/day in 2 doses × 1 day	40 mg/kg/day in 2 doses × 1 day
Alternative:	Oxamniquine[90]*	15 mg/kg once[91]	20 mg/kg/day in 2 doses × 1 day[91]
Schistosoma mekongi			
Drug of	Praziquantel	60 mg/kg/day in 3	60 mg/kg/day in 3

choice:		doses × 1 day	doses × 1 day

Giardiasis *(Giardia duodenalis)*			
Drug of choice:	Metronidaz[	250 mg tid × 5 days	15 mg/kg/day in 3 doses × 5 days
	Nitazoxanide	500 mg bid × 3 days	1-3 yr: 100 mg every 12 hr × 3 days
			4-11 yr: 200 mg every 12 hr × 3 days
	Tinidazole	2 g once	50 mg/kg once (max 2 g)

Bibliography: Nelson current edition.