



La Fondazione / The Foundation

Ivo de Carneri (Cles, Trento 1927, Milano 1993), professore ordinario di *Parassitologia umana* presso l'Università di Pavia, ha dedicato impegno scientifico e attività sul campo alle malattie che l'Organizzazione mondiale della sanità (Oms) definisce "neglette" e che imperversano nelle aree a Sud del mondo. Fra queste vi è l'arcipelago di Zanzibar in Tanzania.

Qui, nell'isola di Pemba, su incarico della Cooperazione italiana, egli svolge (1988) una missione di accertamento sul progetto di lotta alla schistosomiasi e il suo rapporto si conclude sostenendo la necessità di creare un centro per il controllo delle malattie parassitarie e infettive nel loro insieme.

Quella proposta è stata raccolta dalla Fondazione ed è divenuta una operante realtà che reca il suo nome: il Public Health Laboratory Ivo de Carneri (PHL-IdC).

Nel Terzo Mondo, come in Occidente un tempo, la povertà è il "terreno di coltura" di molte malattie. Ecco la ragione per cui la Fondazione, accanto all'azione nel campo della sanità pubblica, ha intrapreso progetti per il miglioramento ambientale, sociale ed economico dell'Isola di Pemba.

Ivo de Carneri (Cles, Trento, 1927 - Milan, 1993), full professor of Human parasitology at the University of Pavia, spent his research career and field work studying diseases the World Health Organization (WHO) refers to as "neglected", which affect areas in the Global South. One of these is the Zanzibar Archipelago in Tanzania.

Here, on Pemba Island, in 1988 on behalf of the Italian Development Cooperation, Professor de Carneri participated in a fact-finding mission on the campaign against schistosomiasis. His report concluded there was a need to set up a centre for parasitic and infectious diseases surveillance.

That conclusion was taken up by the Foundation and turned into an operative reality that bears his name: the Public Health Laboratory Ivo de Carneri (PHL-IdC).

In the Third World, like once in Western countries, poverty is at the basis of several diseases. This is why the Foundation, alongside public health initiatives, has completed interventions for the environmental, social and economic improvement of Pemba Island.

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Ricerche / Researches

(2001-2017)

**Laboratorio di Sanità Pubblica /
Public Health Laboratory Ivo de Carneri**

Fondazione Ivo de Carneri



Quaderni della Fondazione n° 3 / 2017

I Quaderni della Fondazione / *The Foundation Notebooks*

I *Quaderni* sono una sorta di "libro di bordo" della Fondazione: danno infatti conto delle sue attività nei differenti ambiti.

Le istituzioni, gli enti e le organizzazioni che operano nella cooperazione internazionale allo sviluppo sono il pubblico a cui è rivolta l'iniziativa editoriale e, accanto a essi, tutti coloro che, specie i giovani, rivolgono i loro interessi ai temi dello sviluppo nel Sud del mondo.

The Notebooks are a sort of logbook of the Foundation: they describe its activities in the various fields. The series is addressed to the institutions, authorities and organizations operating in the area of international development cooperation and to everyone – especially young people - interested in the topic of underdevelopment in what is often termed 'the global south'.

Il presente Quaderno / This Notebook

Nell'Isola di Pemba, Zanzibar, il Public Health Laboratory Ivo de Carneri / PhI-IdC è stato costruito, fra il 1977 ed il 1999, grazie ai contributi erogati dalla Cooperazione italiana e dalla Provincia Autonoma di Trento ; costituisce uno dei presidi del sistema sanitario nazionale ; è gestito congiuntamente , tramite un apposito accordo, dal Ministry of Health. Government of Zanzibar e dalla Fondazione Ivo de Carneri.

La conduzione di piani di lotta alle malattie parassitarie ed infettive rientra fra i compiti principali del PhI-IdC che, nel 2005, è stato riconosciuto dall' Organizzazione Mondiale della Sanità – "WHO Collaborating Center for Neglected Tropical Diseases " e, nel 2008, "TB national laboratory for Zanzibar".

Questa intensa attività sul campo ha visto la presenza presso il PhI-IdC di numerosi istituti di ricerca internazionali, quali Department of Veterinary Parasitology University of Naples (Italy), The Earth Institute Columbia University (New York, US), Imperial College (London, UK), Institute of Infectious and Tropical Diseases "Luigi Sacco" Hospital (University of Milan, Italy), Institute of Infectious Diseases INMI L. Spallanzani (Rome), Institute of Infectious and Tropical Diseases University of Brescia and University of Florence (Italy) e molte altre che sono indicate nel siglario delle riviste, alle cui équipes si debbono altrettanto numerose indagini che arricchiscono conoscenze e metodi di intervento su questa o quella affezione (malaria, schistosomiasi, parassitosi intestinali,..)

Tutte le ricerche di cui dà conto il presente fascicolo hanno potuto svolgersi grazie alla presenza qualificata di personale locale e alle attrezzature di cui il PhI-IdC è dotato.

On Pemba Island, Zanzibar, the Ivo de Carneri Public Health Laboratory / PhI-IdC was built between 1977 and 1999 thanks to funds contributed through Italian cooperation and the Autonomous Province of Trento. A structure in the national health system, it is managed jointly, through a special agreement, by the Ministry of Health, Government of Zanzibar, and the Ivo de Carneri Foundation.

Management of the projects to fight against parasitic and infectious diseases is one of the main tasks of the PhI-IdC, which in 2005 was recognized by the World Health Organization (WHO) as a "Collaborating Center for Neglected Tropical Diseases" and in 2008 by the TB National Laboratory for Zanzibar.

This intense on-site activity has brought numerous international research institutes Department of Veterinary Parasitology University of Naples (Italy), The Earth Institute Columbia University (New York, US), Imperial College (London, UK), Institute of Infectious and Tropical Diseases "Luigi Sacco" Hospital (University of Milan, Italy), Institute of Infectious Diseases INMI L. Spallanzani (Rome), Institute of Infectious and Tropical Diseases University of Brescia and University of Florence (Italy) and others important ones not mentioned here , to the PhI-IdC, and their teams can be credited with numerous studies that have enriched our knowledge and approaches to such diseases (malaria, schistosomiasis, intestinal parasites and more).

All the studies reported in this publication were conducted thanks to the qualified presence of local staff and the equipment provided by the PhI-IdC.

The Ivo de Carneri Foundation would like to thank Dr Said Ali ,director of PhI-IdC, for providing the information published here. It is also grateful to Margherita Basanisi and Sara Lamperti for overseeing the print layout.

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1.

Trop Med Int Health. 2001 Mar;6(3):227-31.

School enrollment in Zanzibar linked to children's age and helminth infections.

Authors: Montresor A, Ramsan M, Chwaya HM, Ameir H, Foum A, Albonico M, Gyorkos TW, Savioli L.

School health programmes have been identified as a cost-effective strategy to reduce morbidity due to soil-transmitted helminths in the school-age population, but the low rate of school enrollment in developing countries is a major factor limiting their success.

Objective: The present study was conducted to identify reasons for non-enrollment and to evaluate differences in the occurrence of helminth infection between enrolled and non-enrolled children in Zanzibar, United Republic of Tanzania.

Method: A questionnaire was submitted to 520 households to obtain information about enrollment and other socio-economic indicators. In addition, one school-age child was randomly selected in each household and investigated for soil-transmitted helminth infection.

Results: Overall, 71% of school-age children were enrolled. Enrollment increased with age. Only 41% of children under 9 years of age were enrolled compared to 91% in children older than 12 years. Enrollment is delayed because of an insufficient number of schools. Among non-enrolled school-age children, the proportion of heavy intensity infections was twice that of enrolled school-age children.

Conclusions: Most of the non-enrolled school-age children live together with enrolled siblings in the same household, thereby representing an important opportunity for effective outreach activities. The effectiveness of the school-based helminth control programme in reducing the intensity of infection was confirmed. The significant gains achieved by enrolled school-age children in this study must be viewed as an attainable goal for the important numbers of non-enrolled school-age children in endemic areas. Decision-makers must ensure that outreach activities are included in helminth control programmes targeted to school-age children.

PMID: 11299040 [PubMed - indexed for MEDLINE]

2.

Trop Med Int Health. 2001 Jul;6(7):535-7.

Extending anthelmintic coverage to non-enrolled school-age children using a simple and low-cost method.

Authors: Montresor A, Ramsan M, Chwaya HM, Ameir H, Foum A, Albonico M, Gyorkos TW, Savioli L.

School health programmes are the basis of the strategy defined by WHO to reduce morbidity due to soil-transmitted nematodes and schistosomes in school age populations in developing countries. However, low rates of school enrollment can be a major factor limiting their success. In the present study enrolled children were informed by teachers on the date of the next deworming campaign and were invited to pass along this information to parents, siblings and friends of school-age. On the day of the deworming campaign, teachers were instructed to administer anthelmintics to enrolled and not enrolled school-age children present at school. In the month following the treatment day, information about coverage was collected by questionnaire in 257 households in two regions of Unguja Island, Zanzibar. Over 89% of school age children resulted treated (98.9% of those enrolled plus 60% of those not enrolled). The additional cost of treating non-enrolled is limited to the cost of providing additional doses of anthelmintic drug in each school. Non-enrolled school age children can easily, successfully and inexpensively included in school based deworming campaign. Managers of control programmes are invited to test this method adapting it in their particular and cultural environment.

PMID: 11469947 [PubMed - indexed for MEDLINE]

3.

J Clin Microbiol. 2001 Jul;39(7):2681-2.

Efficacy of new low-cost filtration device for recovering *Schistosoma haematobium* eggs from urine.

Authors: Gyorkos TW, Ramsan M, Foum A, Khamis IS.

A new, inexpensive filtration device for the diagnosis of urinary schistosomiasis was tested against the commonly used Millipore device. The experimental protocol was performed with 25 urine samples known to be positive for

Schistosoma haematobium. The results suggest that the new device is as effective as the Millipore device for the diagnosis of urinary schistosomiasis. Its low cost will be attractive to schistosomiasis control programs.

DOI: 10.1128/JCM.39.7.2681-2682.2001 / PMCID: PMC88211 / PMID: 11427595 [PubMed - indexed for MEDLINE]

4.

BMJ. 2001 Dec 15;323(7326):1389-93.

Effects of iron supplementation and anthelmintic treatment on motor and language development of preschool children in Zanzibar: double blind, placebo controlled study.

Authors: Stoltzfus RJ, Kvalsvig JD, Chwaya HM, Montresor A, Albonico M, Tielsch JM, Savioli L, Pollitt E.

Comment in BMJ. 2001 Dec 15;323(7326):1377-8.

Objective: To measure the effects of iron supplementation and anthelmintic treatment on iron status, anaemia, growth, morbidity, and development of children aged 6-59 months.

Design: Double blind, placebo controlled randomised factorial trial of iron supplementation and anthelmintic treatment.

Setting: Community in Pemba Island, Zanzibar.

Participants: 614 preschool children aged 6-59 months.

Main outcome measures: Development of language and motor skills assessed by parental interview before and after treatment in age appropriate subgroups.

Results: Before intervention, anaemia was prevalent and severe, and geohelminth infections were prevalent and light-Plasmodium falciparum infection was nearly universal. Iron supplementation significantly improved iron status, but not haemoglobin status. Iron supplementation improved language development by 0.8 (95% confidence interval 0.2 to 1.4) points on the 20 point scale. Iron supplementation also improved motor development, but this effect was modified by baseline haemoglobin concentrations (P=0.015 for interaction term) and was apparent only in children with baseline haemoglobin concentrations <90 g/l. In children with a baseline haemoglobin concentration of 68 g/l (one standard deviation below the mean value), iron treatment increased scores by 1.1 (0.1 to 2.1) points on the 18 point motor scale. Mebendazole significantly reduced the number and severity of infections caused by Ascaris lumbricoides and Trichuris trichiura, but not by hookworms. Mebendazole increased development scores by 0.4 (-0.3 to 1.1) points on the motor scale and 0.3 (-0.3 to 0.9) points on the language scale.

Conclusions: Iron supplementation improved motor and language development of preschool children in rural Africa. The effects of iron on motor development were limited to children with more severe anaemia (baseline haemoglobin concentration <90 g/l). Mebendazole had a positive effect on motor and language development, but this was not statistically significant.

PMCID: PMC60982 / PMID: 11744561 [PubMed - indexed for MEDLINE]

2002

5.

Trans R Soc Trop Med Hyg. 2002 Mar-Apr;96(2):197-9.

Is the exclusion of children under 24 months from anthelmintic treatment justifiable?

Authors: Montresor A, Stoltzfus RJ, Albonico M, Tielsch JM, Rice AL, Chwaya HM, Savioli L.

There are no reports documenting toxicity or adverse effects after treatment of children aged < 24 months with benzimidazole derivatives and there is an urgent need to clarify this point in light of the potential detrimental effect that soil-transmitted helminthiasis has on this age-group. A total of 653 treatments (317 mebendazole 500 mg; 336 placebo) were administered in 1996/97 to 212 children aged < 24 months as part of a 1-year anthelmintic drug study conducted among preschool-age children in Tanzania. Data on fever, cough, diarrhoea, dysentery and acute respiratory illness were collected 1 week following the treatment. No differences between the occurrence of adverse effects in the 2 groups were observed. In light of the potential nutritional benefit achieved by regular deworming in this young age-group, the policy that excludes children aged < 24 months from treatment should be re-considered.

PMID: 12055814 [PubMed - indexed for MEDLINE]

6.

Trans R Soc Trop Med Hyg. 2002 May-Jun;96(3):323-4.

Field test of the 'dose pole' for praziquantel in Zanzibar.

Authors: Montresor A, Engels D, Ramsan M, Foun A, Savioli L.

A graduated pole for height measurement, estimating the number of praziquantel tablets needed for treatment, was field-tested on 1289 children in Zanzibar. A bathroom-type scale performed better than the dose pole in delivering the optimal dose (40-60 mg/kg) and the 2 methods performed similarly in delivering a dose considered appropriate (30-60 mg/kg).

PMID: 12174788 [PubMed - indexed for MEDLINE]

7.

Trans R Soc Trop Med Hyg. 2002 Sep-Oct;96(5):470-5.

New insights into the transmission biology of urinary schistosomiasis in Zanzibar.

Authors: Stothard JR, Mgeni AF, Khamis S, Seto E, Ramsan M, Hubbard SJ, Kristensen TK, Rollinson D.

A better understanding of the transmission biology of urinary schistosomiasis in Zanzibar, Tanzania was only possible after the development of molecular DNA markers for identification of *Bulinus africanus* group snails, the potential intermediate hosts of *Schistosoma haematobium*. Hitherto, identification of natural populations of *B. globosus* and *B. nasutus* was problematic and the intermediate host status and distribution of either species remained speculative.

By recourse to molecular markers, snail distribution maps could be drawn, revealing an allopatric distribution and, more importantly, leading to the discovery that *B. nasutus* played no role in transmission. Indeed, in Unguja the area of active transmission of *S. haematobium* to humans is confined within the distribution of *B. globosus*. This strong relationship may prove useful for predicting the distribution of urinary schistosomiasis within Zanzibar and, if snail schistosome compatibilities persist, in other areas nearby, e.g. coastal Tanzania and Kenya. The transmission biology of urinary schistosomiasis in Zanzibar is reviewed, the paper reports on ongoing malacological studies in Zanzibar and Kenya and finally closes by posing the question whether medical malacology forms an essential component associated with mass-scale chemotherapy control programmes.

PMID: 12474469 [PubMed - indexed for MEDLINE]

8.

Trans R Soc Trop Med Hyg. 2002 Sep-Oct;96(5):507-14.

Urinary schistosomiasis in schoolchildren on Zanzibar Island (Unguja), Tanzania: a parasitological survey supplemented with questionnaires.

Authors: Stothard JR, Mgeni AF, Khamis S, Seto E, Ramsan M, Rollinson D.

The distribution of urinary schistosomiasis in schoolchildren on Zanzibar Island (Unguja) was surveyed in May 2001 to test a potential correlation with the distribution of snail species of the *Bulinus africanus* group and to record contemporary baseline epidemiological data. Quasi-random samples of 40 schoolchildren of mixed sexes were selected from each of 10 schools. *Schistosoma haematobium* infections were detected upon the basis of micro-haematuria with subsequent confirmation by microscopy examination for schistosome eggs. At the time of urine collection, each child was interviewed with a suite of 12 questions prepared as a standardized questionnaire. Total prevalence of urinary schistosomiasis (known locally as kichocho) was 12% although schistosome infections were absent in 5 schools. Schools located west of 39 degrees 19'E and north of 6 degrees 10'S harboured nearly all of the infections; the highest prevalence (55%) was found at Kinyasini where many *B. globosus* habitats occur nearby. The general level of understanding of kichocho was low (24%) and individual self-diagnosis was poor (sensitivity, 8.5%; specificity, 85%). Grouped freshwater-contact patterns of schoolchildren differed significantly between schools and correlated well with prevalence of infections within schools. Across the island the area of active transmission of *S. haematobium* to humans appears confined within the distribution of *B. globosus*. There was no epidemiological evidence to suggest any involvement of *B. nasutus* in local transmission, confirming previous laboratory findings. In areas where *B. globosus* occurs, targeted snail control should be considered, to reduce schistosome transmission.

PMID: 12474477 [PubMed - indexed for MEDLINE]

9.

Ann Trop Med Parasitol. 2002 Oct;96(7):717-26.

Soil-transmitted nematode infections and mebendazole treatment in Mafia Island schoolchildren.

Authors: Albonico M, Ramsan M, Wright V, Jape K, Haji HJ, Taylor M, Savioli L, Bickle Q.

In August 2000, a cross-sectional study was performed to assess the prevalence and intensity of soil-transmitted nematode infections in schoolchildren on Mafia Island. Hookworm infection was widespread (72.5% prevalence) whereas *Trichuris trichiura* was less prevalent (39.7%) and *Ascaris lumbricoides* was present at a low prevalence (4.2%), mainly in urban areas. In a subsample of the study population, both *Necator americanus* and *Ancylostoma duodenale* were found, although *N. americanus* was more prevalent. This survey was followed by a parasitological evaluation of mebendazole treatment using a single, 500-mg dose.

The data on outcome were used for comparison with those from recent studies of similar treatment regimens in the neighbouring island of Pemba, Zanzibar, where periodic chemotherapy with mebendazole to schoolchildren has been implemented as part of a helminth-control programme since 1994. A higher efficacy of mebendazole against hookworm infection was found in Mafia Island (where a cure 'rate' of 31.3% and an egg-reduction 'rate' of 78.1% were recorded) when compared with that observed in Pemba Island, possibly indicating that hookworms may be developing mebendazole resistance on Pemba Island as a result of intense exposure to the drug there.

DOI: 10.1179/000349802125001942 / PMID: 12537633 [PubMed - indexed for MEDLINE]

10.

Trans R Soc Trop Med Hyg. 2002 Nov-Dec;96(6):685-90.

Evaluation of the efficacy of pyrantel-oxantel for the treatment of soil-transmitted nematode infections.

Authors: Albonico M, Bickle Q, Haji HJ, Ramsan M, Khatib KJ, Montresor A, Savioli L, Taylor M.

A randomized controlled trial comparing the efficacy of pyrantel-oxantel (10 mg/kg) with mebendazole (500 mg) was performed on 1329 schoolchildren aged 6-9 years on Pemba Island in September-October 2000 to evaluate alternative single-dose drugs for regular treatment of intestinal nematode infections. Both mebendazole and pyrantel-oxantel were very effective in eliminating *Ascaris lumbricoides* infection, inducing cure rates of more than 96% and reducing the mean egg counts by more than 95%. Both drugs had a moderate efficacy against *Trichuris trichiura* infection, but pyrantel-oxantel had a higher cure rate (31.5% vs. 23.3%, $P < 0.01$), though the reductions in egg counts did not differ significantly and were more than 80%. Pyrantel-oxantel and mebendazole had a similar, poor efficacy in curing hookworm infections and had a moderate effect in reducing the egg counts by 67% and 68%, respectively. Pyrantel-oxantel (10 mg/kg) offers a valuable alternative to mebendazole as a single-dose treatment for the control of intestinal nematode infections in children in endemic areas of sub-Saharan Africa, due to its comparable efficacy, its low cost and its suitability for use in young children.

PMID: 12625151 [PubMed - indexed for MEDLINE]

2003

11.

Trop Med Int Health. 2003 Jul;8(7):619-24.

Performance of the Haemoglobin Colour Scale in diagnosing severe and very severe anaemia.

Authors: Montresor A, Ramsan M, Khalfan N, Albonico M, Stoltzfus RJ, Tielsch JM, Savioli L.

Objective: To assess the accuracy of Haemoglobin Colour Scale (HCS) in identifying severely anaemic [haemoglobin (Hb) <7 g/dl] and very severely anaemic (Hb <5 g/dl) individuals, and to compare the performances of a group of health workers using HCS after training with a standard method.

Method: The study consisted of two parts. In part 1, the performance of HCS was compared with clinical examination in a hospital population of which more than 450 individuals were severely anaemic and more than 120 very severely anaemic. Part 2 of the study was conducted in eight dispensaries where the performances of 13 health workers using the colour scale were compared with the performances of eight other health workers using clinical signs to estimate Hb.

Results: The colour scale was 92% sensitive for both severe anaemia and very severe anaemia and performed better than clinical examination. Health workers who used the colour scale did better in identifying anaemic and severely anaemic individuals, than those who used clinical examination.

Conclusions: The colour scale improves health workers' capacity to identify severely anaemic individuals and could be used as a basis for referral. Although the diagnostic accuracy of the workers using HCS varied widely, in most cases they did significantly better than those who used clinical investigation alone.

PMID: 12828544 [PubMed - indexed for MEDLINE]

12.

Acta Trop. 2003 May;86(2-3):233-42.

Methods to sustain drug efficacy in helminth control programmes.

Author: Albonico M.

Abstract: Assessment of the efficacy of anthelmintic treatment in public health is a broad concept, which goes beyond parasitological methods and should be clearly defined according to several indicators of morbidity. Several factors may influence the efficacy of anthelmintic drugs. The quality of drug is an issue of great importance, especially when produced locally as a generic product and used in large-scale chemotherapy-based control programmes. Other factors include the drug-patient interaction, the host-parasite relationship, the diagnostic method used, genetic variations between parasite strains and induced drug resistance. Veterinary scientists have warned that drug resistance can be selected through frequent mass treatment of sheep and goats and have developed a body of knowledge on evaluation of efficacy and detection of resistance in nematodes of veterinary importance. In soil-transmitted nematodes infections of humans, the egg reduction rate (ERR), the egg hatch assay (EHA) and novel molecular biological techniques may be used to monitor drug efficacy in helminth control programmes and to detect early occurrence of resistance. Evidence of reduced drug efficacy of some anthelmintics has been suggested by recent studies and strategies to prevent or delay the emergence of drug resistance in human soil-transmitted nematodes.

PMID:12745140 [PubMed - indexed for MEDLINE]

13.

Bull World Health Organ. 2003;81(5):343-52. Epub 2003 Jul 7.

Efficacy of mebendazole and levamisole alone or in combination against intestinal nematode infections after repeated targeted mebendazole treatment in Zanzibar.

Authors: Albonico M, Bickle Q, Ramsan M, Montresor A, Savioli L, Taylor M.

Objective: To evaluate the efficacy of and resistance to mebendazole (500 mg) and levamisole (40 or 80 mg), alone or in combination, for the treatment of *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm infections on Pemba Island – an area exposed to periodic school-based mebendazole treatment since 1994.

Methods: A randomized, placebo-controlled trial was carried out in 914 children enrolled from the first and fifth grades of primary schools. Stool samples collected at baseline and 21 days after treatment were examined by the Kato-Katz technique to assess the prevalence and intensity of helminth infection.

Findings: Efficacies of mebendazole and levamisole as single treatments against intestinal nematode infections were comparable with those in previous trials, but mebendazole treatment of hookworm infections gave significantly lower cure (7.6%) and egg reduction (52.1%) rates than reported in a study undertaken before the beginning of periodic chemotherapy (cure rate, 22.4%; egg reduction rate, 82.4%). Combined treatment with mebendazole and levamisole had a significantly higher efficacy against hookworm infections (cure rate, 26.1%; egg reduction rate, 88.7%) than either drug given alone. No difference in mebendazole efficacy was found in children who had been treated repeatedly compared with those who had not been treated previously.

Conclusions: The overall efficacy of mebendazole against hookworm infections after periodic chemotherapy is reduced. The efficacy of benzimidazoles in chemotherapy-based control programmes should be monitored closely. Combined treatment with mebendazole and levamisole may be useful as a tool to delay the development of benzimidazole resistance.

PMCID: PMC2572452 / PMID: 12856052 [PubMed - indexed for MEDLINE]

14.

J Nutr. 2004 Feb;134(2):348-56.

Low dose daily iron supplementation improves iron status and appetite but not anemia, whereas quarterly anthelmintic treatment improves growth, appetite and anemia in Zanzibari preschool children.

Authors: Stoltzfus RJ, Chway HM, Montresor A, Tielsch JM, Jape JK, Albonico M, Savioli L.

Iron deficiency and helminth infections are two common conditions of children in developing countries. The consequences of helminth infection in young children are not well described, and the efficacy of low dose iron supplementation is not well documented in malaria-endemic settings. A 12-mo randomized, placebo controlled, double-blind trial of 10 mg daily iron and/or mebendazole (500 mg) every 3 mo was conducted in a community-based sample of 459 Zanzibari children age 6-71 mo with hemoglobin > 70 g/L at baseline. The trial was designed to examine treatment effects on growth, anemia and appetite in two age subgroups.

Iron did not affect growth retardation, hemoglobin concentration or mild or moderate anemia (hemoglobin < 110 g/L or < 90 g/L, respectively), but iron significantly improved serum ferritin and erythrocyte protoporphyrin. Mebendazole significantly reduced wasting malnutrition. but only in children <30 mo old. The adjusted odds ratios (AORs) for mebendazole in this age group were 0.38 (95% CI: 0.16, 0.90) for weight-for-height less than -1 Z-score and 0.29 (0.09, 0.91) for small arm circumference. In children <24 mo old, mebendazole also reduced moderate anemia (AOR: 0.41, 0.18, 0.94). Both iron and mebendazole improved children's appetite, according to mothers' report. In this study, iron's effect on anemia was limited, likely constrained by infection, inflammation and perhaps

other nutrient deficiencies. Mebendazole treatment caused unexpected and significant reductions in wasting malnutrition and anemia in very young children with light infections. We hypothesize that incident helminth infections may stimulate inflammatory immune responses in young children, with deleterious effects on protein metabolism and erythropoiesis.

PMID: 14747671 [PubMed - indexed for MEDLINE]

15.

Mol Biochem Parasitol. 2004 Apr;134(2):281-4.

Molecular analysis of the beta-tubulin gene of human hookworms as a basis for possible benzimidazole resistance on Pemba Island.

Authors: Albonico M, Wright V, Bickle Q.

DOI: 10.1016/j.molbiopara.2003.12.008

PMID: 15003848 [PubMed - indexed for MEDLINE]

NOT AVAILBLE FOR FREE

16.

East Afr Med J. 2004 Jun;81(6):307-12.

Epidemiology of streptococcus group A in school aged children in Pemba.

Authors: Braitto A, Galgani I, Mohammed MR, Iozzi C, Ame SM, Haji HS, Zanchi A.

Abstract

Background: In Pemba (Zanzibar) all the risk factors which favour Group A Streptococci spreading, infections and late sequelae are present, though GAS epidemiology is unknown.

Objective: To determine the prevalence of GAS pharyngeal carriers among school-aged-children.

Design: Community-based cross sectional study, carried out at the end of the dry season (January-February 2001).

Setting: Eight primary schools over the four Pemba districts were included in the study.

Methods: Two thousand two hundred and eighty six children aged 7-10 years were selected by random sampling and submitted to throat-swab after informed consent. Swabs were processed according to the "Lennette Manual of Clinical Microbiology" 7th Ed. Isolated were tested for antibiotic susceptibility toward penicillins, erythromycin, clindamycin, josamycin, cloramphenicol, levofloxacin, rifampin and tetracyclines.

Results: Twenty seven point six percent of school-aged children harboured beta-haemolytic Streptococci in their pharynx; most of the isolates were serologically identified as non Group A streptococci group C and G represented more than 70% of all strains, 38.8% of whom were identified as group G; the prevalence of group A streptococci carriers among healthy children all over the island was 8.6%; group A streptococci isolates were sensitive to all the antibiotic tested, except tetracyclines, towards which 83.2% of strains were resistant.

Conclusions: This is the first research in the field of bacteriology carried out in Pemba. According to the epidemiology of group A streptococci and to the environmental and underlying factors which predispose to late group A streptococci sequelae, we suggest to consider antibiotic treatment for children presenting with sore throat with fever and swollen cervical lymphonodes without cough or coryza.

PMID:16167678 [PubMed - indexed for MEDLINE]

17.

J Nutr. 2004 Nov;134(11):3037-41.

Low-dose daily iron supplementation for 12 months does not increase the prevalence of malarial infection or density of parasites in young Zanzibari children.

Authors: Mebrahtu T, Stoltzfus RJ, Chwaya HM, Jape JK, Savioli L, Montresor A, Albonico M, Tielsch JM.

Conflicting evidence exists on the possible role of iron supplementation in the predisposition to malaria infection or the enhancement of its clinical severity. Where anemia prevalence is >40%, current guidelines are to provide low-dose daily iron to young children for up to 18 mo. Earlier studies used doses higher than the current guidelines, intermittent doses, or have supplemented for durations < or = 4 mo. We aimed to assess the effect of low-dose, long-term iron supplementation on malaria infection using a double-blind, placebo-controlled, randomized design, and to examine possible subgroup effects by season and child age. The study was conducted in Pemba Island, Zanzibar, where Plasmodium falciparum malaria has year-round high transmission. A community-based sample of 614 children 4-71 mo old was randomly allocated to 10 mg/d iron or placebo for 12 mo. Outcome measures were the prevalence and density of malaria infection, which was assessed by blood films at monthly intervals. At baseline, 94.4% were anemic (hemoglobin < 110 g/L), 48.1% were stunted (height-for-age Z-score less than -2) and >80% had malaria-positive blood films. No significant differences in malariometric indices were observed between children in the iron-supplemented and placebo groups. Parasite density was higher in certain months and in younger children, but iron supplementation was not associated with any malarial infection outcome in any season or age subgroup. We conclude that in this environment of high malaria transmission, daily oral low-dose supplementation of iron for 12 mo did not affect the prevalence of malaria infection or parasite density.

PMID: 15514272 [PubMed - indexed for MEDLINE]

18.

Mol Biochem Parasitol. 2004 Apr;134(2):281-4.

Molecular analysis of the beta-tubulin gene of human hookworms as a basis for possible benzimidazole resistance on Pemba Island.

Authors: Albonico M, Wright V, Bickle Q.

PMID:15003848 / DOI:10.1016/j.molbiopara.2003.12.008 [PubMed - indexed for MEDLINE]

Text is available only on paid admission on <http://www.sciencedirect.com>

19.

Int J Parasitol. 2004 Oct;34(11):1205-10.

Monitoring drug efficacy and early detection of drug resistance in human soil-transmitted nematodes: a pressing public health agenda for helminth control.

Authors: Albonico M, Engels D, Savioli L.

Abstract : Control of soil-transmitted helminth infection and elimination of lymphatic filariasis by periodic chemotherapy increase drug pressure for possible occurrence of resistance against single dose anthelmintics. In veterinary practice, frequent treatment of closed populations has led to a serious problem of anthelmintic drug resistance which is now largely irreversible. Reduced efficacy of single dose drugs against nematodes of humans should be taken as early warnings to tackle the issue in due time. Research and development of sensitive tools for monitoring and early detection of drug resistance is urgently needed to sustain the benefits of helminth control

programs gained so far. A concerted action with international partners and the creation of a network of scientists to address this issue is the next pressing public health issue for helminth control.

PMID:15491582 / DOI:[10.1016/j.ijpara.2004.08.001](https://doi.org/10.1016/j.ijpara.2004.08.001) [PubMed - indexed for MEDLINE]

2005

20.

2005 Field phase Report.

Haptoglobin gene polymorphism and anaemia in pregnant Zanzibari women.

Authors: Ali S, Hamad JH, Ramsan M, Stoltzfus RJ, Prentice A, Ghattas H.

Not available

21.

Matern Child Nutr. 2005 Jan;1(1):51-8.

Linking traditional treatments of maternal anaemia to iron supplement use: an ethnographic case study from Pemba Island, Zanzibar.

Authors: Young SL, Ali SM.

Iron deficiency anaemia is the most common form of malnutrition in the world. Pregnant women are particularly at risk for anaemia. Insufficient attention has been paid to the reasons underlying the only moderate success of iron supplementation. In this article an additional factor that can affect the use of iron supplements is proposed: their relevance to 'traditional' or nonbiomedical treatments of anaemia. This paper represents what is to our knowledge the first ethnographic description of nonbiomedical treatments for maternal anaemia. The research was conducted over several months on Pemba, one of the islands of the Zanzibar archipelago. Data were collected using a variety of qualitative methods, including in-depth interviews, focus group discussions and participant observation. Informants included 25 mothers and 27 traditional and biomedical health care workers. The resulting ethnography elucidates Pembans' beliefs about the relationship of food, traditional medicine, spirits and biomedical medicine in relation to anaemia. In the analysis of the ethnography, both anthropology and public health perspectives are incorporated to suggest how the understanding of these beliefs is useful for increasing iron supplement use.

DOI: [10.1111/j.1740-8709.2004.00002.x](https://doi.org/10.1111/j.1740-8709.2004.00002.x) / PMID: 16881879 [PubMed - indexed for MEDLINE]

22.

Trop Doct. 2005 Apr;35(2):78-81.

Clinical predictors of malaria and other febrile illnesses in children under five on Pemba Island, Tanzania.

Authors: Yacoub S, Mohammed MJ, Ramsan M, Albonico M.

Under the current guidelines of presumptive treatment of all children with reported fever, the risk of over-prescribing antimalarial drugs and missing other important causes of fever, like acute respiratory tract infection (ARI), is substantial. Clinical algorithms have been shown to be useful in diagnosing malaria, but often with differing results, due to regional variations. We set out to explore the clinical features associated with malaria compared with other febrile illnesses and specifically severe malaria with ARI in children under five in Pemba. Two hundred and seven children aged six months to five years presenting to a hospital clinic with fever were studied in Pemba. Clinical findings were related to the presence of malaria parasitaemia. Malaria accounted for 67.7% of the febrile episodes investigated. Five symptoms and signs, including pallor, drowsiness, splenomegaly, fever duration and no chest crackles, could accurately predict a case of malaria with a sensitivity of 91.3% and specificity of 53% and positive predictive value of 80.3%. Several clinical features were found to differentiate severe malaria from ARI. These results confirm that clinical algorithms can increase the diagnostic accuracy of malaria, although not sufficiently to replace microscopy, and by promoting the use of clinical skills other treatable causes of febrile illnesses may be identified. These findings could have implications in optimizing treatment and malaria control in children on Pemba.

DOI: [10.1258/0049475054036913](https://doi.org/10.1258/0049475054036913) / PMID: 15970025 [PubMed - indexed for MEDLINE]

23.

J Nutr. 2005 Apr;135(4):814-9.

Iron deficiency and physical growth predict attainment of walking but not crawling in poorly nourished Zanzibari infants.

Authors: Kariger PK, Stoltzfus RJ, Olney D, Sazawal S, Black R, Tielsch JM, Frongillo EA, Khalfan SS, Pollitt E.

Locomotion allows infants to explore their environment, promoting development in other domains. Motor progression involves biological systems and experiential factors. Nutritional deficiencies could interfere with systems involved in locomotion. This study examined the associations between height-for-age (HAZ), weight-for-height (WHZ) Z-scores and anemia-iron status on locomotion in 646 Zanzibari infants. Motor milestones were assessed by trained observers using a 14-item scale. Two mutually exclusive samples were created. The crawling sample (n = 167, 6-18 mo old) included infants that crawled only or did not crawl; the walking sample (n = 479, 9-18 mo old) included children that walked alone or did not walk alone. Of the crawling and walking samples, 82.6 and 83.9% respectively, were iron deficient and/or anemic (hemoglobin < 100 g/L; zinc protoporphyrin > or = 90 micromol/mol heme). Stunting (HAZ less than -2) occurred in 30.5% of the crawling sample and 38.4% of the walking sample. Logistic regression models estimated the influence of factors on crawling vs. not crawling or walking vs. not walking. Two models were tested: 1) included sex, age, SES, HAZ and WHZ; 2) added anemia-iron status category to Model 1. HAZ improved the odds of crawling by 30%, but was not significant in either model. Model 2 fit the walking sample data best (P < 0.0001); an increase in HAZ doubled the odds of walking and nonanemic, noniron deficient children were 66% more likely to walk than those with anemia and/or iron deficiency. In this sample of poorly nourished infants, growth and anemia-iron status are significant predictors of walking, but not crawling.

PMID: 15795440 [PubMed - indexed for MEDLINE]

24.

Int J Parasitol. 2005 Jun;35(7):803-11. Epub 2005 Apr 26.

Development of the egg hatch assay for detection of anthelmintic resistance in human hookworms.

Authors: Albonico M, Wright V, Ramsan M, Haji HJ, Taylor M, Savioli L, Bickle Q.

Evidence of development and rapid spread of anthelmintic resistance in veterinary nematodes raises concern that the increasingly frequent treatments used in chemotherapy-based programmes to control human soil-transmitted helminths may select resistant worms. The aim of this study was to adapt, refine, and evaluate the Egg Hatch Assay (EHA) test, which has been used for veterinary nematodes, for field testing of benzimidazole (BZ) susceptibility/resistance in human hookworms. A second objective was to use this EHA to assess whether a population of worms resistant to mebendazole (MBZ) has built up in a

sub-population of frequently treated children in Pemba Island. Stools from 470 school children enrolled in the first (Standard 1) and in the fifth (Standard 5) class were examined at baseline and at 21 days after treatment with 500 mg MBZ or placebo tablets. Standard 1 children had never received any MBZ treatment whilst Standard 5 children had received a total of 13 rounds of treatment. The EHA, involving culture of purified eggs with increasing drug concentrations showed that, for thiabendazole (TBZ), the mean ED(50)s (concentrations required to prevent 50% of the viable eggs from hatching) for all children at baseline were 0.079 microg/ml at 48h and 0.120 microg/ml at 72h (P<0.001). For MBZ, the mean ED(50)s for all children at baseline were 0.895 microg/ml at 48h and 1.50 microg/ml at 72h (P<0.001). For TBZ and for MBZ the ED(50) from Standard 1 were similar to those from Standard 5 children both at 48 and at 72h. At the follow-up for TBZ and for MBZ, there was no significant difference between the ED(50) from children who had received MBZ and children treated with placebo. In Pemba, TBZ ED(50) values of children non-exposed (Standard 1) and of children exposed (Standard 5) to MBZ treatment, and data from children treated with MBZ and placebo indicate that a drug-resistant worm population has not built up within treated individuals, and that periodic treatment has not yet selected for widespread BZ resistance, at least at the threshold detectable by the EHA in this study. However, ED(50) values for strains isolated from Mafia island, an area never exposed to BZ treatment were lower than for Pemba, suggesting lowered sensitivity of hookworm eggs recovered from Pemba children towards BZ.

DOI: 10.1016/j.ijpara.2005.02.016

25.

Am J Clin Nutr. 2005 Aug;82(2):406-12.

Short-term effects of vitamin A and antimalarial treatment on erythropoiesis in severely anemic Zanzibari preschool children.

Authors: Cusick SE, Tielsch JM, Ramsan M, Jape JK, Sazawal S, Black RE, Stoltzfus RJ.

Background: The pathophysiology of anemia in coastal East Africa is complex. Impaired erythropoietin production is one possible mechanism. Plasmodium falciparum malaria has been found to blunt erythropoietin production, whereas vitamin A stimulates erythropoietin production in vitro.

Objective: We investigated the 72-h effects of vitamin A and the antimalarial drug sulfadoxine pyrimethamine (SP) on erythropoietin production in severely anemic (hemoglobin < or = 70 g/L) preschool children in Zanzibar, a region of known vitamin A deficiency. We hypothesized that both treatments would stimulate erythropoietin production directly, within 72 h, before a change in hemoglobin would occur.

Design: One hundred forty-one severely anemic children were identified during the baseline assessment of a morbidity substudy of a community-based micronutrient supplementation trial. All severely anemic children were randomly assigned to receive either vitamin A (100,000 or 200,000 IU depending on age) or SP at baseline; 72 h later they received the opposite treatment plus daily hematinic syrup for 90 d. Erythropoietic and parasitic indicators were assessed at baseline and again after 72 h.

Results: After 72 h, SP reduced the malaria parasite density (by 5029 parasites/microL; P < 0.001), CRP concentrations (by 10.6 mg/L; P = 0.001), and the proportion of children infected with malaria (by 32.4%; P < 0.001). Vitamin A reduced CRP (by 9.6 mg/L; P = 0.011), serum ferritin (by 18.1 microg/L; P = 0.042), and erythropoietin (by 194.7 mIU/mL; P = 0.011) concentrations and increased the reticulocyte production index (by 0.40; P = 0.041).

Conclusions: Contrary to our hypothesis, vitamin A significantly decreased erythropoietin concentration. The most important effect of both vitamin A and SP was the rapid reduction of inflammation. Vitamin A also mobilized iron from stores and stimulated the production of new erythrocytes.

PMID: 16087986 [PubMed - indexed for MEDLINE]

26.

J Helminthol. 2005 Dec;79(4):381-4.

Soil-transmitted helminths and haemoglobin status among Afghan children in World Food Programme assisted schools.

Authors: Gabrielli AF¹, Ramsan M, Naumann C, Tsoqzolmaa D, Bojang B, Khoshal MH, Connolly M, Stothard JR, Montresor A, Savioli L.

PMID:16336723 [PubMed - indexed for MEDLINE]

2006

27.

Adv Parasitol. 2006;61:311-48.

Intervention for the control of soil-transmitted helminthiasis in the community.

Authors: Albonico M, Montresor A, Crompton DW, Savioli L.

Abstract : The global strategy for the control of soil-transmitted helminthiasis, based on regular anthelmintic treatment, health education and improved sanitation standards, is reviewed. The reasons for the development of a control strategy based on population intervention rather than on individual treatment are explained. The evidence and experience from control programmes that created the basis for (i) the definition of the intervention package, (ii) the identification of the groups at risk, (iii) the standardization of the community diagnosis and (iv) the selection of the appropriate intervention for each category in the community are discussed. How to best deliver the appropriate intervention, the impact of the control measures on morbidity and on indicators such as school attendance, cognitive development and productivity are presented. The factors influencing the cost-benefits of helminth control are also considered. The recent progress on the control of soil-transmitted helminth infections is illustrated. Research needs are analysed in relation to the most recent perceptions from private-public partnerships involved in helminth control. The way forward for the control of soil-transmitted helminth infections is

described as a multi-disease approach that goes beyond deworming and fosters a pro-poor strategy that supports the aims of the Millennium Development Goals.

PMID:16735168 / DOI:10.1016/S0065-308X(05)61008-1

28.

Lancet. 2006 Jan 14;367(9505):133-43.

Effects of routine prophylactic supplementation with iron and folic acid on admission to hospital and mortality in preschool children in a high malaria transmission setting: community-based, randomised, placebo-controlled trial.

Authors: Sazawal S, Black RE, Ramsan M, Chwaya HM, Stoltzfus RJ, Dutta A, Dhingra U, Kabole I, Deb S, Othman MK, Kabole FM.

Erratum in: Lancet. 2006 Jan 28;367(9507):302.

Comment in: Lancet. 2006 Jan 14;367(9505):90-1. Lancet. 2006 Mar 11;367(9513):816.

Background: Anaemia caused by iron deficiency is common in children younger than age 5 years in eastern Africa. However, there is concern that universal supplementation of children with iron and folic acid in areas of high malaria transmission might be harmful.

Methods: We did a randomised, placebo-controlled trial, of children aged 1-35 months and living in Pemba, Zanzibar. We assigned children to daily oral supplementation with: iron (12.5 mg) and folic acid (50 mug; n=7950), iron, folic acid, and zinc (n=8120), or placebo (n=8006); children aged 1-11 months received half the dose. Our primary endpoints were all-cause mortality and admission to hospital. Analyses were by intention to treat. This study is registered as an International Standard Randomised Controlled Trial, number ISRCTN59549825.

Findings: The iron and folic acid-containing groups of the trial were stopped early on Aug 19, 2003, on the recommendation of the data and safety monitoring board. To this date, 24 076 children contributed a follow-up of 25,524 child-years. Those who received iron and folic acid with or without zinc were 12% (95% CI 2-23, p=0.02) more likely to die or need treatment in hospital for an adverse event and 11% (1-23%, p=0.03) more likely to be admitted to hospital; there were also 15% (-7 to 41, p=0.19) more deaths in these groups.

Interpretation: Routine supplementation with iron and folic acid in preschool children in a population with high rates of malaria can result in an increased risk of severe illness and death. In the presence of an active programme to detect and treat malaria and other infections, iron-deficient and anaemic children can benefit from supplementation. However, supplementation of those who are not iron deficient might be harmful. As such, current guidelines for universal supplementation with iron and folic acid should be revised.

DOI: 10.1016/S0140-6736(06)67962-2 / PMID: 16413877 [PubMed - indexed for MEDLINE]

29.

J Nutr. 2006 Sep;136(9):2427-34.

Combined iron and folic acid supplementation with or without zinc reduces time to walking unassisted among Zanzibari infants 5- to 11-mo old.

Authors: Olney DK, Pollitt E, Kariger PK, Khalfan SS, Ali NS, Tielsch JM, Sazawal S, Black R, Allen LH, Stoltzfus RJ.

Iron and zinc deficiencies have been associated with delayed motor development in nutritionally at-risk children, albeit inconsistently. In this community-based, randomized double-blind trial, iron+folic acid (FeFA) (12.5 mg Fe + 50 mug folic acid), zinc (Zn) (10 mg), and iron+folic acid+zinc (FeFA+Zn) supplements or a placebo were given daily for 1 y to nutritionally at-risk children in Pemba, Zanzibar. The effects of these treatments on attaining unassisted walking were evaluated using survival analysis for 354 children aged 5-11 mo at the start of supplementation. Treatment effects on changes in hemoglobin (Hb) and zinc protoporphyrin (ZPP) and height-for-age (HAZ) and weight-for-age (WAZ) Z scores were evaluated using linear regression. Attained motor milestone was recorded every 2 wk for 1 y. Hb, ZPP, HAZ, and WAZ were measured at baseline and after 6 mo of treatment. FeFA with or without Zn reduced the time it took for children to walk unassisted. Children who received any iron walked unassisted sooner than those who received no iron [median difference approximately 15 d, P = 0.035, risk ratio (RR) = 1.28, 95% CI = 1.02, 1.61] and this effect was stronger in those who had iron deficiency anemia (IDA) at baseline (median difference was approximately 30 d; P = 0.002; RR = 1.68; 95% CI = 1.21, 2.32). FeFA alone and Zn alone improved Hb and ZPP compared with placebo. There were no significant treatment effects on changes in HAZ or WAZ. The effects of treatment on time

to walking may have been mediated by improvements in iron status or hemoglobin, but were not mediated through improvements in growth.

PMID: 16920865 [PubMed - indexed for MEDLINE]

30.

International Federation of Gynecology and Obstetrics. 2006 Oct; 95(1): 24–28

Measurement of blood loss at childbirth and postpartum

Authors: J.A. Kavle, S.S. Khalfan, R.J. Stoltzfus, F. Witter, J.M. Tielsch, L.E. Caulfield

Objective : To accurately measure blood loss during childbirth in a developing country.

Method : The alkaline hematin technique was used to quantify blood lost during delivery and 24 h postpartum in 158 women in Pemba Island, Zanzibar.

Result: Women were found to lose less blood during childbirth and 24 h postpartum than previously reported. Compared with laboratory values, nurse–midwives approximated blood loss accurately (mean difference, i.e., mean underestimation by nurse–midwives, 4.90 mL); however, their imprecision was greater for higher laboratory values.

Conclusion: This study may prompt further investigation, as no comparable data exist for developing countries where maternal mortality is high and severe anemia prevalent.

2007

31.

J Health Popul Nutr. 2007 Mar;25(1):62-6.

Effect of zinc added to multi-vitamin supplementation containing low-dose vitamin A on plasma retinol level in children--a double-blind randomized, controlled trial.

Authors: Sazawal S, Dhingra U, Deb S, Bhan MK, Menon VP, Black RE.

In a community-based double-blind randomized trial in children aged 6-35 months, both intervention and control groups received a multi-vitamin syrup containing vitamin A, while the intervention group had zinc gluconate (equivalent to 10 mg of elemental zinc) additional in the syrup. There was a significant decrease in diarrhoea and pneumonia in the intervention group. This study was undertaken to investigate if addition of zinc to vitamin A had improved plasma retinol levels, which, in turn, was responsible for the effects observed in the intervention group. In a randomly-selected subsample of 200 children--100 each from the intervention and the control group, plasma retinol levels after 120 days of supplementation were measured. There was no difference in the mean plasma retinol levels [the difference in the mean 0.46 microg/dL (95% confidence interval -1.42-2.36)] between the two groups following supplementation. No difference in plasma retinol levels was observed in the subgroups based on base-line nutritional status and plasma zinc levels. Addition of zinc to low-dose vitamin A in this study did not improve the vitamin A status of children and cannot explain morbidity effects of the intervention.

PMCID: PMC3013264 / PMID: 17615904 [PubMed - indexed for MEDLINE]

32.

Lancet. 2007 Mar 17;369(9565):927-34.

Effect of zinc supplementation on mortality in children aged 1-48 months: a community-based randomised placebo-controlled trial.

Authors: Sazawal S, Black RE, Ramsan M, Chwaya HM, Dutta A, Dhingra U, Stoltzfus RJ, Othman MK, Kabole FM.

Background: Studies from Asia have suggested that zinc supplementation can reduce morbidity and mortality in children, but evidence from malarious populations in Africa has been inconsistent. Our aim was to assess the effects of zinc supplementation on overall mortality in children in Pemba, Zanzibar.

Methods: We enrolled 42,546 children aged 1-36 months, contributing a total of 56,507 child-years in a randomised, double-blind, placebo-controlled trial in Pemba, Zanzibar. Randomisation was by household. 21 274 children received daily supplementation with zinc 10 mg (5 mg in children younger than 12 months) for mean 484.7 days (SD 306.6). 21,272 received placebo. The primary endpoint was overall mortality, and analysis was by intention to treat. This study is registered as an International Standard Randomised Clinical Trial, number ISRCTN59549825.

Findings: Overall, there was a non-significant 7% (95% CI -6% to 19%; p=0.29) reduction in the relative risk of all-cause mortality associated with zinc supplementation.

Interpretation: We believe that a meta-analysis of all studies of mortality and morbidity, will help to make evidence-based recommendations for the role of zinc supplementation in public health policy to improve mortality, morbidity, growth, and development in young children.

DOI: 10.1016/S0140-6736(07)60452-8 / PMID: 17368154 [PubMed - indexed for MEDLINE]

33.

Am J Trop Med Hyg. 2007 Mar;76(3):541-8.

Helicobacter pylori infection is associated with severe anemia of pregnancy on Pemba Island, Zanzibar.

Authors: Farag TH, Stoltzfus RJ, Khalfan SS, Tielsch JM.

Helicobacter pylori infection has recently been associated with iron deficiency and anemia in developed countries. To determine the association of H. pylori and anemia in a tropical region, we measured hemoglobin concentration (Hb) and H. pylori infection by the 13C urea breath test among 857 pregnant women attending antenatal care clinics. Parasitology, anthropometry, obstetric history, sociodemographic and dietary variables were also assessed. Logistic regression showed an odds ratio of 7.63 (95% confidence interval=1.73-33.55) for H. pylori infection comparing women with and without severe anemia (Hb<7 g/dL), controlling for hookworm infection, body mass index and parity, but only among women with a diet low in foods containing heme iron. Infection with H. pylori with low bacterial load was associated with lower Hb concentration while high bacterial load was associated with higher Hb concentration. Further research is needed to establish causality because high worldwide prevalence means that even a small associated risk would be of public health significance.

PMID: 17360881 [PubMed - indexed for MEDLINE]

34.

Am J Trop Med Hyg. 2007 Apr;76(4):725-31.

A comparison of methods for detecting the eggs of Ascaris, Trichuris, and hookworm in infant stool, and the epidemiology of infection in Zanzibari infants.

Authors: Goodman D, Haji HJ, Bickle QD, Stoltzfus RJ, Tielsch JM, Ramsan M, Savioli L, Albonico M.

This study compared five methods for detecting the eggs of the human parasitic geohelminths Ascaris, Trichuris, and hookworm in infant stool, and describes the epidemiology of infection in infants from a parasite-endemic area. A total of 424 infants 5-11 months old were enrolled from three villages on Pemba Island, Zanzibar. Methods used included the Kato-Katz technique, formol ethyl acetate sedimentation, modified formol ethyl acetate sedimentation, modified Wisconsin floatation, and simple gravity sedimentation. Of methods used alone, Wisconsin floatation and simple gravity sedimentation each provided the highest sensitivity for detecting eggs of these three geohelminths (89.6%). Of methods used in combination, the Kato-Katz technique/simple gravity sedimentation and Wisconsin floatation/simple gravity sedimentation each provided the highest sensitivity (99.0%). Prevalence of geohelminth infection was 26.5%. Between five and nine months of age the mean prevalence was 9.4%, while at 10 and 11 months of age the mean prevalence was 43.4%. Village prevalence varied from 3.6% to 43.8%. Infant geohelminth infection can occur at a high prevalence, and what method is best depends on research specifics.

PMID: 17426179 [PubMed - indexed for MEDLINE]

35.

Trans R Soc Trop Med Hyg. 2007 Aug;101(8):766-72. Epub 2007 Jun 12.

Geophagia is not associated with Trichuris or hookworm transmission in Zanzibar, Tanzania. / Association of geophagia with Ascaris, Trichuris and hookworm transmission in Zanzibar, Tanzania

Authors: Young SL, Goodman D, Farag TH, Ali SM, Khatib MR, Khalfan SS, Tielsch JM, Stoltzfus RJ.

Geophagia may be harmful as a method for the transmission of geohelminths. In this study, we pose two questions in a representative sample of 970 pregnant women from Pemba Island, Zanzibar, Tanzania. Can consumed earth be a vector for geohelminth infection? And do geophagists have differential parasitic infection? The parasitological content of 59 non-food substance samples was analysed.

Cross-sectional data regarding pica behaviour were collected through interviews conducted by local researchers. Ascaris, Trichuris and hookworm status was ascertained through Kato-Katz smears. The prevalence of geophagia

at baseline was 5.6% and the overall prevalence of *Ascaris*, *Trichuris* and hookworm infection was 5.6%, 33.2% and 32.9%, respectively. No consumed soil samples contained infectious parasitic stages, and only one of the consumed pica substances (charcoal) contained parasites of potential risk to human health. In bivariate analyses, neither the prevalence nor the intensity of infection with *Ascaris*, *Trichuris* or hookworm differed significantly by geophagia status. Furthermore, in multivariate models, geophagia was not a significant predictor of helminth infection status. We conclude that geophagia is not a source of *Trichuris* or hookworm infection among pregnant women in Pemba (insufficient power to evaluate the effect of *Ascaris*), which is in contrast to existing findings of helminth infection and geophagia.

DOI: 10.1016/j.trstmh.2007.04.016 / PMCID: PMC1995549 / PMID: 17568644 [PubMed - indexed for MEDLINE]

36.

Trop Med Int Health. 2007 Sep;12(9):1011-7.

Risk factors for HIV/AIDS in a low HIV prevalence site of sub-Saharan Africa.

Authors: Croce F, Fedeli P, Dahoma M, Dehò L, Ramsan M, Adorni F, Corvasce S, Galli M.

We conducted a hospital-based survey on prevalence and risk factors of HIV-1/2 and other viral infections in Zanzibar archipelago. Blood samples, socio-demographic and behavioural data were collected from 2697 patients. The overall HIV prevalence was 2.9%. About 1.4%, 2.1%, 4.2% of antenatal clinic (ANC) attendees and 2.1%, 3.7%, 5.3% of blood donors were, respectively, HIV-Abs-, HTLV-Abs- and HBs-Ag-positive; 5.5% of blood donors were HCV-affected.

Co-infections were rare. Exactly 3.4% of the children aged 6-10 years were HIV-positive. People aged 26-35 years [adjusted odds ratio (AOR) 4.4, 95% CI (confidence interval) 1.72-11.22; P = 0.002], illiterate subjects (AOR 3.6, 95% CI 1.65-7.98; P = 0.001) mobile workers (AOR 7.0, 95% CI 1.41-34.62; P = 0.02) and previously operated patients (AOR 1.9, 95% CI 1.02-3.66; P = 0.04) were at higher risk for HIV/AIDS. Any of the examined factors were associated with hepatitis B virus, hepatitis C virus and human T lymphotropic virus type 1/2 transmission. HIV/AIDS prevention strategies must primarily be addressed to traditional high-risk groups and secondarily to unsafe health care procedures in relatively preserved sub-Saharan areas.

DOI: 10.1111/j.1365-3156.2007.01880.x / PMID: 17875012 [PubMed - indexed for MEDLINE]

37.

Trans R Soc Trop Med Hyg. 2007 Sep;101(9):915-22. Epub 2007 Jul 6.

Unexpectedly low prevalence of *Helicobacter pylori* infection among pregnant women on Pemba Island, Zanzibar.

Authors: Farag TH, Stoltzfus RJ, Khalfan SS, Tielsch JM.

Helicobacter pylori is strongly associated with peptic ulcer and gastric cancer and may be the most common human bacterial infection. The epidemiology of *H. pylori* has been poorly studied in Africa, where its relevance to disease has not been fully appreciated. Following a cross-sectional study design, *H. pylori* infection was measured by (13)C-urea breath test among 857 pregnant women attending antenatal care clinics. Location, water use practices, anthropometry, and social and demographic variables were assessed as covariates. The prevalence of *H. pylori* infection was 17.5%. Multiple logistic regression showed that *H. pylori* was positively associated with location of enrollment clinic along the main road leading from the southern seaport (odds ratio (OR)=2.5), presence of costlier household lighting in the home (OR=1.6) and height (10 cm) (OR=1.5). The prevalence of *H. pylori* infection was unexpectedly low for a developing country population, where prevalence is typically very high. Higher prevalence along the road from the southern seaport suggests that infection was imported from the mainland. The reason for very low prevalence should be investigated further because the discovery of bacterial or dietary factors that limit infection in this population could have useful public health applications.

DOI: 10.1016/j.trstmh.2007.05.003 / PMID: 17617430 [PubMed - indexed for MEDLINE]

38.

Ann Ig. 2007 Sep-Oct;19(5):395-403.

Prevalence of *E. coli*, thermotolerant coliforms, *Salmonella* spp. and *Vibrio* spp. in ready-to-eat foods: Pemba Island, United Republic of Tanzania.

Authors: Viganò A, Pellissier N, Hamad HJ, Ame SA, Pontello M.

This study is aimed to evaluate the microbiological quality of ready-to-eat foods in Pemba island. A total of 300 food samples have been analysed: 66 household preparations, 115 samples of raw cow milk, and 119 fried sea-foods. The thermotolerant coliforms have been detected in 34% sea-foods, 58% household meals, and 98% milk samples; the coliforms count is $5 \times 10(2)$, $10(3)$, and $3 \times 10(4)$ cfu/g, respectively. *E. coli* is the species most frequently isolated: 60 on 100 strains agglutinate one of the tested polyvalent antisera. *Salmonella* spp. have been found exclusively in cow milk (11%); in 15% sea-foods *V. alginolyticus* has been isolated. The prevalence of faecal contamination is extremely high in cow milk, a critical vehicle for the transmission of pathogens, probably for a lacking thermal treatment (pasteurization). *Salmonella* spp., *V. cholerae*, and *V. parahaemolyticus* have not been isolated from boiled or fried foodstuffs, but in any case the cooked foods are faecally contaminated: their contamination occurs likely after preparation and before consumption. The identification of risk factors for the faecal contamination could be helpful to plan educational programmes involving food operators and may be an effective preventive measure, especially in settings where financial resources are lacking for the construction of adequate infrastructures.

PMID: 18210770 [PubMed - indexed for MEDLINE]

39.

J Nutr. 2007 Dec;137(12):2756-62.

Young Zanzibari children with iron deficiency, iron deficiency anemia, stunting, or malaria have lower motor activity scores and spend less time in locomotion.

Authors: Olney DK, Pollitt E, Kariger PK, Khalfan SS, Ali NS, Tielsch JM, Sazawal S, Black R, Mast D, Allen LH, Stoltzfus RJ.

Motor activity improves cognitive and social-emotional development through a child's exploration of his or her physical and social environment. This study assessed anemia, iron deficiency, hemoglobin (Hb), length-for-age Z-score (LAZ), and malaria infection as predictors of motor activity in 771 children aged 5-19 mo. Trained observers conducted 2- to 4-h observations of children's motor activity in and around their homes. Binary logistic regression assessed the predictors of any locomotion. Children who did not locomote during the observation (nonmovers) were excluded from further analyses. Linear regression evaluated the predictors of total motor activity (TMA) and time spent in locomotion for all children who locomoted during the observation combined (movers) and then separately for crawlers and walkers. Iron deficiency (77.0%), anemia (58.9%), malaria infection (33.9%), and stunting (34.6%) were prevalent.

Iron deficiency with and without anemia, Hb, LAZ, and malaria infection significantly predicted TMA and locomotion in all movers. Malaria infection significantly predicted less TMA and locomotion in crawlers. In walkers, iron deficiency anemia predicted less activity and locomotion, whereas higher Hb and LAZ significantly predicted more activity and locomotion, even after controlling for attained milestone. Improvements in iron status and growth and prevention or effective treatment of malaria may improve children's motor, cognitive, and social-emotional development either directly or through improvements in motor activity. However, the relative importance of these factors is dependent on motor development, with malaria being important for the younger, less developmentally advanced children and Hb and LAZ becoming important as children begin to attain walking skills.

PMID: 18029495 [PubMed - indexed for MEDLINE]

2008

40.

Early Hum Dev. 2008 Jun;84(6):389-98. Epub 2007 Nov 26.

Maternal reports of sleep in 6-18 month-old infants from Nepal and Zanzibar: association with iron deficiency anemia and stunting.

Authors: Kordas K, Siegel EH, Olney DK, Katz J, Tielsch JM, Chwaya HM, Kariger PK, Leclercq SC, Khattri SK, Stoltzfus RJ.

Background: Infants with iron deficiency anemia (IDA) and stunting explore and interact less with their environment. They may also be fatigued more often, suggesting their sleep may be affected. It is unclear whether fatigue in these infants is due to poor nighttime sleep or if it is compensated for with frequent naps or longer sleep.

Aims: In 2 studies from Pemba Island, Zanzibar and 1 from Nepal we investigated the relationship between IDA, stunting, and maternal reports of sleep in 6-18 mo old infants.

Methods: Parents reported on the number and duration of naps, hours of nighttime sleep, and frequency of night waking. Anemia was defined as Hb<10 g/dL, iron deficiency as zinc protoporphyrin (ZPP > or = 90 micromol/mol heme), stunting as HAZ<-2 SD, and IDA as Hb<10 g/dL and ZPP > or = 90 micromol/mol heme.

Results: The prevalence of IDA and stunting was 34-84% and 22-37%, respectively. Most infants napped during the day and took approximately 1.5 naps (mean nap duration 1.4-1.7 h). Mean nighttime sleep duration was 8.3-9.7 h and infants awoke 2.1-2.5 times per night. Both IDA and stunting were associated with differences in reported sleep characterized by shorter night sleep duration and higher frequency of night waking; stunting was also related to shorter nap duration.

Conclusions: We found reduced sleep duration and increased night waking among infants with IDA and stunting. Because sleep plays an essential role in infant development, our findings indicate a clear need for further research into these relationships.

PMID: 18022771 / DOI: 10.1016/j.earlhumdev.2007.10.007 [PubMed - indexed for MEDLINE]

41.

J Health Popul Nutr. 2008 Jun;26(2):232-40.

Association between anaemia during pregnancy and blood loss at and after delivery among women with vaginal births in Pemba Island, Zanzibar, Tanzania.

Authors: Kavle JA, Stoltzfus RJ, Witter F, Tielsch JM, Khalfan SS, Caulfield LE.

The study sought to identify determinants of blood loss at childbirth and 24 hours postpartum. The study was nested in a community-based randomized trial of treatments for anaemia during pregnancy in Wete Town, Pemba Island, Zanzibar, United Republic of Tanzania. Status of anaemia during pregnancy, nutritional information, obstetric history, and socioeconomic status were assessed at enrollment during routine antenatal care. Pregnant women presented for spontaneous vaginal delivery, and nurse-midwives collected information on labour and delivery via partograph. Blood-stained sanitary napkins and pads from childbirth and 24 hours postpartum were quantified using the alkaline hematin method. Moderate-to-severe anaemia (Hb <90 g/L) at enrollment was strongly associated with blood loss at delivery and the immediate postpartum period, after adjusting for maternal covariates and variables of biological relevance to blood loss. Greater blood loss was associated ($p<0.10$) with duration of the first stage of labour, placental weight, receipt of oxytocin, preterm birth, and grand multiparity. The findings provide unique evidence of a previously-suspected link between maternal anaemia and greater blood loss at childbirth and postpartum. Further research is needed to confirm these findings on a larger sample of women to determine whether women with moderate-to-severe anaemia are more likely to experience postpartum haemorrhage and whether appropriate antenatal or peripartum care can affect the relationships described here.

PMCID: PMC2740668 / PMID: 18686556 [PubMed - indexed for MEDLINE]

42.

Trans R Soc Trop Med Hyg. 2008 Nov;102(11):1164-5. doi: 10.1016/j.trstmh.2008.08.019. Epub 2008 Sep 18.

Diet as a factor in unexpectedly low prevalence of Helicobacter pylori infection.

Authors: Farag TH, Fahey JW, Khalfan SS, Tielsch JM.

We recently described an unexpectedly low prevalence of Helicobacter pylori infection in a tropical African population, finding that only 17.5% of women attending antenatal care clinics on Pemba Island, Zanzibar, were infected (Farag et al., 2007). We also reviewed previous research that showed unexpectedly low prevalence of infection in Malaysia and Indonesia. An unexpectedly low prevalence has also been reported in Sri Lanka (de Silva, 1999; Devanarayana et al., 2008; Fernando et al., 2001). As Uyub and colleagues suggest in their letter in this issue of Transactions, the epidemiological evidence points to one or more extrinsic factors. Host and pathogen-specific factors are unlikely to be relevant because the populations of Zanzibar, Malaysia, Indonesia and Sri Lanka are not isolated and have long ...

DOI: 10.1016/j.trstmh.2008.08.019

PMID: 18804252 [PubMed - indexed for MEDLINE].

43.

PLoS Negl Trop Dis. 2008 Mar 26;2(3):e126. doi: 10.1371/journal.pntd.0000126.

Controlling soil-transmitted helminthiasis in pre-school-age children through preventive chemotherapy.

Authors: Albonico M, Allen H, Chitsulo L, Engels D, Gabrielli AF, Savioli L.

Abstract: Pre-school age children account for 10%-20% of the 2 billion people worldwide who are infected with soil-transmitted helminths (STHs): *Ascaris lumbricoides* (roundworm), *Trichuris trichiura* (whipworm), and *Ancylostoma duodenale*/*Necator americanus* (hookworms). Through a systematic review of the published literature and using information collated at World Health Organization headquarters, this paper summarizes the available evidence to support the recommendation that pre-school children should be included in regular deworming programmes. The first section describes the burden of STH disease in this age group, followed by a summary of how infection impacts iron status, growth, vitamin A status, and cognitive development and how STHs may exacerbate other high mortality infections. The second section explores the safety of the drugs themselves, given alone or co-administered, drug efficacy, and the importance of safe administration. The third section provides country-based evidence to demonstrate improved health outcomes after STH treatment. The final section provides country experiences in scaling up coverage of pre-school children by using other large scale public health interventions, including vitamin A programmes, immunization campaigns, and Child Health days. The paper concludes with a number of open research questions and a summary of some of the operational challenges that still need to be addressed.

PMID:18365031 / PMCID:PMC2274864 / DOI:10.1371/journal.pntd.0000126 [PubMed - indexed for MEDLINE]

2009

44.

J Health Popul Nutr 2009 Feb.;27(1):41-52

Bacterial populations in complementary foods and drinking water in households with children 10–15 months old in Pemba Island, Tanzania

Authors: Jacqueline K Kung'u, Kathryn J Boor, Shaali M Ame, Nadra S Ali, Anna E Jackson and Rebecca J Stoltzfus

Abstract: Bacteria were quantified in samples of drinking-water and in two porridges prepared for infant-feeding [fortified instant soy-rice porridge (SRP) and cooked porridge (Lishe bora, LB)] in 54 households. Bacterial numbers were measured again after the porridges had been held at room temperature for four hours (T4). Findings were benchmarked against bacterial numbers in traditional complementary foods sampled from 120 households. Total bacteria, coliform, and Enterobacteriaceae counts were enumerated using Petrifilm™. The mean log bacterial numbers were the lowest for LB at T0 (2.24±0.84 CFU/g aerobic counts) and the highest for SRP at T4 (4.63±0.56 CFU/g aerobic counts). The total bacteria, coliform and Enterobacteriaceae counts were higher at T4 than at T0 for LB (p≤0.001); however, only the coliform and Enterobacteriaceae counts were higher at T4 than at T0 for SRP (p<0.001). Drinking-water, SRP0, traditional foods, and SRP4 all had the mean aerobic counts higher than the acceptable cut-off but the total bacterial count in SRP0 was not significantly (p=0.543) different from drinking-water. However, coliform and Enterobacteriaceae counts in SRP0 were higher than in drinking-water (p<0.001). Also, although the aerobic counts of SRP4 were not significantly (p>0.999) different from traditional foods, the coliform and Enterobacteriaceae counts were significantly higher in SRP4 than in traditional foods (p<0.001). It is, therefore, recommended that food safety concerns be addressed when improving complementary foods.

45.

Am J Trop Med Hyg. 2009 May;80(5):712-7.

Accuracy of malaria diagnosis by microscopy, rapid diagnostic test, and PCR methods and evidence of antimalarial overprescription in non-severe febrile patients in two Tanzanian hospitals.

Authors: Nicastri E, Bevilacqua N, Sañé Schepisi M, Paglia MG, Meschi S, Ame SM, Mohamed JA, Mangi S, Fumakule R, Di Caro A, Capobianchi MR, Kitua A, Molteni F, Racalbutto V, Ippolito G.

The study was aimed to evaluate the malaria over/underdiagnosis and over/underprescription of antimalarial drugs. Between February and March 2007 blood samples were collected from 336 non-severe febrile outpatients attended in two peripheral Tanzanian hospitals. Microscopy and a rapid diagnostic test (RDT) were done locally

and the accuracy evaluated by qualitative polymerase chain reaction (PCR) for Plasmodium spp. The testing was performed at National Institute for Infectious Diseases Lazzaro Spallanzani (INMI), Rome, Italy. As a result of PCR, we identified 26 malaria cases out of 336 (7.7%) patients. Microscopy and RDT accuracies were 93.5% and 97.6%, respectively. Overprescription and underdiagnosis rates were 29.3% and 30.8%, respectively. On-field training, clinical management of febrile illness, and malaria microscopy in remote settings should be considered.

PMID: 19407111 [PubMed - indexed for MEDLINE]

46.

PLoS Negl Trop Dis. 2009;3(5):e433. doi: 10.1371/journal.pntd.0000433. Epub 2009 May 19.

Early exposure of infants to GI nematodes induces Th2 dominant immune responses which are unaffected by periodic anthelmintic treatment.

Authors: Wright VJ, Ame SM, Haji HS, Weir RE, Goodman D, Pritchard DI, Mohamed MR, HajiHJ, Tielsch JM, Stoltzfus RJ, Bickle QD.

We have previously shown a reduction in anaemia and wasting malnutrition in infants <3 years old in Pemba Island, Zanzibar, following repeated anthelmintic treatment for the endemic gastrointestinal (GI) nematodes *Ascaris lumbricoides*, hookworm and *Trichuris trichiura*. In view of the low intensity of worm infections in this age group, this was unexpected, and it was proposed that immune responses to the worms rather than their direct effects may play a significant role in morbidity in infants and that anthelmintic treatment may alleviate such effects.

Therefore, the primary aims of this study were to characterise the immune response to initial/early GI nematode infections in infants and the effects of anthelmintic treatment on such immune responses. The frequency and levels of Th1/Th2 cytokines (IL-5, IL-13, IFN-gamma and IL-10) induced by the worms were evaluated in 666 infants aged 6-24 months using the Whole Blood Assay. *Ascaris* and hookworm antigens induced predominantly Th2 cytokine responses, and levels of IL-5 and IL-13 were significantly correlated. The frequencies and levels of responses were higher for both *Ascaris* positive and hookworm positive infants compared with worm negative individuals, but very few infants made *Trichuris*-specific cytokine responses. Infants treated every 3 months with mebendazole showed a significantly lower prevalence of infection compared with placebo-treated controls at one year following baseline. At follow-up, cytokine responses to *Ascaris* and hookworm antigens, which remained Th2 biased, were increased compared with baseline but were not significantly affected by treatment. However, blood eosinophil levels, which were elevated in worm-infected children, were significantly lower in treated children. Thus the effect of deworming in this age group on anaemia and wasting malnutrition, which were replicated in this study, could not be explained by modification of cytokine responses but may be related to eosinophil function.

DOI: 10.1371/journal.pntd.0000433 / PMCID: PMC2677666 / PMID: 19436745 [PubMed - indexed for MEDLINE]

2010

47.

BMC Infect Dis. 2010 Jun 22;10:180. doi: 10.1186/1471-2334-10-180.

Evaluation of the Widal tube agglutination test for the diagnosis of typhoid fever among children admitted to a rural hospital in Tanzania and a comparison with previous studies.

Authors: Ley B, Mtove G, Thriemer K, Amos B, von Seidlein L, Hendriksen I, Mwambuli A, Shoo A, Malahiyo R, Ame SM, Kim DR, Ochiai LR, Clemens JD, Reyburn H, Wilfing H, Magesa S, Deen JL.

Background: The diagnosis of typhoid fever is confirmed by culture of *Salmonella enterica* serotype Typhi (*S. typhi*). However, a more rapid, simpler, and cheaper diagnostic method would be very useful especially in developing countries. The Widal test is widely used in Africa but little information exists about its reliability.

Methods: We assessed the performance of the Widal tube agglutination test among febrile hospitalized Tanzanian children. We calculated the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of various anti-TH and -TO titers using culture-confirmed typhoid fever cases as the "true positives" and all other febrile children with blood culture negative for *S. typhi* as the "true negatives."

Results: We found that 16 (1%) of 1,680 children had culture-proven typhoid fever. A single anti-TH titer of 1:80 and higher was the optimal indicator of typhoid fever. This had a sensitivity of 75%, specificity of 98%, NPV of 100%, but PPV was only 26%. We compared our main findings with those from previous studies.

Conclusions: Among febrile hospitalized Tanzanian children with a low prevalence of typhoid fever, a Widal titer of $> \text{ or } = 1:80$ performed well in terms of sensitivity, specificity, and NPV. However a test with improved PPV that is similarly easy to apply and cost-efficient is desirable.

DOI: 10.1186/1471-2334-10-180 / PMCID: PMC2898821 / PMID: 20565990 [PubMed - indexed for MEDLINE]

48.

Am J Trop Med Hyg. 2010 Jul;83(1):144-51. doi: 10.4269/ajtmh.2010.09-0442.

Association of pica with anemia and gastrointestinal distress among pregnant women in Zanzibar, Tanzania.

Authors: Young SL, Khalfan SS, Farag TH, Kavle JA, Ali SM, Hajji H, Rasmussen KM, Pelto GH, Tielsch JM, Stoltzfus RJ.

The etiology of pica, the purposive consumption of non-food substances, is not understood, despite its ubiquity among gravidae. We examined correlates of pica in a representative obstetric population ($n = 2,368$) on Pemba Island, Zanzibar, Tanzania to examine proposed etiologies. Cross-sectional data were collected on socioeconomic characteristics, food intake, geophagy (earth consumption), amylophagy (raw starch consumption), anthropometry, iron status, parasitic burden, and gastrointestinal morbidities. Amylophagy was reported by 36.3%, geophagy by 5.2%, and any pica by 40.1%. There was a strong additive relationship of geophagy and amylophagy with lower hemoglobin (Hb) concentration and iron deficiency anemia. By multivariate logistic regression, any pica was associated with Hb level (odds ratio [OR] = 0.76, 95% confidence interval [CI] = 0.72-0.81), nausea (OR = 1.45, 95% CI = 1.20-1.73), and abdominal pain (OR = 1.22, 95% CI = 1.01-1.48). These striking results indicate that the nature of the relationship between pica, pregnancy, gastrointestinal distress, and iron deficiency anemia merits further investigation.

DOI: 10.4269/ajtmh.2010.09-0442 / PMCID: PMC2912591 / PMID: 20595493 [PubMed - indexed for MEDLINE]

2011

49.

PLoS Negl Trop Dis. 2011 Mar 29;5(3):e948. doi: 10.1371/journal.pntd.0000948.

Assessment of the anthelmintic efficacy of albendazole in school children in seven countries where soil-transmitted helminths are endemic.

Authors: Veracruz J, Behnke JM, Albonico M, Ame SM, Angebault C, Bethony JM, Engels D, Guillard B, Nguyen TV, Kang G, Kattula D, Kotze AC, McCarthy JS, Mekonnen Z, Montresor A, Periago MV, Sumo L, Tchuente LA, Dang TC, Zeynudin A, Levecke B.

Comment in PLoS Negl Trop Dis. 2011;5(3):e1010.

Background: The three major soil-transmitted helminths (STH) *Ascaris lumbricoides*, *Trichuris trichiura* and *Necator americanus/Ancylostoma duodenale* are among the most widespread parasites worldwide. Despite the global expansion of preventive anthelmintic treatment, standard operating procedures to monitor anthelmintic drug efficacy are lacking. The objective of this study, therefore, was to define the efficacy of a single 400 milligram dose of albendazole (ALB) against these three STH using a standardized protocol.

Principal findings: Seven trials were undertaken among school children in Brazil, Cameroon, Cambodia, Ethiopia, India, Tanzania and Vietnam. Efficacy was assessed by the Cure Rate (CR) and the Fecal Egg Count Reduction (FECR) using the McMaster egg counting technique to determine fecal egg counts (FEC). Overall, the highest CRs were observed for *A. lumbricoides* (98.2%) followed by hookworms (87.8%) and *T. trichiura* (46.6%). There was considerable variation in the CR for the three parasites across trials (country), by age or the pre-intervention FEC (pre-treatment). The latter is probably the most important as it had a considerable effect on the CR of all three STH. Therapeutic efficacies, as reflected by the FECRs, were very high for *A. lumbricoides* (99.5%) and hookworms (94.8%) but significantly lower for *T. trichiura* (50.8%), and were affected to different extents among the 3 species by the pre-intervention FEC counts and trial (country), but not by sex or age.

Conclusions: Our findings suggest that a FECR (based on arithmetic means) of $>95\%$ for *A. lumbricoides* and $>90\%$ for hookworms should be the expected minimum in all future surveys, and that therapeutic efficacy below this level following a single dose of ALB should be viewed with concern in light of potential drug resistance. A standard threshold for efficacy against *T. trichiura* has yet to be established, as a single-dose of ALB is unlikely to be satisfactory for this parasite.

TRIAL REGISTRATION: ClinicalTrials.gov NCT01087099.

DOI: 10.1371/journal.pntd.0000948 / PMCID: PMC3066140 / PMID: 21468309 [PubMed - indexed for MEDLINE]

50.

BMC Infectious Diseases 2011; 11:147

Assessment and comparative analysis of a rapid diagnostic test (Tubex®) for the diagnosis of typhoid fever among hospitalized children in rural Tanzania

Authors: Benedikt Ley, Kamala Thriemer, Shaali M Ame, George M Mtove, Lorenz von Seidlein, Ben Amos, Ilse CE Hendriksen, Abraham Mwambuli, Aikande Shoo, Deok R Kim, Leon R Ochiai, Michael Favorov, John D Clemens, Harald Wilfing, Jacqueline L Deen and Said M Ali

Background: Typhoid fever remains a significant health problem in many developing countries. A rapid test with a performance comparable to that of blood culture would be highly useful. A rapid diagnostic test for typhoid fever, Tubex®, is commercially available that uses particle separation to detect immunoglobulin M directed towards *Salmonella* Typhi O9 lipopolysaccharide in sera.

Methods: We assessed the sensitivity and specificity of the Tubex test among Tanzanian children hospitalized with febrile illness using blood culture as gold standard. Evaluation was done considering blood culture confirmed *S. Typhi* with non-typhi salmonella (NTS) and non-salmonella isolates as controls as well as with non-salmonella isolates only.

Results: Of 139 samples tested with Tubex, 33 were positive for *S. Typhi* in blood culture, 49 were culture-confirmed NTS infections, and 57 were other non-salmonella infections. Thirteen hemolyzed samples were excluded. Using all non-*S. Typhi* isolates as controls, we showed a sensitivity of 79% and a specificity of 89%. When the analysis was repeated excluding NTS from the pool of controls we showed a sensitivity of 79% and a specificity of 97%. There was no significant difference in the test performance using the two different control groups ($p > 0.05$).

Conclusions: This first evaluation of the Tubex test in an African setting showed a similar performance to those seen in some Asian settings. Comparison with the earlier results of a Widal test using the same samples showed no significant difference ($p > 0.05$) for any of the performance indicators, irrespective of the applied control group.

51.

PLoS Negl Trop Dis. 2011 Jun;5(6):e1201. doi: 10.1371/journal.pntd.0001201. Epub 2011 Jun 14.

A comparison of the sensitivity and fecal egg counts of the McMaster egg counting and Kato-Katz thick smear methods for soil-transmitted helminths.

Authors: Levecke B, Behnke JM, Ajjampur SS, Albonico M, Ame SM, Charlier J, Geiger SM, Hoa NT, Kamwa Ngassam RI, Kotze AC, McCarthy JS, Montresor A, Periaño MV, Roy S, Tchuem Tchuente LA, Thach DT, Vercruyse J.

Background: The Kato-Katz thick smear (Kato-Katz) is the diagnostic method recommended for monitoring large-scale treatment programs implemented for the control of soil-transmitted helminths (STH) in public health, yet it is difficult to standardize. A promising alternative is the McMaster egg counting method (McMaster), commonly used in veterinary parasitology, but rarely so for the detection of STH in human stool.

Principal findings: The Kato-Katz and McMaster methods were compared for the detection of STH in 1,543 subjects resident in five countries across Africa, Asia and South America. The consistency of the performance of both methods in different trials, the validity of the fixed multiplication factor employed in the Kato-Katz method and the accuracy of these methods for estimating 'true' drug efficacies were assessed. The Kato-Katz method detected significantly more *Ascaris lumbricoides* infections (88.1% vs. 75.6%, $p < 0.001$), whereas the difference in sensitivity between the two methods was non-significant for hookworm (78.3% vs. 72.4%) and *Trichuris trichiura* (82.6% vs. 80.3%). The sensitivity of the methods varied significantly across trials and magnitude of fecal egg counts (FEC). Quantitative comparison revealed a significant correlation ($R_s > 0.32$) in FEC between both methods, and indicated no significant difference in FEC, except for *A. lumbricoides*, where the Kato-Katz resulted in significantly higher FEC (14,197 eggs per gram of stool (EPG) vs. 5,982 EPG). For the Kato-Katz, the fixed multiplication factor resulted in significantly higher FEC than the multiplication factor adjusted for mass of feces examined for *A. lumbricoides* (16,538 EPG vs. 15,396 EPG) and *T. trichiura* (1,490 EPG vs. 1,363 EPG), but not for hookworm. The McMaster provided more accurate efficacy results (absolute difference to 'true' drug efficacy: 1.7% vs. 4.5%).

Conclusions: The McMaster is an alternative method for monitoring large-scale treatment programs. It is a robust (accurate multiplication factor) and accurate (reliable efficacy results) method, which can be easily standardized.

52.

Int J Parasitol Drugs Drug Resist. 2011 Oct 14;1(1):14-27. doi: 10.1016/j.ijpddr.2011.09.002. eCollection 2011.

Is anthelmintic resistance a concern for the control of human soil-transmitted helminths?

Authors: Vercruyse J, Albonico M, Behnke JM, Kotze AC, Prichard RK, McCarthy JS, Montresor A, Levecke B.

Abstract: The major human soil-transmitted helminths (STH), *Ascaris lumbricoides*, hookworms (*Necator americanus* and *Ancylostoma duodenale*) and *Trichuris trichiura* have a marked impact on human health in many parts of the world. Current efforts to control these parasites rely predominantly on periodic mass administration of anthelmintic drugs to school age children and other at-risk groups. After many years of use of these same drugs for controlling roundworms in livestock, high levels of resistance have developed, threatening the sustainability of these livestock industries in some locations. Hence, the question arises as to whether this is likely to also occur in the human STH, thereby threatening our ability to control these parasites. This is particularly important because of the recent increase in mass control programmes, relying almost exclusively on benzimidazole anthelmintics. It will be important to ensure that resistance is detected as it emerges in order to allow the implementation of mitigation strategies, such as use of drug combinations, to ensure that the effectiveness of the few existing anthelmintic drugs is preserved. In this review we address these issues by firstly examining the efficacy of anthelmintics against the human STH, and assessing whether there are any indications to date that resistance has emerged. We then consider the factors that influence the effect of current drug-use patterns in selecting for resistant parasite populations. We describe the tools currently available for resistance monitoring (field-based coprological methods), and those under development (in vitro bioassays and molecular tests), and highlight confounding factors that need to be taken into account when interpreting such resistance-monitoring data. We then highlight means to ensure that the currently available tools are used correctly, particularly with regard to study design, and we set appropriate drug-efficacy thresholds. Finally, we make recommendations for monitoring drug efficacy in the field, as components of control programmes, in order to maximise the ability to detect drug resistance, and if it arises to change control strategy and prevent the spread of resistance.

Keywords: Anthelmintic resistance; Anthelmintics; Guidelines; Soil-transmitted helminths

PMID:24533260 / PMCID:PMC3913213 / DOI:10.1016/j.ijpddr.2011.09.00

2012

53.

PLoS One. 2012;7(8):e44109. doi: 10.1371/journal.pone.0044109. Epub 2012 Aug 27.

Improvement of tuberculosis laboratory capacity on Pemba Island, Zanzibar: a health cooperation project.

Authors: Paglia MG, Bevilacqua N, Haji HS, Vairo F, Girardi E, Nicastrì E, Muhsin J, Racalbuto V, Jiddawi MS, Ippolito G.

Abstract: Low-income countries with high Tuberculosis burden have few reference laboratories able to perform TB culture. In 2006, the Zanzibar National TB Control Programme planned to decentralize TB diagnostics. The Italian Cooperation Agency with the scientific support of the "L. Spallanzani" National Institute for Infectious Diseases sustained the project through the implementation of a TB reference laboratory in a low-income country with a high prevalence of TB. The implementation steps were: 1) TB laboratory design according to the WHO standards; 2) laboratory equipment and reagent supplies for microscopy, cultures, and identification; 3) on-the-job training of the local staff; 4) web- and telemedicine-based supervision. From April 2007 to December 2010, 921 sputum samples were received from 40 peripheral laboratories: 120 TB cases were diagnosed. Of all the smear-positive cases, 74.2% were culture-positive. During the year 2010, the smear positive to culture positive rate increased up to 100%. In March 20, 2010 the Ministry of Health and Social Welfare of Zanzibar officially recognized the Public Health Laboratory- Ivo de Carneri as the National TB Reference Laboratory for the Zanzibar Archipelago. An advanced TB laboratory can represent a low cost solution to strengthen the TB diagnosis, to provide capacity building and mid-term sustainability.

PMID:22952891 / PMCID:PMC3428332 / DOI:10.1371/journal.pone.0044109 [PubMed - indexed for MEDLINE]

54.

Trop Med Int Health. 2012 Apr;17(4):423-9. doi: 10.1111/j.1365-3156.2011.02944.x. Epub 2012 Feb 1.

Evaluation of the diagnostic accuracy of the Haemoglobin Colour Scale to detect anaemia in young children attending primary healthcare clinics in Zanzibar.

Authors: Aldridge C, Foster HM, Albonico M, Ame SM, Montresor A.

Objectives: This study evaluates the diagnostic accuracy of Haemoglobin Colour Scale (HCS), compared with clinical diagnosis, to detect anaemia and severe anaemia in preschool-age children attending primary healthcare clinics in rural Zanzibar.

Methods: In all participants, haemoglobin (Hb) concentration was independently estimated by clinical examination for palmar pallor, HCS and HemoCue™. HemoCue was considered the reference method. Data collection was integrated into the usual health services and performed by local healthcare workers (HCWs). Sensitivity, specificity, positive and negative predictive values were calculated for HCS and clinical examination for palmar pallor. The limits of agreement between HCS and HemoCue, and inter-observer variability for HCS, were also defined.

Results: A total of 799 children age 2-59 months were recruited to the study. The prevalence of anaemia (Hb<11 g/dl) and severe anaemia (<5 g/dl) were 71% and 0.8% respectively. The sensitivity of HCS to detect anaemia was 33% [95% confidence interval (CI) 29-36] and specificity was 87% (83-91). The sensitivity of HCS to detect severe anaemia was 14% (95% CI 0-58) and specificity was 100% (99-100). The sensitivity of palmar pallor to detect anaemia was low, but superior to HCS (58% vs. 33%, P<0.001); specificity was inferior to HCS (55% vs. 87%, P<0.001). There was no evidence of a difference in either sensitivity (P>0.1) or specificity (P>0.1) between HCS and palmar pallor to detect severe anaemia.

Conclusions: Haemoglobin Colour Scale does not improve the capacity of HCWs to diagnose anaemia in this population. Accuracy is limited by considerable variability in the performances of test operators. However, optimizing the training protocol for those using the test may improve performance.

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DOI: 10.1111/j.1365-3156.2011.02944.x / PMID: 22296167 [PubMed - indexed for MEDLINE]

55.

BMC Res Notes. 2012 Feb 21;5:113. doi: 10.1186/1756-0500-5-113.

Replacing paper data collection forms with electronic data entry in the field: findings from a study of community-acquired bloodstream infections in Pemba, Zanzibar.

Authors: Thriemer K, Ley B, Ame SM, Puri MK, Hashim R, Chang NY, Salim LA, Ochiai RL, Wierzbica TF, Clemens JD, von Seidlein L, Deen JL, Ali SM, Ali M.

Background: Entering data on case report forms and subsequently digitizing them in electronic media is the traditional way to maintain a record keeping system in field studies. Direct data entry using an electronic device avoids this two-step process. It is gaining in popularity and has replaced the paper-based data entry system in many studies. We report our experiences with paper- and PDA-based data collection during a fever surveillance study in Pemba Island, Zanzibar, Tanzania.

Methods: Data were collected on a 14-page case report paper form in the first period of the study. The case report paper forms were then replaced with handheld computers (personal digital assistants or PDAs). The PDAs were used for screening and clinical data collection, including a rapid assessment of patient eligibility, real time errors, and inconsistency checking.

Results: A comparison of paper-based data collection with PDA data collection showed that direct data entry via PDA was faster and 25% cheaper. Data was more accurate (7% versus 1% erroneous data) and omission did not occur with electronic data collection. Delayed data turnaround times and late error detections in the paper-based system which made error corrections difficult were avoided using electronic data collection.

Conclusions: Electronic data collection offers direct data entry at the initial point of contact. It has numerous advantages and has the potential to replace paper-based data collection in the field. The availability of information and communication technologies for direct data transfer has the potential to improve the conduct of public health research in resource-poor settings.

DOI: 10.1186/1756-0500-5-113 / PMCID: PMC3392743 / PMID: 22353420 [PubMed - indexed for MEDLINE]

56.

PLoS One. 2012;7(2):e30350. doi: 10.1371/journal.pone.0030350. Epub 2012 Feb 17.

The burden of invasive bacterial infections in Pemba, Zanzibar.

Thriemer K, Ley B, Ame S, von Seidlein L, Pak GD, Chang NY, Hashim R, Schmied WH, Busch CJ, Nixon S, Morrissey A, Puri MK, Ali M, Ochiai RL, Wierzbza T, Jiddawi MS, Clemens JD, Ali SM, Deen JL.

Background: We conducted a surveillance study to determine the leading causes of bloodstream infection in febrile patients seeking treatment at three district hospitals in Pemba Island, Zanzibar, Tanzania, an area with low malaria transmission.

Methods: All patients above two months of age presenting to hospital with fever were screened, and blood was collected for microbiologic culture and malaria testing. Bacterial sepsis and malaria crude incidence rates were calculated for a one-year period and were adjusted for study participation and diagnostic sensitivity of blood culture.

Results: Blood culture was performed on 2,209 patients. Among them, 166 (8%) samples yielded bacterial growth; 87 (4%) were considered as likely contaminants; and 79 (4%) as pathogenic bacteria. The most frequent pathogenic bacteria isolated were Salmonella Typhi (n = 46; 58%), followed by Streptococcus pneumoniae (n = 12; 15%). The crude bacteremia rate was 6/100,000 but when adjusted for potentially missed cases the rate may be as high as 163/100,000. Crude and adjusted rates for S. Typhi infections and malaria were 4 and 110/100,000 and 4 and 47/100,000, respectively. Twenty three (51%), 22 (49%) and 22 (49%) of the S. Typhi isolates were found to be resistant toward ampicillin, chloramphenicol and cotrimoxazole, respectively. Multidrug resistance (MDR) against the three antimicrobials was detected in 42% of the isolates.

Conclusions: In the presence of very low malaria incidence we found high rates of S. Typhi and S. pneumoniae infections on Pemba Island, Zanzibar. Preventive measures such as vaccination could reduce the febrile disease burden.

DOI: 10.1371/journal.pone.0030350 / PMCID: PMC3281825 / PMID: 22363426 [PubMed - indexed for MEDLINE]

57.

Trans R Soc Trop Med Hyg. 2012 Mar;106(3):199-201. doi: 10.1016/j.trstmh.2011.11.006. Epub 2012 Jan 18.

Comparison of the Kato-Katz thick smear and McMaster egg counting techniques for monitoring drug efficacy against soil-transmitted helminths in schoolchildren on Pemba Island, Tanzania.

Authors: Albonico M, Ame SM, Vercruysse J, Levecke B.

The Kato-Katz thick smear technique is widely used to assess prevalence and intensity in soil-transmitted helminth (STH) control programmes, but its usefulness in monitoring anthelmintic drug efficacy needs to be validated and compared with other methods. A promising alternative is the McMaster egg counting technique. In the present study, the efficacy of single-dose albendazole against STH infections in 430 schoolchildren on Pemba Island was assessed using both the Kato-Katz and McMaster techniques. The study revealed comparable drug efficacy results for both methods and confirmed the potency of the McMaster technique as an alternative method for monitoring large-scale deworming programmes.

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DOI: 10.1016/j.trstmh.2011.11.006 / PMID: 22261186 [PubMed - indexed for MEDLINE]

58.

PLoS Negl Trop Dis. 2012;6(6):e1685. doi: 10.1371/journal.pntd.0001685. Epub 2012 Jun 5.

Efficacy and safety of nitazoxanide, albendazole, and nitazoxanide-albendazole against Trichuris trichiura infection: a randomized controlled trial.

Authors: Speich B, Ame SM, Ali SM, Alles R, Hattendorf J, Utzinger J, Albonico M, Keiser J.

Background: The currently used anthelmintic drugs, in single oral application, have low efficacy against Trichuris trichiura infection, and hence novel anthelmintic drugs are needed. Nitazoxanide has been suggested as potential drug candidate.

Methodology: The efficacy and safety of a single oral dose of nitazoxanide (1,000 mg), or albendazole (400 mg), and a nitazoxanide-albendazole combination (1,000 mg-400 mg), with each drug administered separately on two consecutive days, were assessed in a double-blind, randomized, placebo-controlled trial in two schools on Pemba, Tanzania. Cure and egg reduction rates were calculated by per-protocol analysis and by available case analysis. Adverse events were assessed and graded before treatment and four times after treatment.

Principal findings: Complete data for the per-protocol analysis were available from 533 *T. trichiura*-positive children. Cure rates against *T. trichiura* were low regardless of the treatment (nitazoxanide-albendazole, 16.0%; albendazole, 14.5%; and nitazoxanide, 6.6%). Egg reduction rates were 54.9% for the nitazoxanide-albendazole combination, 45.6% for single albendazole, and 13.4% for single nitazoxanide. Similar cure and egg reduction rates were calculated using the available case analysis. Children receiving nitazoxanide had significantly more adverse events compared to placebo recipients. Most of the adverse events were mild and had resolved within 24 hours posttreatment.

Conclusions: Nitazoxanide shows no effect on *T. trichiura* infection. The low efficacy of albendazole against *T. trichiura* in the current setting characterized by high anthelmintic drug pressure is confirmed. There is a pressing need to develop new anthelmintics against trichuriasis.

DOI: 10.1371/journal.pntd.0001685 / PMCID: PMC3367984 / PMID: 22679525 [PubMed - indexed for MEDLINE]

59.

PLoS One. 2012;7(7):e41527. doi: 10.1371/journal.pone.0041527. Epub 2012 Jul 23.

Improving community coverage of oral cholera mass vaccination campaigns: lessons learned in Zanzibar.

Authors: Schaetti C, Ali SM, Chaignat CL, Khatib AM, Hutubessy R, Weiss MG.

Background: Recent research in two cholera-endemic communities of Zanzibar has shown that a majority (~94%) of the adult population was willing to receive free oral cholera vaccines (OCVs). Since OCV uptake in the 2009 campaign reached only ~50% in these communities, an evaluation of social and cultural factors and of barriers was conducted to understand this difference for future cholera control planning.

Principal findings: A random sample of 367 adult peri-urban and rural community residents (46.6% immunized vs. 53.4% unimmunized) was studied with a semi-structured interview that inquired about social and cultural features of cholera depicted in a vignette and barriers to OCV uptake. Symptoms (rectal pain, loose skin only in rural community) and perceived causes (uncovered food, contact with contaminated water) specific for severe diarrhea were associated with uptake. Purchasing drugs from pharmacies to stop diarrhea and vomiting was negatively associated with uptake. Increasing household size, age and previous enteric illness episode were positively related to uptake, the latter only at the rural site. The most prominent barrier to uptake was competing obligations or priorities (reported by 74.5%, identified as most important barrier by 49.5%).

Next most prominent barriers were lacking information about the campaign (29.6%, 12.2%), sickness (14.3%, 13.3%) and fear of possible vaccine side effects (15.3%, 5.6%). The majority of unvaccinated respondents requested repetition of the vaccination with free OCVs.

Conclusions: Factors associated with uptake indicated a positive impact of the vaccination campaign and of sensitization activities on vaccine acceptance behavior. Unlike communities opposed to cholera control or settings where public confidence in vaccines is lacking, identified barriers to uptake indicated a good campaign implementation and trust in the health system. Despite prospects and demand for repeating the vaccination, local decision-makers should reconsider how careful logistical arrangements may improve community coverage and thus effectiveness of vaccination campaigns.

DOI: 10.1371/journal.pone.0041527 / PMCID: PMC3402403

60.

Hum Vaccin Immunother. 2012 Sep;8(9):1223-9. doi: 10.4161/hv.20901. Epub 2012 Aug 16.

Social and cultural determinants of oral cholera vaccine uptake in Zanzibar.

Authors: Schaetti C, Ali SM, Hutubessy R, Khatib AM, Chaignat CL, Weiss MG.

Effectiveness of mass cholera vaccination campaigns requires not only technical and financial capacity but also consideration of social and cultural factors affecting vaccine acceptance. This study examined the influence of local community views of cholera on oral cholera vaccine (OCV) uptake in a mass vaccination campaign in 2009 in peri-urban and rural areas of Zanzibar. It used data from interviews conducted before the campaign and followed previous research assessing determinants of anticipated OCV acceptance. OCV uptake was lower than the reported anticipated acceptance. Less than half of the 356 adult respondents (49.7%) drank the required two doses of OCV. Variables referring to socio-cultural features of diarrheal illness that respondents identified with a cholera case vignette explained uptake better than analysis only of socio-demographic characteristics. Somatic features of illness not specific for cholera were negative determinants. Recognition of unconsciousness as a serious sign of dehydration and concern that cholera outbreaks would overwhelm the local healthcare system in the rural area were positive determinants of acceptance.

Female gender, rural residence and older age were also positive determinants of OCV uptake. For further vaccine action with OCVs, cholera as a cause of severe dehydration should be distinguished from other causes of diarrhea. Planning should acknowledge rural concern about the relationship of limited capacity of the healthcare system to cope with cholera outbreaks and the priority of a cholera vaccine. Findings recommend particular efforts to increase cholera immunization coverage among young adults, in peri-urban areas and for men.

DOI: 10.4161/hv.20901 / PMCID: PMC3579902 / PMID: 22894965 [PubMed - indexed for MEDLINE]

61.

PLoS One. 2012;7(12):e51823. doi: 10.1371/journal.pone.0051823. Epub 2012 Dec 20.

Authors: **Clinical and epidemiological features of typhoid fever in Pemba, Zanzibar: assessment of the performance of the WHO case definitions.**

Thriemer K, Ley B, Ame SS, Deen JL, Pak GD, Chang NY, Hashim R, Schmied WH, Busch CJ, Nixon S, Morrissey A, Puri MK, Ochiai RL, Wierzba T, Clemens JD, Ali M, Jiddawi MS, von Seidlein L, Ali SM.

Background: The gold standard for diagnosis of typhoid fever is blood culture (BC). Because blood culture is often not available in impoverished settings it would be helpful to have alternative diagnostic approaches. We therefore investigated the usefulness of clinical signs, WHO case definition and Widal test for the diagnosis of typhoid fever.

Principal findings: Participants with a body temperature $\geq 37.5^{\circ}\text{C}$ or a history of fever were enrolled over 17 to 22 months in three hospitals on Pemba Island, Tanzania. Clinical signs and symptoms of participants upon presentation as well as blood and serum for BC and Widal testing were collected. Clinical signs and symptoms of typhoid fever cases were compared to other cases of invasive bacterial diseases and BC negative participants. The relationship of typhoid fever cases with rainfall, temperature, and religious festivals was explored. The performance of the WHO case definitions for suspected and probable typhoid fever and a local cut off titre for the Widal test was assessed. 79 of 2209 participants had invasive bacterial disease. 46 isolates were identified as typhoid fever. Apart from a longer duration of fever prior to admission clinical signs and symptoms were not significantly different among patients with typhoid fever than from other febrile patients. We did not detect any significant seasonal patterns nor correlation with rainfall or festivals. The sensitivity and specificity of the WHO case definition for suspected and probable typhoid fever were 82.6% and 41.3% and 36.3 and 99.7% respectively. Sensitivity and specificity of the Widal test was 47.8% and 99.4 both for O-agglutinin and H-agglutinin at a cut-off titre of 1:80.

Conclusions: Typhoid fever prevalence rates on Pemba are high and its clinical signs and symptoms are non-specific. The sensitivity of the Widal test is low and the WHO case definition performed better than the Widal test.

DOI: 10.1371/journal.pone.0051823 / PMCID: PMC3527440 / PMID: 23284780 [PubMed - indexed for MEDLINE]

62.

PLoS Negl Trop Dis. 2012;6(10):e1844. doi: 10.1371/journal.pntd.0001844. Epub 2012 Oct 4.

Costs of illness due to cholera, costs of immunization and cost-effectiveness of an oral cholera mass vaccination campaign in Zanzibar.

Authors: Schaetti C, Weiss MG, Ali SM, Chaignat CL, Khatib AM, Reyburn R, Duintjer Tebbens RJ, Hutubessy R.

Background: The World Health Organization (WHO) recommends oral cholera vaccines (OCVs) as a supplementary tool to conventional prevention of cholera. Dukoral, a killed whole-cell two-dose OCV, was used in a mass vaccination campaign in 2009 in Zanzibar. Public and private costs of illness (COI) due to endemic cholera and costs of the mass vaccination campaign were estimated to assess the cost-effectiveness of OCV for this particular campaign from both the health care provider and the societal perspective.

Principal findings: Public and private COI were obtained from interviews with local experts, with patients from three outbreaks and from reports and record review. Cost data for the vaccination campaign were collected based on actual expenditure and planned budget data. A static cohort of 50,000 individuals was examined, including herd protection. Primary outcome measures were incremental cost-effectiveness ratios (ICER) per death, per case and per disability-adjusted life-year (DALY) averted. One-way sensitivity and threshold analyses were conducted. The ICER was evaluated with regard to WHO criteria for cost-effectiveness. Base-case ICERs were USD 750,000 per death averted, USD 6,000 per case averted and USD 30,000 per DALY averted, without differences between the health care provider and the societal perspective. Threshold analyses using Shanchol and assuming high incidence and case-fatality rate indicated that the purchase price per course would have to be as low as USD 1.2 to render the mass vaccination campaign cost-effective from a health care provider perspective (societal perspective: USD 1.3).

Conclusions: Based on empirical and site-specific cost and effectiveness data from Zanzibar, the 2009 mass vaccination campaign was cost-ineffective mainly due to the relatively high OCV purchase price and a relatively low incidence. However, mass vaccination campaigns in Zanzibar to control endemic cholera may meet criteria for cost-effectiveness under certain circumstances, especially in high-incidence areas and at OCV prices below USD 1.3.

DOI: 10.1371/journal.pntd.0001844 / PMCID: PMC3464297 / PMID: 23056660 [PubMed - indexed for MEDLINE]

63.

BMC Public Health. 2012 Oct 30;12:930. doi: 10.1186/1471-2458-12-930.

Study and implementation of urogenital schistosomiasis elimination in Zanzibar (Unguja and Pemba islands) using an integrated multidisciplinary approach.

Authors: Knopp S, Mohammed KA, Ali SM, Khamis IS, Ame SM, Albonico M, Gouvras A, Fenwick A, Savioli L, Colley DG, Utzinger J, Person B, Rollinson D.

Background: Schistosomiasis is a parasitic infection that continues to be a major public health problem in many developing countries being responsible for an estimated burden of at least 1.4 million disability-adjusted life years (DALYs) in Africa alone. Importantly, morbidity due to schistosomiasis has been greatly reduced in some parts of the world, including Zanzibar. The Zanzibar government is now committed to eliminate urogenital schistosomiasis. Over the next 3-5 years, the whole at-risk population will be administered praziquantel (40 mg/kg) biannually. Additionally, snail control and behaviour change interventions will be implemented in selected communities and the outcomes and impact measured in a randomized intervention trial.

Methods: In this 5-year research study, on both Unguja and Pemba islands, urogenital schistosomiasis will be assessed in 45 communities with urine filtration and reagent strips in 4,500 schoolchildren aged 9-12 years annually, and in 4,500 first-year schoolchildren and 2,250 adults in years 1 and 5.

Additionally, from first-year schoolchildren, a finger-prick blood sample will be collected and examined for *Schistosoma haematobium* infection biomarkers. Changes in prevalence and infection intensity will be assessed annually. Among the 45 communities, 15 were randomized for biannual snail control with niclosamide, in concordance with preventive chemotherapy campaigns. The reduction of *Bulinus globosus* snail populations and *S. haematobium*-infected snails will be investigated. In 15 other communities, interventions triggering behaviour change have been designed and will be implemented in collaboration with the community. A change in knowledge, attitudes and practices will be assessed annually through focus group discussions and in-depth interviews with schoolchildren, teachers, parents and community leaders. In all 45 communities, changes in the health system, water and sanitation infrastructure will be annually tracked by standardized questionnaire-interviews with community leaders. Additional issues potentially impacting on study outcomes and all incurring costs will be recorded and monitored longitudinally.

Discussion: Elimination of schistosomiasis has become a priority on the agenda of the Zanzibar government and the international community. Our study will contribute to identifying what, in addition to preventive chemotherapy, needs to be done to prevent, control, and ultimately eliminate schistosomiasis, and to draw lessons for current and future schistosomiasis elimination programmes in Africa and elsewhere.

TRIAL REGISTRATION: ISRCTN48837681.

DOI: 10.1186/1471-2458-12-930 / PMCID: PMC3533998 / PMID: 23110494 [PubMed - indexed for MEDLINE].

64.

Lancet Infect Dis. 2012 Nov;12(11):837-44. doi: 10.1016/S1473-3099(12)70196-2. Epub 2012 Sep 4.

Effectiveness of an oral cholera vaccine in Zanzibar: findings from a mass vaccination campaign and observational cohort study.

Authors: Khatib AM, Ali M, von Seidlein L, Kim DR, Hashim R, Reyburn R, Ley B, Thriemer K, Enwere G, Hutubessy R, Aguado MT, Kieny MP, Lopez AL, Wierzbza TF, Ali SM, Saleh AA, Mukhopadhyay AK, Clemens J, Jiddawi MS, Deen J.

Background: Zanzibar, in east Africa, has been severely and repeatedly affected by cholera since 1978. We assessed the effectiveness of oral cholera vaccination in high-risk populations in the archipelago to estimate the indirect (herd) protection conferred by the vaccine and direct vaccine effectiveness.

Methods: We offered two doses of a killed whole-cell B-subunit cholera vaccine to individuals aged 2 years and older in six rural and urban sites. To estimate vaccine direct protection, we compared the incidence of cholera between recipients and non-recipients using generalised estimating equations with the log link function while controlling for potential confounding variables. To estimate indirect effects, we used a geographic information

systems approach and assessed the association between neighbourhood-level vaccine coverage and the risk for cholera in the non-vaccinated residents of that neighbourhood, after controlling for potential confounding variables. This study is registered with ClinicalTrials.gov, number NCT00709410.

Findings: Of 48,178 individuals eligible to receive the vaccine, 23,921 (50%) received two doses. Between February, 2009, and May, 2010, there was an outbreak of cholera, enabling us to assess vaccine effectiveness. The vaccine conferred 79% (95% CI 47-92) direct protection against cholera in participants who received two doses. Indirect (herd) protection was shown by a decrease in the risk for cholera of non-vaccinated residents within a household's neighbourhood as the vaccine coverage in that neighbourhood increased.

Interpretation: Our findings suggest that the oral cholera vaccine offers both direct and indirect (herd) protection in a sub-Saharan African setting. Mass oral cholera immunisation campaigns have the potential to provide not only protection for vaccinated individuals but also for the unvaccinated members of the community and should be strongly considered for wider use. Because this is an internationally-licensed vaccine, we could not undertake a randomised placebo-controlled trial, but the absence of vaccine effectiveness against non-cholera diarrhoea indicates that the noted protection against cholera could not be explained by bias.

FUNDING: Bill & Melinda Gates Foundation, Swedish International Development Cooperation Agency, and the South Korean Government.

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65.

J Trop Med. 2012;2012:590463. doi: 10.1155/2012/590463. Epub 2012 Dec 24.

Safety of a New Chewable Formulation of Mebendazole for Preventive Chemotherapy Interventions to Treat Young Children in Countries with Moderate-to-High Prevalence of Soil Transmitted Helminth Infections.

Authors: Friedman AJ, Ali SM, Albonico M.

The primary objective was to evaluate the safety and tolerability of the new chewable formulation of mebendazole to treat soil-transmitted helminth (STH) infections in children ≤ 10 years old with the goal of using this formulation in preventive chemotherapy programs and expand treatment to young children who are unable to swallow solid tablets. In this open-label, single-arm, phase 3 study conducted at Pemba Island, Zanzibar, Tanzania, children aged 2 to 10 years (median age: 4 years) were administered a single dose of the mebendazole 500 mg chewable tablet. Safety was assessed 30 minutes after dose and 3 days later. Of the 390 (98%) children who completed the study, 195 (55%) had ≥ 1 STH infection and 157 (45%) had no infection at baseline. The most common STH infections were *Trichuris trichiura* (51%), hookworm (16%), and *Ascaris lumbricoides* (7%). Treatment-emergent adverse events (TEAEs) were experienced by 11% of children. There was no difference in the percentage of children experiencing TEAEs between the age strata of 2-5 years and 6-10 years. Diarrhea was reported only in children aged 2-5 years. No correlation was observed between the type or percentage of AEs and presence or severity of infection. A single dose of mebendazole 500 mg chewable tablet was safe and well tolerated in children aged 2 to 10 years.

DOI: 10.1155/2012/590463 / PMCID: PMC3540782 / PMID: 23319961 [PubMed]

2013

66.

Am J Trop Med Hyg. 2013 Jan;88(1):144-52. doi: 10.4269/ajtmh.2012.12-0288. Epub 2012 Dec 3.

Utilization and accessibility of healthcare on Pemba Island, Tanzania: implications for health outcomes and disease surveillance for typhoid fever.

Authors: Kaljee LM, Pach A, Thriemer K, Ley B, Ali SM, Jiddawi M, Puri M, von Seidlein L, Deen J, Ochiai L, Wierzbica T, Clemens J.

Salmonella enterica serotype Typhi (S. Typhi) was estimated to cause over 200,000 deaths and more than 21 million illnesses worldwide, including over 400,000 illnesses in Africa. The current study was conducted in four villages on Pemba Island, Zanzibar, in 2010. We present data on policy makers', health administrators', and village residents' and leaders' perceptions of typhoid fever, and hypothetical and actual health care use among village residents for typhoid fever. Qualitative data provided descriptions of home-based treatment practices and use of western pharmaceuticals, and actual healthcare use for culture-confirmed typhoid fever. Survey data indicate health facility use was associated with gender, education, residency, and perceptions of severity for symptoms associated with typhoid fever. Data have implications for education of policy makers and health administrators, design and implementation of surveillance studies, and community-based interventions to prevent disease

outbreaks, decrease risks of complications, and provide information about disease recognition, diagnosis, and treatment.

DOI: 10.4269/ajtmh.2012.12-0288 / PMCID: PMC3541726 / PMID: 23208887 [PubMed - indexed for MEDLINE]

67.

Parasit Vectors. 2013 Jan 4;6:3. doi: 10.1186/1756-3305-6-3.

Prevalence of intestinal protozoa infection among school-aged children on Pemba Island, Tanzania, and effect of single-dose albendazole, nitazoxanide and albendazole-nitazoxanide.

Authors: Speich B, Marti H, Ame SM, Ali SM, Bogoch II, Utzinger J, Albonico M, Keiser J.

Background: Pathogenic intestinal protozoa infections are common in school-aged children in the developing world and they are frequently associated with malabsorption syndromes and gastrointestinal morbidity. Since diagnosis of these parasites is difficult, prevalence data on intestinal protozoa is scarce.

Methods: We collected two stool samples from school-aged children on Pemba Island, Tanzania, as part of a randomized controlled trial before and 3 weeks after treatment with (i) single-dose albendazole (400 mg); (ii) single-dose nitazoxanide (1,000 mg); (iii) nitazoxanide-albendazole combination (1,000 mg-400 mg), with each drug given separately on two consecutive days; and (iv) placebo. Formalin-fixed stool samples were examined for the presence of intestinal protozoa using an ether-concentration method to determine the prevalence and estimate cure rates (CRs).

Results: Almost half (48.7%) of the children were diagnosed with at least one of the (potentially) pathogenic protozoa *Giardia intestinalis*, *Entamoeba histolytica*/E. dispar and *Blastocystis hominis*. Observed CRs were high for all treatment arms, including placebo. Nitazoxanide showed a significant effect compared to placebo against the non-pathogenic protozoon *Entamoeba coli*.

Conclusions: Intestinal protozoa infections might be of substantial health relevance even in settings where they are not considered as a health problem. Examination of a single stool sample with the ether-concentration method lacks sensitivity for the diagnosis of intestinal protozoa, and hence, care is indicated when interpreting prevalence estimates and treatment effects.

DOI: 10.1186/1756-3305-6-3 / PMCID: PMC3558385 / PMID: 23289920 [PubMed - indexed for MEDLINE]

68.

J Clin Microbiol. 2013 Mar;51(3):1040-5. doi: 10.1128/JCM.03162-12. Epub 2013 Jan 16.

Molecular characterization of high-level-cholera-toxin-producing El Tor variant *Vibrio cholerae* strains in the Zanzibar Archipelago of Tanzania.

Authors: Naha A, Chowdhury G, Ghosh-Banerjee J, Senoh M, Takahashi T, Ley B, Thriemer K, Deen J, Seidlein LV, Ali SM, Khatib A, Ramamurthy T, Nandy RK, Nair GB, Takeda Y, Mukhopadhyay AK.

Analysis of 1,180 diarrheal stool samples in Zanzibar detected 247 *Vibrio cholerae* O1, Ogawa strains in 2009. Phenotypic traits and PCR-based detection of *rstR*, *rtxC*, and *tcpA* alleles showed that they belonged to the El Tor biotype.

Genetic analysis of *ctxB* of these strains revealed that they were classical type, and production of classical cholera toxin B (CTB) was confirmed by Western blotting. These strains produced more CT than the prototype El Tor and formed a separate cluster by pulsed-field gel electrophoresis (PFGE) analysis.

DOI: 10.1128/JCM.03162-12 / PMCID: PMC3592071 / PMID: 23325815 [PubMed - indexed for MEDLINE]

69.

Am J Trop Med Hyg. 2013 Apr;88(4):626-9. doi: 10.4269/ajtmh.12-0742. Epub 2013 Mar 11.

Mobile phone microscopy for the diagnosis of soil-transmitted helminth infections: a proof-of-concept study.

Authors: Bogoch II, Andrews JR, Speich B, Utzinger J, Ame SM, Ali SM, Keiser J.

We created a mobile phone microscope and assessed its accuracy for the diagnosis of soil-transmitted helminths compared with conventional microscopy. Mobile phone microscopy has a sensitivity of 69.4% for detecting any helminth egg and sensitivities of 81.0%, 54.4%, and 14.3% for the diagnosis of *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm respectively.

70.

Trans R Soc Trop Med Hyg. 2013 Aug;107(8):493-501. doi: 10.1093/trstmh/trt051.

Comparison of three copromicroscopic methods to assess albendazole efficacy against soil-transmitted helminth infections in school-aged children on Pemba Island.

Authors: Albonico M, Rinaldi L, Sciascia S, Morgoglione ME, Piemonte M, Maurelli MP, Musella V, Utzinger J, Ali SM, Ame SM, Cringoli G.

Background: The diagnostic accuracy of three faecal egg count techniques (Kato-Katz, McMaster and FLOTAC) to assess albendazole efficacy against soil-transmitted helminth (STH) infections was compared.

Methods: The study is registered with Current Controlled Trials [identifier: ISRCTN90088840]. During September-November 2009, 304 school-aged children on Pemba Island, Tanzania, were screened and those infected with *Ascaris lumbricoides*, hookworm or *Trichuris trichiura* were treated with a single dose of albendazole (400 mg). Twenty-one days post-treatment, children provided a single stool sample which was examined using the same diagnostic methods. All stool samples were divided into two aliquots and one was fixed in 5% formalin and examined using FLOTAC and McMaster approximately 6 months after collection.

Results: Using fresh stool samples, comparable prevalences were demonstrated for the three methods at baseline (90-92.2% for *T. trichiura*, 41.1-52.8% for hookworm, 32.9-37.2% for *A. lumbricoides*); FLOTAC was the most sensitive method at baseline and follow-up. Albendazole showed high cure rate (CR) against *A. lumbricoides* (90-97%), moderate CR against hookworm (63-72%) and very low CR against *T. trichiura* (6-9%), regardless of the technique used. Egg counts (eggs per gram) at baseline were similar for *A. lumbricoides* and for hookworm among the three methods, and higher using McMaster and Kato-Katz compared with FLOTAC for *T. trichiura*. All methods were similar for hookworm and *A. lumbricoides* egg reduction rate (ERR) estimation, but Kato-Katz indicated a significantly higher ERR than McMaster and FLOTAC for *T. trichiura*. Preserved stool samples revealed consistently lower FECs at baseline and follow-up for all STHs.

Conclusions: Further development and validation of standard protocols for anthelmintic drug efficacy evaluation must be pursued.

DOI: 10.1093/trstmh/trt051 / PMID: 23843559 [PubMed - indexed for MEDLINE]

71.

BMC Med. 2013 Sep 18;11:206. doi: 10.1186/1741-7015-11-206.

Comparing sociocultural features of cholera in three endemic African settings.

Authors: Schaetti C, Sundaram N, Merten S, Ali SM, Nyambedha EO, Lapika B, Chaignat CL, Hutubessy R, Weiss MG.

Background: Cholera mainly affects developing countries where safe water supply and sanitation infrastructure are often rudimentary. Sub-Saharan Africa is a cholera hotspot. Effective cholera control requires not only a professional assessment, but also consideration of community-based priorities. The present work compares local sociocultural features of endemic cholera in urban and rural sites from three field studies in southeastern Democratic Republic of Congo (SE-DRC), western Kenya and Zanzibar.

Methods: A vignette-based semistructured interview was used in 2008 in Zanzibar to study sociocultural features of cholera-related illness among 356 men and women from urban and rural communities. Similar cross-sectional surveys were performed in western Kenya (n = 379) and in SE-DRC (n = 360) in 2010. Systematic comparison across all settings considered the following domains: illness identification; perceived seriousness, potential fatality and past household episodes; illness-related experience; meaning; knowledge of prevention; help-seeking behavior; and perceived vulnerability.

Results: Cholera is well known in all three settings and is understood to have a significant impact on people's lives. Its social impact was mainly characterized by financial concerns. Problems with unsafe water, sanitation and dirty environments were the most common perceived causes across settings; nonetheless, non-biomedical explanations were widespread in rural areas of SE-DRC and Zanzibar. Safe food and water and vaccines were prioritized for prevention in SE-DRC. Safe water was prioritized in western Kenya along with sanitation and health education. The latter two were also prioritized in Zanzibar. Use of oral rehydration solutions and rehydration was a top priority everywhere; healthcare facilities were universally reported as a primary source of help. Respondents in SE-DRC and Zanzibar reported cholera as affecting almost everybody without differentiating much for gender, age and class. In contrast, in western Kenya, gender differentiation was pronounced, and children and the poor were regarded as most vulnerable to cholera.

Conclusions: This comprehensive review identified common and distinctive features of local understandings of cholera. Classical treatment (that is, rehydration) was highlighted as a priority for control in the three African study settings and is likely to be identified in the region beyond. Findings indicate the value of insight from community studies to guide local program planning for cholera control and elimination.

DOI: 10.1186/1741-7015-11-206 / PMCID: PMC4016292 / PMID: 24047241 [PubMed - indexed for MEDLINE]

72.

PLoS Negl Trop Dis. 2013 Oct 17;7(10):e2474. doi: 10.1371/journal.pntd.0002474. eCollection 2013.

Elimination of schistosomiasis transmission in Zanzibar: baseline findings before the onset of a randomized intervention trial.

Authors: Knopp S, Person B, Ame SM, Mohammed KA, Ali SM, Khamis IS, Rabone M, Allan F, Gouvras A, Blair L, Fenwick A, Utzinger J, Rollinson D.

Background: Gaining and sustaining control of schistosomiasis and, whenever feasible, achieving local elimination are the year 2020 targets set by the World Health Organization. In Zanzibar, various institutions and stakeholders have joined forces to eliminate urogenital schistosomiasis within 5 years. We report baseline findings before the onset of a randomized intervention trial designed to assess the differential impact of community-based praziquantel administration, snail control, and behavior change interventions.

Methodology: In early 2012, a baseline parasitological survey was conducted in ~20,000 people from 90 communities in Unguja and Pemba. Risk factors for schistosomiasis were assessed by administering a questionnaire to adults. In selected communities, local knowledge about schistosomiasis transmission and prevention was determined in focus group discussions and in-depths interviews. Intermediate host snails were collected and examined for shedding of cercariae.

Principal findings: The baseline *Schistosoma haematobium* prevalence in school children and adults was 4.3% (range: 0-19.7%) and 2.7% (range: 0-26.5%) in Unguja, and 8.9% (range: 0-31.8%) and 5.5% (range: 0-23.4%) in Pemba, respectively. Heavy infections were detected in 15.1% and 35.6% of the positive school children in Unguja and Pemba, respectively. Males were at higher risk than females (odds ratio (OR): 1.45; 95% confidence interval (CI): 1.03-2.03). Decreasing adult age (OR: 1.04; CI: 1.02-1.06), being born in Pemba (OR: 1.48; CI: 1.02-2.13) or Tanzania (OR: 2.36; CI: 1.16-4.78), and use of freshwater (OR: 2.15; CI: 1.53-3.03) showed higher odds of infection. Community knowledge about schistosomiasis was low. Only few infected *Bulinus* snails were found.

Conclusions: The relatively low *S. haematobium* prevalence in Zanzibar is a promising starting point for elimination. However, there is a need to improve community knowledge about disease transmission and prevention. Control measures tailored to the local context, placing particular attention to hot-spot areas, high-risk groups, and individuals, will be necessary if elimination is to be achieved.

DOI: 10.1371/journal.pntd.0002474 / PMCID: PMC3798599 / PMID: 24147165 [PubMed - indexed for MEDLINE]

2014

73.

N Engl J Med. 2014 Feb 13;370(7):610-20. doi: 10.1056/NEJMoa1301956.

Oxantel pamoate-albendazole for *Trichuris trichiura* infection.

Authors: Speich B, Ame SM, Ali SM, Alles R, Huwyler J, Hattendorf J, Utzinger J, Albonico M, Keiser J.

Background: Infections with soil-transmitted helminths (*Ascaris lumbricoides*, hookworm, and *Trichuris trichiura*) are widespread and often occur concomitantly. These parasitic-worm infections are typically treated with albendazole or mebendazole, but both drugs show low efficacy against *T. trichiura*. Albendazole is the drug of choice against hookworm.

Methods: In this double-blind trial conducted on Pemba Island, Tanzania, we randomly assigned children, 6 to 14 years of age, to receive one of four treatments: oxantel pamoate at a dose of 20 mg per kilogram of body weight, plus 400 mg of albendazole, administered on consecutive days; oxantel pamoate at a single dose of 20 mg per kilogram; albendazole at a single dose of 400 mg; or mebendazole at a single dose of 500 mg. We assessed the efficacy and safety profile of oxantel pamoate-albendazole when used in the treatment of *T. trichiura* infection (primary outcome) and concomitant soil-transmitted helminth infection (secondary outcome). Efficacy was determined by means of assessment of the cure rate and egg-reduction rate. Adverse events were assessed four times after treatment.

Results: Complete data were available for 458 children, of whom 450 were infected with *T. trichiura*, 443 with hookworm, and 293 with *A. lumbricoides*. The cure rate of *T. trichiura* infection was significantly higher with oxantel pamoate-albendazole than with mebendazole (31.2% vs. 11.8%, $P=0.001$), as was the egg-reduction rate (96.0% [95% confidence interval {CI}, 93.5 to 97.6] vs. 75.0% [95% CI, 64.2 to 82.0]). The cure rate with albendazole (2.6%) and the egg-reduction rate with albendazole (45.0%; 95% CI, 32.0 to 56.4) were significantly lower than the rates with mebendazole ($P=0.02$ for the comparison of cure rates). Oxantel pamoate had low efficacy against hookworm and *A. lumbricoides*. Adverse events (mainly mild) were reported by 30.9% of all children.

Conclusions: Treatment with oxantel pamoate-albendazole resulted in higher cure and egg-reduction rates for *T. trichiura* infection than the rates with standard therapy. (Funded by the Medicor Foundation and the Swiss National Science Foundation; Current Controlled Trials number, ISRCTN54577342.).

DOI: 10.1056/NEJMoa1301956 / PMID: 24521107 [PubMed - indexed for MEDLINE]

74.

Acta Trop. 2014 Feb;130:11-6. doi: 10.1016/j.actatropica.2013.10.008. Epub 2013 Oct 18.

"Freezing" parasites in pre-Himalayan region, Himachal Pradesh: Experience with mini-FLOTAC.

Authors: Barda B, Ianniello D, Salvo F, Sadutshang T, Rinaldi L, Cringoli G, Burioni R, Albonico M.

Background: Helminths and protozoa infections pose a great burden especially in developing, countries, due to morbidity caused both by acute and chronic infections. Data on distribution of intestinal parasitic infections among the native and expatriates populations in Himachal Pradesh are scarce. The aim of our survey was to analyze the intestinal parasitic burden in communities from Dharamsala, Kangra district, in clinical and public health settings. We also field-tested the mini- FLOTAC, an innovative diagnostic device.

Methods: Subjects referring to the Tibetan Delek Hospital for abdominal discomfort and all children of the Tibetan Primary School in Dharamsala were screened for intestinal parasitic infections with direct smear, formol-ether concentration (FEC) method and mini-FLOTAC, their clinical history was recorded, and correlations between clinical symptoms and infections analyzed.

Results: 152 subjects were screened for intestinal parasites, of which 72 subjects in the outpatients department (OPD) (36 expatriates and 36 natives) and 80 in the school. 60% of schoolchildren and 57% of OPD patients were found positive for any infection, the most represented were protozoa infections (50%), whereas helminthic infections accounted only for 13% and 20% in OPD patients and schoolchildren, respectively. The most prevalent among helminths was *Ascaris lumbricoides* (11%). *Giardia intestinalis* was more present among schoolchildren than the OPD patients (20% vs 6%) and *E. histolytica/dispar* was more prevalent among the OPD patients (42%) than the school children (23%). Correlations were found between nausea and loose or watery stools and parasitic infections, particularly in expatriates, whereas schoolchildren, despite being as infected as adults, were completely asymptomatic. Mini-FLOTAC detected higher number of helminth infections whereas FEC method was more accurate for the diagnosis of protozoa.

Conclusions: This study presents an accurate snapshot of intestinal parasitic infections in Dharamsala, and their high prevalence calls for more awareness and control measures. Mini-FLOTAC is a promising and simple technique for the diagnosis of helminth infections.

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PMID:24145157 / DOI:10.1016/j.actatropica.2013.10.008 [PubMed - indexed for MEDLINE].

75.

Eur J Clin Microbiol Infect Dis. 2014 May;33(5):815-22. doi: 10.1007/s10096-013-2019-1. Epub 2013 Nov 23.

Comparison of the Kato-Katz method and ether-concentration technique for the diagnosis of soil-transmitted helminth infections in the framework of a randomised controlled trial.

Authors: Speich B, Utzinger J, Marti H, Ame SM, Ali SM, Albonico M, Keiser J.

Soil-transmitted helminth infections are a major public health problem. An accurate diagnosis is important in order to identify individuals and communities in need of intervention, and for monitoring drug efficacy and potential emergence of resistance. We compared the accuracy of the Kato-Katz method and ether-concentration technique for the diagnosis of soil-transmitted helminth infections within a randomised controlled trial. Quadruplicate Kato-Katz thick smears (duplicate Kato-Katz from two stool samples each) were examined before (baseline) and 3 weeks after treatment (follow-up). Additionally, at baseline and follow-up, the first stool sample was subjected to an ether-concentration method. We determined the prevalence, sensitivity, negative predictive value, diagnostic agreement and cure rates for single and duplicate Kato-Katz thick smears from the first stool sample, quadruplicate Kato-Katz thick smears produced from two stool samples and single ether-concentration as compared to our 'gold' standard (i.e. quadruplicate Kato-Katz plus ether-concentration). Quadruplicate Kato-Katz

revealed a higher sensitivity than single ether-concentration for *Trichuris trichiura* at baseline (94.3 % vs. 88.5 %, $p = 0.002$) and follow-up (93.8 % vs.

83.5 %, $p < 0.001$). In contrary, at follow-up, ether-concentration showed a higher sensitivity than quadruplicate Kato-Katz for *Ascaris lumbricoides* diagnosis (86.7 % vs. 46.7 %, $p = 0.012$). The ether-concentration method showed

similar or slightly higher sensitivity than the Kato-Katz technique based on a single stool sample for all soil-transmitted helminth infections. The estimated cure rates were heavily dependent on the diagnostic technique and sampling effort. In conclusion, data on the prevalence of soil-transmitted helminth infections and the efficacy of anthelmintics are greatly influenced by the diagnostic method and sampling effort. The ether-concentration technique is a valuable alternative to the Kato-Katz method for helminth diagnosis.

DOI: 10.1007/s10096-013-2019-1 / PMID: 24272064 [PubMed - indexed for MEDLINE]

76.

J Health Popul Nutr. 2014 Sep;32(3):377-85.

Cost of illness due to typhoid Fever in pemba, zanzibar, East Africa.

Authors: Riewpaiboon A, Piatti M, Ley B, Deen J, Thriemer K, von Seidlein L, Salehjiddawi M, Busch CJ, Schmieid WH, Ali SM, The Typhoid Economic Study Group GiDeok Pak Leon R Ochiai Mahesh K Puri Na Yoon Chang Thomas F Wierzbica And John D Clemens.

The aim of this study was to estimate the economic burden of typhoid fever in Pemba, Zanzibar, East Africa. This study was an incidence-based cost-of-illness analysis from a societal perspective. It covered new episodes of blood culture-confirmed typhoid fever in patients presenting at the outpatient or inpatient departments of three district hospitals between May 2010 and December 2010. Cost of illness was the sum of direct costs and costs for productivity loss. Direct costs covered treatment, travel, and meals. Productivity costs were loss of income by patients and caregivers. The analysis included 17 episodes. The mean age of the patients, was 23 years (range=5-65, median=22). Thirty-five percent were inpatients, with a mean of 4.75 days of hospital stay (range=3-7, median=4.50). The mean cost for treatment alone during hospital care was US\$ 21.97 at 2010 prices (US\$ 1=1,430.50 Tanzanian Shilling—TSH). The average societal cost was US\$ 154.47 per typhoid episode. The major expenditure was productivity cost due to lost wages of US\$ 128.02 (83%). Our results contribute to the further economic evaluation of typhoid fever vaccination in Zanzibar and other sub-Saharan African countries.

PMCID: PMC4221443 / PMID: 25395900 [PubMed - in process]

77.

Trans R Soc Trop Med Hyg. 2014 May;108(5):297-304. doi: 10.1093/trstmh/tru037. Epub 2014 Mar 5.

Do shoes reduce hookworm infection in school-aged children on Pemba Island, Zanzibar? A pragmatic trial.

Authors: Bird C, Ame S, Albonico M, Bickle Q.

Abstract

Background: A non-blinded, cluster randomized controlled trial to test whether footwear reduces prevalence and intensity of hookworm infection in school-aged children on Pemba Island, Zanzibar.

Methods: Six schools were randomised to receive shoes and standard care (deworming with albendazole and health education) and six control schools to receive standard care only. Children provided a stool sample to assess prevalence and intensity of infection with soil transmitted helminthiases (*Ascaris lumbricoides*, *Trichuris trichiura* and hookworm). Shoes were then distributed to pupils in the intervention schools; deworming took place as part of the government's mass drug administration programme and a further round of stool samples were collected six months later.

Results: Nine hundred and fifteen children were traced at follow-up (1056 at baseline). As many children wore shoes in the control arm as the intervention arm. There was no difference in hookworm prevalence (23.4% for intervention schools, 21.3% for control schools, $p=0.48$), and no difference in mean hookworm infection in eggs/gram of stool (18, 1-36 in intervention schools, 18, 7-29 in control schools, $p=0.23$). Shoe-wearing increased across all schools, from 47.4 to 82.4%. If a child wore shoes at the end of the study, the relative risk of hookworm infection was 0.7 (CI 0.53-0.91).

Conclusions: Due to contamination, the trial could not conclude that shoes were protective against hookworm infection but the intervention led to behavioural change, and observational data suggest that shoes are protective against hookworm. This trial is registered at ClinicalTrials.gov, [NCT01869127](https://clinicaltrials.gov/ct2/show/study/NCT01869127).

78.

PLoS Negl Trop Dis. 2014 Oct 9;8(10):e3204. doi: 10.1371/journal.pntd.0003204. eCollection 2014.

Assessment of anthelmintic efficacy of mebendazole in school children in six countries where soil-transmitted helminths are endemic.

Authors: Levecke B, Montresor A, Albonico M, Ame SM, Behnke JM, Bethony JM, Nounmedem CD, Engels D, Guillard B, Kotze AC, Krolewiecki AJ, McCarthy JS, Mekonnen Z, Periago MV, Sopheak H, Tchuem-Tchuente LA, Duong TT, Huong NT, Zeynudin A, Vercruyse J.

Background: Robust reference values for fecal egg count reduction (FECR) rates of the most widely used anthelmintic drugs in preventive chemotherapy (PC) programs for controlling soil-transmitted helminths (STHs; *Ascaris lumbricoides*, *Trichuris trichiura*, and hookworm) are still lacking. However, they are urgently needed to ensure detection of reduced efficacies that are predicted to occur due to growing drug pressure. Here, using a standardized methodology, we assessed the FECR rate of a single oral dose of mebendazole (MEB; 500 mg) against STHs in six trials in school children in different locations around the world. Our results are compared with those previously obtained for similarly conducted trials of a single oral dose of albendazole (ALB; 400 mg).

Methodology: The efficacy of MEB, as assessed by FECR, was determined in six trials involving 5,830 school children in Brazil, Cambodia, Cameroon, Ethiopia, United Republic of Tanzania, and Vietnam. The efficacy of MEB was compared to that of ALB as previously assessed in 8,841 school children in India and all the above-mentioned study sites, using identical methodologies.

Principal findings: The estimated FECR rate [95% confidence interval] of MEB was highest for *A. lumbricoides* (97.6% [95.8; 99.5]), followed by hookworm (79.6% [71.0; 88.3]). For *T. trichiura*, the estimated FECR rate was 63.1% [51.6; 74.6]. Compared to MEB, ALB was significantly more efficacious against hookworm (96.2% [91.1; 100], $p < 0.001$) and only marginally, although significantly, better against *A. lumbricoides* infections (99.9% [99.0; 100], $p = 0.012$), but equally efficacious for *T. trichiura* infections (64.5% [44.4; 84.7], $p = 0.906$).

Conclusions: A minimum FECR rate of 95% for *A. lumbricoides*, 70% for hookworm, and 50% for *T. trichiura* is expected in MEB-dependent PC programs. Lower FECR results may indicate the development of potential drug resistance.

DOI: 10.1371/journal.pntd.0003204 / PMCID: PMC4191962 / PMID: 25299391 [PubMed - indexed for MEDLINE]

79.

Parasitol Int. 2014 Apr;63(2):438-41. doi: 10.1016/j.parint.2013.11.004. Epub 2013 Nov 19.

Genetic characterization of *Giardia duodenalis* by sequence analysis in humans and animals in Pemba Island, Tanzania.

Authors: Di Cristanziano V, Santoro M, Parisi F, Albonico M, Shaali MA, Di Cave D, Berrilli F.

Abstract: *Giardia duodenalis* represents one of the most widespread human enteric parasites: about 200 million people in Asia, Africa and Latin America are infected. *Giardia* exerts a deep impact on public health because of high prevalence and possible effects on growth and cognitive functions in infected children. The major aim of this study was to detect and genetically characterize *G. duodenalis* in both human and animal fecal samples collected in Pemba Island, in the archipelago of Zanzibar (Tanzania), in order to deepen the knowledge of genotypes of *Giardia* in this area. Between October 2009 and October 2010, we collected 45 human fecal samples from children from 2 primary schools and 60 animal fecal samples: 19 from zebras (*Bos primigenius indicus*) and 41 from goats (*Capra hircus*). Detection and genetic identification were performed by multilocus analysis of *ssu-rDNA* and *gdh* genes. In humans we found a higher prevalence of assemblage B (sub-assemblage BIV), in goats of assemblage E and in zebra of assemblage A. Our study represents an important contribution to the epidemiological knowledge of *G. duodenalis* in this area of Tanzania.

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80.

J Health Popul Nutr. 2014 Sep;32(3):377-85.

Cost of illness due to typhoid Fever in pemba, zanzibar, East Africa.

Authors: Riewpaiboon A, Piatti M, Ley B, Deen J, Thriemer K, von Seidlein L, Salehjiddawi M, Busch CJ, Schmiel WH, Ali SM, The Typhoid Economic Study Group GiDeok Pak Leon R Ochiai Mahesh K Puri Na Yoon Chang Thomas F Wierzbica And John D Clemens.

Abstract: The aim of this study was to estimate the economic burden of typhoid fever in Pemba, Zanzibar, East Africa. This study was an incidence-based cost-of-illness analysis from a societal perspective. It covered new episodes of blood culture-confirmed typhoid fever in patients presenting at the outpatient or inpatient departments of three district hospitals between May 2010 and December 2010. Cost of illness was the sum of direct costs and costs for productivity loss. Direct costs covered treatment, travel, and meals. Productivity costs were loss of income by patients and caregivers. The analysis included 17 episodes. The mean age of the patients, was 23 years (range=5-65, median=22). Thirty-five percent were inpatients, with a mean of 4.75 days of hospital stay (range=3-7, median=4.50). The mean cost for treatment alone during hospital care was US\$ 21.97 at 2010 prices (US\$ 1=1,430.50 Tanzanian Shilling— TSH). The average societal cost was US\$ 154.47 per typhoid episode. The major expenditure was productivity cost due to lost wages of US\$ 128.02 (83%). Our results contribute to the further economic evaluation of typhoid fever vaccination in Zanzibar and other sub-Saharan African countries.

PMID:25395900 / PMCID:PMC4221443 [PubMed - in process]

81.

Am J Trop Med Hyg. 2014 Dec;91(6):1138-41. doi: 10.4269/ajtmh.14-0253. Epub 2014 Sep 22. **Quantitative evaluation of a handheld light microscope for field diagnosis of soil-transmitted helminth infection.**

Authors: Bogoch II, Andrews JR, Speich B, Ame SM, Ali SM, Stothard JR, Uttinger J, Keiser J.

Abstract: We evaluated the Newton Nm1, a commercially available handheld light microscope and compared it with conventional light microscopy for the diagnosis of soil-transmitted helminth infections. A total of 91 Kato-Katz thick smears were examined by experienced microscopists and helminth eggs were counted and expressed as eggs per gram of stool (EPG). Mean egg counts were significantly higher with the conventional light microscope (5,190 EPG versus 2,386 EPG for *Ascaris lumbricoides*; 826 versus 456 for *Trichuris trichiura*; both $P < 0.05$). Using regression coefficients and accounting for intensity of infection, we found that the agreement between the two devices was excellent for both species ($\kappa = 0.90$, 95% confidence interval = 0.82-0.99 for *A. lumbricoides* and $\kappa = 0.96$, 95% CI = 0.91-1.00 for *T. trichiura*). The Newton Nm1 microscope may be a useful tool for the detection and quantification of soil-transmitted helminth infection in clinical, epidemiologic, and public health settings.

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PMID:25246697 / PMCID:PMC4257635 / DOI:10.4269/ajtmh.14-0253 [PubMed - indexed for MEDLINE]

82.

PLoS Negl Trop Dis. 2014 Oct 9;8(10):e3204. doi: 10.1371/journal.pntd.0003204. eCollection 2014

Assessment of anthelmintic efficacy of mebendazole in school children in six countries where soil-transmitted helminths are endemic.

Authors: Levecke B, Montresor A, Albonico M, Ame SM, Behnke JM, Bethony JM, Noumedem CD, Engels D, Guillard B, Kotze AC, Krolewiecki AJ, McCarthy JS, Mekonnen Z, Periago MV, Sopheak H, Tchuem-Tchuente LA, Duong TT, Huong NT, Zeynudin A, Vercruyse J.

Background: Robust reference values for fecal egg count reduction (FECR) rates of the most widely used anthelmintic drugs in preventive chemotherapy (PC) programs for controlling soil-transmitted helminths (STHs; *Ascaris lumbricoides*, *Trichuris trichiura*, and hookworm) are still lacking. However, they are urgently needed to ensure detection of reduced efficacies that are predicted to occur due to growing drug pressure. Here, using a standardized methodology, we assessed the FECR rate of a single oral dose of mebendazole (MEB; 500 mg) against STHs in six trials in school children in different locations around the world. Our results are compared with those previously obtained for similarly conducted trials of a single oral dose of albendazole (ALB; 400 mg).

Methodology: The efficacy of MEB, as assessed by FECR, was determined in six trials involving 5,830 school children in Brazil, Cambodia, Cameroon, Ethiopia, United Republic of Tanzania, and Vietnam. The efficacy of MEB was compared to that of ALB as previously assessed in 8,841 school children in India and all the above-mentioned study sites, using identical methodologies.

Principal findings: The estimated FECR rate [95% confidence interval] of MEB was highest for *A. lumbricoides* (97.6% [95.8; 99.5]), followed by hookworm (79.6% [71.0; 88.3]). For *T. trichiura*, the estimated FECR rate was 63.1% [51.6; 74.6]. Compared to MEB, ALB was significantly more efficacious against hookworm (96.2% [91.1; 100], $p < 0.001$) and only marginally, although significantly, better against *A. lumbricoides* infections (99.9% [99.0; 100], $p = 0.012$), but equally efficacious for *T. trichiura* infections (64.5% [44.4; 84.7], $p = 0.906$).

Conclusions: A minimum FECR rate of 95% for *A. lumbricoides*, 70% for hookworm, and 50% for *T. trichiura* is expected in MEB-dependent PC programs. Lower FECR results may indicate the development of potential drug resistance.

Trial registration: ClinicalTrials.gov [NCT01087099](#) [NCT01379326](#) [NCT01087099](#) [NCT01379326](#).

PMID:25299391 / PMCID:PMCID:4191962 / DOI:10.1371/journal.pntd.0003204 [PubMed - indexed for MEDLINE]

83.

Malar Res Treat. 2014;2014:625905. doi: 10.1155/2014/625905. Epub 2014 Jan 19.

Effect of iron/folic Acid supplementation on the outcome of malaria episodes treated with sulfadoxine-pyrimethamine.

Authors: [Sazawal S](#), [Black RE](#), [Kabole I](#), [Dutta A](#), [Dhingra U](#), [Ramsan M](#).

Abstract: Folic acid supplementation may potentially alter the efficacy of sulfadoxine-pyrimethamine (SP) treatment in children with malaria. However, there is lack of evidence from randomized controlled trials and effects of folic acid supplementation on clinical efficacy of SP therapy remain moderately understood among children. In a double masked, placebo-controlled trial among preschool children in Pemba Island (Tanzania), iron and folic acid supplementation (Fe/FA) showed an increased risk of hospitalizations and death. In the present paper, we evaluated if folic acid supplementation reduced the efficacy of malaria treatment and thereby contributed to observed adverse effects. During the study, 1648 children had confirmed malarial episodes and received either sulphadoxine-pyrimethamine (SP) treatment and iron folic acid or SP treatment and placebo. These children were evaluated for recovery and incidence of hospitalization during the next 15, 30, and 140 days. Two groups did not differ in malarial episode or hospitalization rate on subsequent 15, 30, and 140 days. Altered efficacy of SP by folic acid was not observed and did not contribute to adverse events in the previous trial. This trial is registered with Controlled-trials.com ISRCTN59549825.

PMID:24575311 / PMCID:PMCID:3915546 / DOI:10.1155/2014/625905

2015

84.

Parasit Vectors. 2015 Feb 5;8:82. doi: 10.1186/s13071-015-0702-z.

Quality control in the diagnosis of *Trichuris trichiura* and *Ascaris lumbricoides* using the Kato-Katz technique: experience from three randomised controlled trials.

Authors: [Speich B](#), [Ali SM](#), [Ame SM](#), [Albonico M](#), [Uttinger J](#), [Keiser J](#).

Background: An accurate diagnosis of soil-transmitted helminthiasis is important for individual patient management, for drug efficacy evaluation and for monitoring control programmes. The Kato-Katz technique is the most widely used method detecting soil-transmitted helminth eggs in faecal samples. However, detailed analyses of quality control, including false-positive and faecal egg count (FEC) estimates, have received little attention.

Methods: Over a 3-year period, within the frame of a series of randomised controlled trials conducted in Pemba, United Republic of Tanzania, 10% of randomly selected Kato-Katz thick smears were re-read for *Trichuris trichiura* and *Ascaris lumbricoides* eggs. In case of discordant result (i.e. positive versus negative) the slides were re-examined a third time. A result was assumed to be false-positive or false-negative if the result from the initial reading did not agree with the quality control as well as the third reading. We also evaluated the general agreement in FECs between the first and second reading, according to internal and World Health Organization (WHO) guidelines.

Results: From the 1,445 Kato-Katz thick smears subjected to quality control, 1,181 (81.7%) were positive for *T. trichiura* and 290 (20.1%) were positive for *A. lumbricoides*. During quality control, very low rates of false-positive results were observed; 0.35% (n=5) for *T. trichiura* and 0.28% (n=4) for *A. lumbricoides*. False-negative readings of Kato-Katz thick smears were obtained in 28 (1.94%) and 6 (0.42%) instances for *T. trichiura* and *A. lumbricoides*, respectively. A high frequency of discordant results in FECs was observed (i.e. 10.0-23.9% for *T. trichiura*, and 9.0-11.4% for *A. lumbricoides*).

Conclusions: Our analyses show that the rate of false-positive diagnoses of soil-transmitted helminths is low. As the probability of false-positive results increases after examination of multiple stool samples from a single individual, the potential influence of false-positive results on epidemiological studies and anthelmintic drug efficacy studies should be determined. Existing WHO guidelines for quality control might be overambitious and might have to be revised, specifically with regard to handling disagreements in FECs.

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85.

Lancet Infect Dis. 2015 Mar;15(3):277-84. doi: 10.1016/S1473-3099(14)71050-3. Epub 2015 Jan 12.

Efficacy and safety of albendazole plus ivermectin, albendazole plus mebendazole, albendazole plus oxantel pamoate, and mebendazole alone against *Trichuris trichiura* and concomitant soil-transmitted helminth infections: a four-arm, randomised controlled trial.

Authors: Speich B, Ali SM, Ame SM, Bogoch II, Alles R, Huwlyer J, Albonico M, Hattendorf J, Utzinger J, Keiser J.

Comment in Lancet Infect Dis. 2015 Mar;15(3):250-1.

Background: Existing anthelmintic drugs (eg, albendazole and mebendazole) have low efficacy against the intestinal nematode species *Trichuris trichiura* and the drug pipeline is exhausted. We aimed to investigate the strategy of combination chemotherapy with existing drugs to establish whether their efficacy could be enhanced and broadened.

Methods: In this randomised controlled trial, we compared three drug combinations and one standard drug alone in children aged 6-14 years in two schools on Pemba Island, Tanzania infected with *T trichiura* and concomitant intestinal nematodes. We assigned children, via a randomisation list with block sizes of either four or eight, to orally receive albendazole (400 mg) plus ivermectin (200 µg/kg); albendazole (400 mg) plus mebendazole (500 mg); albendazole (400 mg) plus oxantel pamoate (20 mg/kg); or mebendazole (500 mg) alone. The primary endpoints were the proportion of children cured of *T trichiura* infection and the reduction of *T trichiura* eggs in stool based on geometric means, both analysed by available case. This study is registered with ISRCTN, number ISRCTN80245406.

Findings: We randomly assigned 440 eligible children infected with *T trichiura* between Sept 2, and Oct 18, 2013, to one of the four treatment groups (110 children per group). Data for 431 children were included in the analysis for the primary endpoints. Albendazole plus oxantel pamoate (74 of 108 children cured [68·5%, 95% CI 59·6-77·4]; egg reduction 99·2%, 98·7-99·6) and albendazole plus ivermectin (30 of 109 cured [27·5%, 19·0-36·0]; egg reduction 94·5%, 91·7-96·3) were significantly more effective against *T trichiura* than mebendazole alone (nine of 107 cured [8·4%, 3·1-13·8]; egg reduction 58·5%, 45·2-70·9). Albendazole plus mebendazole had similar low efficacy (nine of 107 cured [8·4%, 3·1-13·8; egg reduction 51·6%, 35·0-65·3) to mebendazole alone. About a fifth of the children reported adverse events, which were mainly mild. Abdominal cramps and headache were the most common adverse events after treatment; abdominal cramps were reported by 13 (12·0%) children for albendazole plus ivermectin, 10 (9·3%) for albendazole plus mebendazole, 20 (18·2%) for albendazole plus oxantel pamoate, and 16 (14·5%) for mebendazole; headaches were reported by 5 (4·6%) children for albendazole plus ivermectin, 6 (5·6%) for albendazole plus mebendazole, 12 (10·9%) for albendazole plus oxantel pamoate, and 7 (6·4%) for mebendazole.

Interpretation: Our head-to-head comparison of three combination chemotherapies showed the highest efficacy for albendazole plus oxantel pamoate for the treatment of infection with *T trichiura*. Further studies should investigate the combination of albendazole plus oxantel pamoate so that it can be considered for soil-transmitted helminthiasis control programmes.

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86.

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Cessation of mass drug administration for lymphatic filariasis in Zanzibar in 2006: was transmission interrupted?

Authors: Rebollo MP, Mohammed KA, Thomas B, Ame S, Ali SM, Cano J, Escalada AG, Bockarie MJ.

Background: Lymphatic filariasis (LF) is targeted for elimination through annual mass drug administration (MDA) for 4-6 years. In 2006, Zanzibar stopped MDA against LF after five rounds of MDA revealed no microfilaraemic individuals during surveys at selected sentinel sites. We asked the question if LF transmission was truly interrupted in 2006 when MDA was stopped.

Principal findings: In line with ongoing efforts to shrink the LF map, we performed the WHO recommended transmission assessment surveys (TAS) in January 2012 to verify the absence of LF transmission on the main Zanzibar islands of Unguja and Pemba. Altogether, 3275 children were tested on both islands and 89 were found to be CFA positive; 70 in Pemba and 19 in Unguja. The distribution of schools with positive children was heterogeneous with pronounced spatial variation on both islands. Based on the calculated TAS cut-offs of 18 and 20 CFA positive children for Pemba and Unguja respectively, we demonstrated that transmission was still ongoing in Pemba where the cut-off was exceeded.

Conclusions: Our findings indicated ongoing transmission of LF on Pemba in 2012. Moreover, we presented evidence from previous studies that LF transmission was also active on Unguja shortly after stopping MDA in 2006. Based on these observations the government of Zanzibar decided to resume MDA against LF on both islands in 2013.

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87.

PLoS Negl Trop Dis. 2015 Apr 7;9(4):e0003698. doi: 10.1371/journal.pntd.0003698. eCollection 2015.

How long can stool samples be fixed for an accurate diagnosis of soil-transmitted helminth infection using Mini-FLOTAC?

Authors: Barda B, Albonico M, Ianniello D, Ame SM, Keiser J, Speich B, Rinaldi L, Cringoli G, Burioni R, Montresor A, Utzinger J.

Background: Kato-Katz is a widely used method for the diagnosis of soil-transmitted helminth infection. Fecal samples cannot be preserved, and hence, should be processed on the day of collection and examined under a microscope within 60 min of slide preparation. Mini-FLOTAC is a technique that allows examining fixed fecal samples. We assessed the performance of Mini-FLOTAC using formalin-fixed stool samples compared to Kato-Katz and determined the dynamics of prevalence and intensity estimates of soil-transmitted helminth infection over a 31-day time period.

Methodology: The study was carried out in late 2013 on Pemba Island, Tanzania. Forty-one children were enrolled and stool samples were subjected on the day of collection to a single Kato-Katz thick smear and Mini-FLOTAC examination; 12 aliquots of stool were fixed in 5% formalin and subsequently examined by Mini-FLOTAC up to 31 days after collection.

Principal findings: The combined results from Kato-Katz and Mini-FLOTAC revealed that 100% of children were positive for *Trichuris trichiura*, 85% for *Ascaris lumbricoides*, and 54% for hookworm. Kato-Katz and Mini-FLOTAC techniques found similar prevalence estimates for *A. lumbricoides* (85% versus 76%), *T. trichiura* (98% versus 100%), and hookworm (42% versus 51%). The mean eggs per gram of stool (EPG) according to Kato-Katz and Mini-FLOTAC was 12,075 and 11,679 for *A. lumbricoides*, 1,074 and 1,592 for *T. trichiura*, and 255 and 220 for hookworm, respectively. The mean EPG from day 1 to 31 of fixation was stable for *A. lumbricoides* and *T. trichiura*, but gradually declined for hookworm, starting at day 15.

Conclusions: The findings of our study suggest that for a qualitative diagnosis of soil-transmitted helminth infection, stool samples can be fixed in 5% formalin for at least 30 days. However, for an accurate quantitative diagnosis of hookworm, we suggest a limit of 15 days of preservation. Our results have direct implication for integrating soil-transmitted helminthiasis into transmission assessment surveys for lymphatic filariasis.

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PMCID: PMC4388498

PMID: 25848772 [PubMed - indexed for MEDLINE].

88.

Trans R Soc Trop Med Hyg. 2015 Apr;109(4):262-7. doi: 10.1093/trstmh/tru180. Epub 2014 Nov 16.

Soil-transmitted helminthiasis: the relationship between prevalence and classes of intensity of infection.

Authors: Montresor A, À Porta N, Albonico M, Gabrielli AF, Jankovic D, Fitzpatrick C, Vercruyssen J, Levecke B.

Abstract

Background: programs to control the morbidity of soil-transmitted helminths (STHs). To make predictions, this model needs baseline information about the proportion of infections classified as low, moderate and high intensity, for each of the three STH species. However, epidemiological data available are often limited to prevalence estimates.

Methods: We reanalyzed available data from 19 surveys in 10 countries and parameterized the relationship between prevalence of STH infections and the proportion of moderate and heavy intensity infections.

Results: The equations derived allow feeding the WHO model with estimates of the proportion of the different classes of infection intensity when only prevalence data is available.

Conclusions: The prediction capacities of the STH model using the equations developed in the present study, should be tested by comparing it with the changes on STH epidemiological data observed in control programs operating for several years.

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89.

[PLoS Negl Trop Dis](https://doi.org/10.1371/journal.pntd.0003752). 2015 May 14;9(5):e0003752. doi: 10.1371/journal.pntd.0003752.eCollection 2015.

Sensitivity and Specificity of a Urine Circulating Anodic Antigen Test for the Diagnosis of *Schistosoma haematobium* in Low Endemic Settings.

Authors: [Knopp S](#), [Corstjens PL](#), [Koukounari A](#), [Cercamondi CI](#), [Ame SM](#), [Ali SM](#), [de Dood CJ](#), [Mohammed KA](#), [Utzinger J](#), [Rollinson D](#), [van Dam GJ](#).

Methodology: A total of 1,740 urine samples were collected in 2013 from children on Pemba Island, from schools where the *S. haematobium* prevalence was <2%, 2-5%, and 5-10%, based on a single urine filtration. On the day of collection, all samples were tested for microhematuria with reagent strips and for the presence of *S. haematobium* eggs with microscopy. Eight months later, 1.5 ml of urine from each of 1,200 samples stored at -20°C were analyzed by UCP-LF CAA assay, while urine filtration slides were subjected to quality control (QCUF). In the absence of a true 'gold' standard, the diagnostic performance was calculated using latent class analyses (LCA).

Principal findings: The 'empirical' *S. haematobium* prevalence revealed by UCP-LF CAA, QCUF, and reagent strips was 14%, 5%, and 4%, respectively. LCA revealed a sensitivity of the UCP-LF CAA, QCUF, and reagent strips of 97% (95% confidence interval (CI): 91-100%), 86% (95% CI: 72-99%), and 67% (95% CI: 52-81%), respectively. Test specificities were consistently above 90%.

Conclusions: The UCP-LF CAA assay shows high sensitivity for the diagnosis of *S. haematobium* in low-endemicity settings. Empirically, it detects a considerably higher number of infections than microscopy. Hence, the UCP-LF CAA employed in combination with QCUF, is a promising tool for monitoring and surveillance of urogenital schistosomiasis in low-transmission settings targeted for elimination.

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90.

[Lancet](https://doi.org/10.1016/S0140-6736(15)61536-7). 2015 Aug 22;386(9995):739. doi: 10.1016/S0140-6736(15)61536-7.

An achievable goal: control and elimination of schistosomiasis.

Authors: [Savioli L](#), [Fenwick A](#), [Rollinson D](#), [Albonico M](#), [Ame SM](#).

DOI: [10.1016/S0140-6736\(15\)61536-7](https://doi.org/10.1016/S0140-6736(15)61536-7) / PMID: [26333971](https://pubmed.ncbi.nlm.nih.gov/26333971/) [PubMed - indexed for MEDLINE]

91.

[Parasit Vectors](https://doi.org/10.1186/s13071-015-1044-6). 2015 Aug 20;8:432. doi: 10.1186/s13071-015-1044-6.

Development of novel multiplex microsatellite polymerase chain reactions to enable high-throughput population genetic studies of *Schistosoma haematobium*.

Authors: [Webster BL](#), [Rabone M](#), [Pennance T](#), [Emery AM](#), [Allan F](#), [Gouvras A](#), [Knopp S](#), [Garba A](#), [Hamidou AA](#), [Mohammed KA](#), [Ame SM](#), [Rollinson D](#), [Webster JP](#).

Background: Human urogenital schistosomiasis caused by *Schistosoma haematobium* is widely distributed across Africa and is increasingly targeted for control and regional elimination. The development of new high-throughput, cost-effective molecular tools and approaches are needed to monitor and evaluate the impact of control programs on the parasite populations. Microsatellite loci are genetic markers that can be used to investigate how parasite populations change over time and in relation to external influences such as control interventions.

Findings: Here, 18 existing *S. haematobium* microsatellite loci were optimised to enable simultaneous amplification across two novel multiplex microsatellite PCR's, each containing nine loci. Methods were developed for the cost effective and rapid processing and microsatellite analysis of *S. haematobium* larval stages stored on Whatman-FTA cards and proved robust on miracidia and cercariae collected from Zanzibar and Niger.

Conclusions: The development of these novel and robust multiplex microsatellite assays, in combination with an improved protocol to elute gDNA from Whatman-FTA fixed schistosome larval stages, enables the high-throughput population genetic analysis of *S. haematobium*. The molecular resources and protocols described here advance the way researchers can perform multi locus-based population genetic analyses of *S. haematobium* as part of the evaluation and monitoring of schistosomiasis control programmes.

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92.

Parasit Vectors. 2015 Oct 9;8:519. doi: 10.1186/s13071-015-1134-5.

Erratum to: Development of novel multiplex microsatellite polymerase chain reactions to enable high-throughput population genetic studies of *Schistosoma haematobium*.

Authors: Webster BL, Rabone M, Pennance T, Emery AM, Allan F, Gouvras A, Knopp S, Garba A, Hamidou AA, Mohammed KA, Ame SM, Rollinson D, Webster JP.

DOI: 10.1186/s13071-015-1134-5 / PMCID: PMC4600265 / PMID: 26453014 [PubMed]

93.

PLoS Negl Trop Dis. 2015 Oct 22;9(10):e0004165. doi: 10.1371/journal.pntd.0004165. eCollection 2015.

Methodological Bias Can Lead the Cochrane Collaboration to Irrelevance in Public Health Decision-Making.

Authors: Montresor , Addiss D, Albonico M, Ali SM, Ault SK, Gabrielli AF, Garba A, Gasimov E, Gyorkos T, Jamsheed MA, Levecke B, Mbabazi P, Mupfasoni D, Savioli L, Vercruyse J, Yajima A.

DOI: 10.1371/journal.pntd.0004165 / PMCID: PMC4619606 / PMID: 26492178 [PubMed - indexed for MEDLINE]

94.

BMC Pregnancy Childbirth. 2015 Dec 28;15:354. doi: 10.1186/s12884-015-0760-4.

Trial of improved practices approach to explore the acceptability and feasibility of different modes of chlorhexidine application for neonatal cord care in Pemba, Tanzania.

Authors: Dhingra U, Sazawal S, Dhingra P, Dutta A, Ali SM, Ame SM, Deb S, Suleiman AM, Black RE.

Background: Infections are responsible for 30-40 % of 4 million neonatal deaths annually. Use of chlorhexidine (CHX), a broad-spectrum topical antiseptic with strong residual activity, for umbilical cord cleansing has been shown to reduce infections during the neonatal period. However, the challenge remains with regard to selection of best mode of CHX delivery. As a part of formative research, we undertook a qualitative study in Pemba Island as a pilot to explore the attitudes; beliefs and practices of the community and health workers related to delivery, newborn and cord care. During the second phase of formative research, we used Trials of Improved Practices (TIPs) methodology to explore the acceptance and impediments, for the three possible modes of chlorhexidine application- 100 ml bottle with cotton swab, 10 ml single use dropper bottle and 3 g single application squeeze tube containing gel, as an umbilical cord care intervention.

Methods: In this pilot study, 204 mother-newborn pairs were enrolled from hospital and community setting in Pemba, Tanzania using a randomized three period crossover design. Mothers/guardians, Trained Birth Attendants (TBA)/ medical staff and community health workers (CHWs) were requested to try three different modes of CHX application for cord cleaning. All participants were demonstrated the method of cord cleaning using all three modes of delivery; each delivery mode was used for 3 days and an interview was conducted on day 10 to collect summary of their experience. Acceptance and preference scores were calculated based on feedback from the participants.

Results: Of 204 mother-newborn pairs, 27 were lost to follow up. 177 mothers performed the intervention and applied CHX to the newborn cord for all 9 days. Mothers rated 10 ml dropper bottle (49.7 %) as most convenient in terms of ease and application. They selected 10 ml dropper bottle (44.6 %) as their first choice; gel tube (33.9 %) and 100 ml bottle (21.5 %) as their second and third choice. TBAs, medical staff and CHWs also preferred 10 ml dropper bottle (43.3 %) over 100 ml bottle (12.9 %) and gel (38.8 %).

Conclusions: Overall acceptability of CHX application for cord cleansing was high. 10 ml single use dropper bottle was given highest preference for CHX application. An understanding of the attitudes, beliefs and cultural practices in the community and selection of the most acceptable mode of CHX delivery is essential to the design and implementation of the intervention trials examining the efficacy of CHX cord care in reducing neonatal mortality and subsequent implementation in the programs.

DOI: 10.1186/s12884-015-0760-4 / PMCID: PMC4693417 / PMID: 26711437 [PubMed - indexed for MEDLINE]

95.

PLoS Negl Trop Dis. 2015 Nov 5;9(11):e0004150. doi: 10.1371/journal.pntd.0004150. eCollection 2015.

Mass Administration of Ivermectin for the Elimination of *Onchocerciasis* Significantly Reduced and Maintained Low the Prevalence of *Strongyloides stercoralis* in Esmeraldas, Ecuador.

Authors: Anselmi M, Buonfrate D, Guevara Espinoza A, Prandi R, Marquez M, Gobbo M, Montresor A, Albonico

M^c Racines Orbe M, Martin Moreira J, Bisoffi Z.

Abstract

Objectives: To evaluate the effect of ivermectin mass drug administration on strongyloidiasis and other soil transmitted helminthiasis.

Methods: We conducted a retrospective analysis of data collected in Esmeraldas (Ecuador) during surveys conducted in areas where ivermectin was annually administered to the entire population for the control of onchocerciasis. Data from 5 surveys, conducted between 1990 (before the start of the distribution of ivermectin) and 2013 (six years after the interruption of the intervention) were analyzed. The surveys also comprised areas where ivermectin was not distributed because onchocerciasis was not endemic. Different laboratory techniques were used in the different surveys (direct fecal smear, formol-ether concentration, IFAT and IVD ELISA for *Strongyloides stercoralis*).

Results: In the areas where ivermectin was distributed the strongyloidiasis prevalence fell from 6.8% in 1990 to zero in 1996 and 1999. In 2013 prevalence in children was zero with stool examination and 1.3% with serology, in adult 0.7% and 2.7%. In areas not covered by ivermectin distribution the prevalence was 23.5% and 16.1% in 1996 and 1999, respectively. In 2013 the prevalence was 0.6% with fecal exam and 9.3% with serology in children and 2.3% and 17.9% in adults. Regarding other soil transmitted helminthiasis: in areas where ivermectin was distributed the prevalence of *T. trichiura* was significantly reduced, while *A. lumbricoides* and hookworms were seemingly unaffected.

Conclusions: Periodic mass distribution of ivermectin had a significant impact on the prevalence of strongyloidiasis, less on trichuriasis and apparently no effect on ascariasis and hookworm infections.

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96.

BMC Med. 2015 Dec 8;13:291. doi: 10.1186/s12916-015-0527-9.

Improving performance of the Tariff Method for assigning causes of death to verbal autopsies.

Authors: Serina P, Riley I, Stewart A, James SL, Flaxman AD, Lozano R, Hernandez B, Mooney MD, Luning R, Black R, Ahuja R, Alam N, Alam SS, Ali SM, Atkinson C, Baqui AH, Chowdhury HR, Dandona L, Dandona R, Dantzer E, Darmstadt GL, Das V, Dhingra U, Dutta A, Fawzi W, Freeman M, Gomez S, Gouda HN, Joshi R, Kalter HD, Kumar A, Kumar V, Lucero M, Maraga S, Mehta S, Neal B, Ohno SL, Phillips D, Pierce K, Prasad R, Praveen D, Premji Z, Ramirez-Villalobos D, Rarau P, Remolador H, Romero M, Said M, Sanvictores D, Sazawal S, Streatfield PK, Tallo V, Vadhatpour A, Vano M, Murray CJ, Lopez AD.

Background: Reliable data on the distribution of causes of death (COD) in a population are fundamental to good public health practice. In the absence of comprehensive medical certification of deaths, the only feasible way to collect essential mortality data is verbal autopsy (VA). The Tariff Method was developed by the Population Health Metrics Research Consortium (PHMRC) to ascertain COD from VA information. Given its potential for improving information about COD, there is interest in refining the method. We describe the further development of the Tariff Method.

Methods: This study uses data from the PHMRC and the National Health and Medical Research Council (NHMRC) of Australia studies. Gold standard clinical diagnostic criteria for hospital deaths were specified for a target cause list. VAs were collected from families using the PHMRC verbal autopsy instrument including health care experience (HCE). The original Tariff Method (Tariff 1.0) was trained using the validated PHMRC database for which VAs had been collected for deaths with hospital records fulfilling the gold standard criteria (validated VAs). In this study, the performance of Tariff 1.0 was tested using VAs from household surveys (community VAs) collected for the PHMRC and NHMRC studies. We then corrected the model to account for the previous observed biases of the model, and Tariff 2.0 was developed. The performance of Tariff 2.0 was measured at individual and population levels using the validated PHMRC database.

Results: For median chance-corrected concordance (CCC) and mean cause-specific mortality fraction (CSMF) accuracy, and for each of three modules with and without HCE, Tariff 2.0 performs significantly better than the Tariff 1.0, especially in children and neonates. Improvement in CSMF accuracy with HCE was 2.5%, 7.4%, and 14.9% for adults, children, and neonates, respectively, and for median CCC with HCE it was 6.0%, 13.5%, and 21.2%, respectively. Similar levels of improvement are seen in analyses without HCE.

Conclusions: Tariff 2.0 addresses the main shortcomings of the application of the Tariff Method to analyze data from VAs in community settings. It provides an estimation of COD from VAs with better performance at the individual and population level than the previous version of this method, and it is publicly available for use.

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97.

J Glob Antimicrob Resist. 2015 Dec;3(4):229-236. doi: 10.1016/j.jgar.2015.08.004. Epub 2015 Oct 9.

Monitoring the efficacy of drugs for neglected tropical diseases controlled by preventive chemotherapy.

Authors: Albonico M, Levecke B, LoVerde PT, Montresor A, Prichard R, Vercruysse J, Webster JP.

Abstract

In the last decade, pharmaceutical companies, governments and global health organisations under the leadership of the World Health Organization (WHO) have pledged large-scale donations of anthelmintic drugs, including ivermectin (IVM), praziquantel (PZQ), albendazole (ALB) and mebendazole (MEB). This worldwide scale-up in drug donations calls for strong monitoring systems to detect any changes in anthelmintic drug efficacy. This review reports on the outcome of the WHO Global Working Group on Monitoring of Neglected Tropical Diseases Drug Efficacy, which consists of three subgroups: (i) soil-transmitted helminthiases (ALB and MEB); (ii) onchocerciasis and lymphatic filariasis (IVM); and (iii) schistosomiasis (PZQ). Progress of ongoing work, challenges and research needs for each of the four main drugs used in helminthic preventive chemotherapy (PC) are reported, laying the ground for appropriate implementation of drug efficacy monitoring programmes under the co-ordination and guidelines of the WHO. Best practices for monitoring drug efficacy should be made available and capacity built as an integral part of neglected tropical disease (NTD) programme monitoring. Development of a disease-specific model to predict the impact of PC programmes, to detect outliers and to solicit responses is essential. Research studies on genetic polymorphisms in relation to low-efficacy phenotypes should be carried out to identify markers of putative resistance against all NTD drugs and ultimately to develop diagnostic assays. Development of combination and co-administration of NTD drugs as well as of new drug entities to boost the armamentarium of the few drugs available for NTD control and elimination should be pursued in parallel.

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98.

BMC Public Health. 2016 Jan 14;16:36. doi: 10.1186/s12889-016-2710-0.

Sociocultural determinants of anticipated oral cholera vaccine acceptance in three African settings: a meta-analytic approach.

Authors: Sundaram N, Schaetti C, Merten S, Schindler C, Ali SM, Nyambedha EO, Lapika B, Chaignat CL, Hutubessy R, Weiss MG.

Abstract

Background: Controlling cholera remains a significant challenge in Sub-Saharan Africa. In areas where access to safe water and sanitation are limited, oral cholera vaccine (OCV) can save lives. Establishment of a global stockpile for OCV reflects increasing priority for use of cholera vaccines in endemic settings. Community acceptance of vaccines, however, is critical and sociocultural features of acceptance require attention for effective implementation. This study identifies and compares sociocultural determinants of anticipated OCV acceptance across populations in Southeastern Democratic Republic of Congo, Western Kenya and Zanzibar.

Methods: Cross-sectional studies were conducted using similar but locally-adapted semistructured interviews among 1095 respondents in three African settings. Logistic regression models identified sociocultural determinants of OCV acceptance from these studies in endemic areas of Southeastern Democratic Republic of Congo (SE-DRC), Western Kenya (W-Kenya) and Zanzibar. Meta-analytic techniques highlighted common and distinctive determinants in the three settings.

Results: Anticipated OCV acceptance was high in all settings. More than 93% of community respondents overall indicated interest in a no-cost vaccine. Higher anticipated acceptance was observed in areas with less access to public health facilities. In all settings awareness of cholera prevention methods (safe food consumption and garbage disposal) and relating ingestion to cholera causation were associated with greater acceptance. Higher age, larger households, lack of education, social vulnerability and knowledge of oral rehydration solution for self-treatment were negatively associated with anticipated OCV acceptance. Setting-specific determinants of acceptance included reporting a reliable income (W-Kenya and Zanzibar, not SE-DRC). In SE-DRC, intention to purchase an OCV appeared unrelated to ability to pay. Rural residents were less likely than urban counterparts to accept an OCV in W-Kenya, but more likely in Zanzibar. Prayer as a form of self-treatment was associated with vaccine acceptance in SE-DRC and W-Kenya, but not in Zanzibar.

Conclusions: These cholera-endemic African communities are especially interested in no-cost OCVs. Health education and attention to local social and cultural features of cholera and vaccines would likely increase vaccine coverage. High demand and absence of insurmountable sociocultural barriers to vaccination with OCVs indicate potential for mass vaccination in planning for comprehensive control or elimination.

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99.

Lancet Infect Dis. 2016 Jan;16(1):53-60. doi: 10.1016/S1473-3099(15)00271-6. Epub 2015 Sep 18.

Efficacy and safety of oxantel pamoate in school-aged children infected with *Trichuris trichiura* on Pemba Island, Tanzania: a parallel, randomised, controlled, dose-ranging study.

Authors: Moser W, Ali SM, Ame SM, Speich B, Puchkov M, Huwylar J, Albonico M, Hattendorf J, Keiser J.

Background: Commonly used drugs for preventive chemotherapy against soil-transmitted helminths (ie, albendazole and mebendazole) show low efficacy against *Trichuris trichiura*. Recent studies with oxantel pamoate revealed good cure rates and high egg-reduction rates against *T trichiura*. We aimed to assess the nature of the dose-response relation to determine the optimum dose.

Methods: We did a parallel, randomised, placebo-controlled, single-blind trial with oxantel pamoate in school-aged children (aged 6-14 years) infected with *T trichiura* on Pemba Island, Tanzania. Children were asked to provide two stool samples and children positive for *T trichiura* were eligible to participate in the trial. Children were excluded if they suffered from any systematic illness. Children were randomly assigned to six different oxantel pamoate doses (5-30 mg/kg) or a placebo. Randomisation was stratified by baseline infection intensity using random block sizes of seven and 14. The primary endpoints were cure rates and egg-reduction rates against *T trichiura*, both analysed by available case. Drug safety was assessed 2 h and 24 h after treatment. The trial is registered at www.isrctn.com, number ISRCTN86603231.

Findings: Between Oct 14, and Nov 28, 2014, we enrolled 480 participants and randomly assigned 350 children to the different oxantel pamoate doses or the placebo. 5 mg/kg oxantel pamoate was the minimum effective dose (10 of 46 children cured [cure rate 22%, 95% CI 11-36]; egg-reduction rate 85·0%, 64·5-92·9). An increased probability of being cured and reduced egg counts with escalating doses was recorded. At 25 mg/kg oxantel pamoate 27 of 45 children were cured (cure rate 60%, 95% CI 44-65) with an egg-reduction rate of 97·5% (94·4-98·9), and at 30 mg/kg 27 of 46 children were cured (59%, 43-73) with an egg-reduction rate of 98·8% (96·8-99·6). Oxantel pamoate was well tolerated across all treatment groups; only mild adverse events were reported by the participants 2 h (27 [10%]) and 24 h (12 [4%]) after treatment.

Interpretation: Our dose-finding study revealed an excellent tolerability profile of oxantel pamoate in children infected with *T trichiura*. An optimum therapeutic dose range of 15-30 mg/kg oxantel pamoate was defined. With a weight independent dose of 500 mg oxantel pamoate 95% of children aged 7-14 years in sub-Saharan Africa would receive doses of 11·7-32·0 mg/kg. Future research should include studies with oxantel pamoate in younger children and on different continents with the ultimate goal to be able to add oxantel pamoate to soil-transmitted helminth control programmes.

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100.

Parasit Vectors. 2016 Jan 4;9:5. doi: 10.1186/s13071-015-1244-0.

Praziquantel coverage in schools and communities targeted for the elimination of urogenital schistosomiasis in Zanzibar: a cross-sectional survey.

Authors: Knopp S, Person B, Ame SM, Ali SM, Muhsin J, Juma S, Khamis IS, Rabone M, Blair L, Fenwick A, Mohammed KA, Rollinson D.

Background: Biannual mass drug administration (MDA) with praziquantel and additional interventions to eliminate urogenital schistosomiasis has been implemented on the Zanzibar islands, United Republic of Tanzania, since 2012. We aimed to assess the coverage of school-based treatment (SBT) and community-wide treatment (CWT), to validate the coverage reported by the Zanzibar Ministry of Health (MoH) and to identify reasons for non-compliance.

Methods: We conducted a post-MDA cross-sectional survey in 93 schools and 92 communities on Pemba and Unguja islands in early 2014, 3-5 months after the last MDA round. Pupils and adults were asked whether they had received and taken the praziquantel treatment provided in the last SBT or CWT, respectively, and the

observed and reported coverage were compared. Reasons for non-compliance were recorded in a pretested questionnaire and assessed in qualitative interviews. Urine samples of participants were examined for *Schistosoma haematobium* eggs with a single urine filtration.

Results: Around 8000 pupils and 4000 adults were included in the analysis. Our survey revealed a SBT coverage of 85.2% in Pemba and of 86.9% in Unguja, which was in line with MoH reports from Pemba (84.3%) and higher than reports from Unguja (63.9%). However, 15 among the 48 schools surveyed in Unguja had not received SBT. Among the interviewed adults, 53.6% in Pemba and 64.9% in Unguja had received praziquantel during CWT, which was less than the 59.0% and 67.7%, respectively, indicated by MoH reports. Moreover, only 43.8% and 54.0% of adults in Pemba and Unguja, respectively, had taken all the tablets as recommended. The main reasons for not receiving or taking praziquantel were absence during CWT, no drug distributor coming, being busy, fear of adverse events, pregnancy, breastfeeding or feeling healthy.

Conclusion: To increase coverage and compliance in Zanzibar, SBT should target all schools and mobilization, sensitization and implementation of the CWT need to be improved. To reach elimination of urogenital schistosomiasis transmission in Zanzibar and elsewhere, a very high treatment coverage and compliance at national and local level is key and additional control measures such as snail control and behaviour change interventions will need to be implemented area wide.

TRIAL REGISTRATION: ISRCTN48837681.

DOI: 10.1186/s13071-015-1244-0 / PMCID: PMC4700672 / PMID: 26727915 [PubMed - in process]

101.

BMC Public Health. 2016 Jan 14;16:36. doi: 10.1186/s12889-016-2710-0.

Sociocultural determinants of anticipated oral cholera vaccine acceptance in three African settings: a meta-analytic approach.

Authors: Sundaram N, Schaetti C, Merten S, Schindler C, Ali SM, Nyambedha EO, Lapika B, Chaignat CL, Hutubessy R, Weiss MG.

Background: Controlling cholera remains a significant challenge in Sub-Saharan Africa. In areas where access to safe water and sanitation are limited, oral cholera vaccine (OCV) can save lives. Establishment of a global stockpile for OCV reflects increasing priority for use of cholera vaccines in endemic settings. Community acceptance of vaccines, however, is critical and sociocultural features of acceptance require attention for effective implementation. This study identifies and compares sociocultural determinants of anticipated OCV acceptance across populations in Southeastern Democratic Republic of Congo, Western Kenya and Zanzibar.

Methods: Cross-sectional studies were conducted using similar but locally-adapted semistructured interviews among 1095 respondents in three African settings. Logistic regression models identified sociocultural determinants of OCV acceptance from these studies in endemic areas of Southeastern Democratic Republic of Congo (SE-DRC), Western Kenya (W-Kenya) and Zanzibar. Meta-analytic techniques highlighted common and distinctive determinants in the three settings.

Results: Anticipated OCV acceptance was high in all settings. More than 93% of community respondents overall indicated interest in a no-cost vaccine. Higher anticipated acceptance was observed in areas with less access to public health facilities. In all settings awareness of cholera prevention methods (safe food consumption and garbage disposal) and relating ingestion to cholera causation were associated with greater acceptance. Higher age, larger households, lack of education, social vulnerability and knowledge of oral rehydration solution for self-treatment were negatively associated with anticipated OCV acceptance. Setting-specific determinants of acceptance included reporting a reliable income (W-Kenya and Zanzibar, not SE-DRC). In SE-DRC, intention to purchase an OCV appeared unrelated to ability to pay. Rural residents were less likely than urban counterparts to accept an OCV in W-Kenya, but more likely in Zanzibar. Prayer as a form of self-treatment was associated with vaccine acceptance in SE-DRC and W-Kenya, but not in Zanzibar.

Conclusions: These cholera-endemic African communities are especially interested in no-cost OCVs. Health education and attention to local social and cultural features of cholera and vaccines would likely increase vaccine coverage. High demand and absence of insurmountable sociocultural barriers to vaccination with OCVs indicate potential for mass vaccination in planning for comprehensive control or elimination.

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102.

Parasit Vectors. 2016 Mar 2;9:123. doi: 10.1186/s13071-016-1406-8.

Efficacy and reinfection with soil-transmitted helminths 18-weeks post-treatment with albendazole-ivermectin, albendazole-mebendazole, albendazole-oxantel pamoate and mebendazole.

Authors: Speich B, Moser W, Ali SM, Ame SM, Albonico M, Hattendorf , Keiser J.

Background: Preventive chemotherapy with albendazole or mebendazole is the current strategy to control soil-transmitted helminth (STH) infections (i.e. *Ascaris lumbricoides*, hookworm and *Trichuris trichiura*). STH reinfections, in particular *A. lumbricoides* and *T. trichiura* occur rapidly after treatment with the standard drugs. However, their low efficacy against *T. trichiura*, made an accurate assessment of reinfection patterns impossible.

Methods: In 2013 a randomised controlled trial was conducted on Pemba Island, Tanzania. School-aged children diagnosed positive for *T. trichiura*, were randomly allocated to (i) albendazole-ivermectin; (ii) albendazole-mebendazole; (iii) albendazole-oxantel pamoate; or (iv) mebendazole. Here we report the efficacy [cure rates (CR) and egg-reduction rates (ERR)], reinfection rates and new infections determined 18 weeks post-treatment.

Results: For a total of 405 children complete baseline and follow-up data were available. Similar to the efficacy determined after 3 weeks, 18 weeks after treatment albendazole-oxantel pamoate showed a significantly higher efficacy against *T. trichiura* (CR: 54.0 %, 95 % CI: 43.7-64.0; ERR: 98.6 %, 95 % CI: 97.8-99.2) compared to the other treatment arms. Children treated with albendazole-oxantel pamoate or albendazole-ivermectin had fewer moderate infections compared to children treated with albendazole. The reinfection rates 18 weeks post-treatment among all treatment arms were 37.2 % for *T. trichiura* (95 % CI: 28.3-46.8), 34.6 % for *A. lumbricoides* (95 % CI: 27.3-42.3) and 25.0 % for hookworms (95 % CI: 15.5-36.6).

Conclusions: The moderate reinfection rates with STHs 18 weeks post-treatment support the concept of regular anthelmintic treatment in highly endemic settings. Combination chemotherapy might achieve decreased morbidity in children since in the albendazole plus oxantel pamoate and albendazole plus ivermectin treatment arms only few moderate *T. trichiura* infections remained. Further trials should investigate the long term efficacy of albendazole-oxantel pamoate (i.e. 6 and 12 month post-treatment) and after several rounds of treatment in order to develop recommendations for appropriate control approaches for STH infections.

DOI: 10.1186/s13071-016-1406-8 / PMCID: PMC4776366 / PMID: 26935065 [PubMed - in process]

103.

PLoS Negl Trop Dis. 2016 Jul 11;10(7):e0004814. doi: 10.1371/journal.pntd.0004814. eCollection 2016.

Community Knowledge, Perceptions, and Practices Associated with Urogenital Schistosomiasis among School-Aged Children in Zanzibar, United Republic of Tanzania.

Authors: Person B, Ali SM, A'Kadir FM, Ali JN, Mohammed UA, Mohammed KA, Rollinson D, Knopp S

Background: On the Zanzibar islands, United Republic of Tanzania, elimination of urogenital schistosomiasis is strived for in the coming years. This qualitative study aimed to better understand community knowledge, perceptions, and practices associated with schistosomiasis among school-aged children on Unguja and Pemba islands, in order to inform the development of behavior change interventions contributing to eliminate urogenital schistosomiasis.

Methodology: In 2011, we conducted 35 children's discussion groups, 41 in-depth interviews with parents and teachers, and 5 focus group discussions with community members in Zanzibar. Using a modified-grounded theory approach, we transcribed and coded the narrative data followed by thematic analysis of the emergent themes.

Principal findings: Urogenital schistosomiasis is a common experience among children in Zanzibar and typically considered a boys' disease. Children engage in multiple high-risk behaviors for acquiring schistosomiasis because of poor knowledge on disease transmission, lack of understanding on severity of disease-associated consequences, and lack of alternative options for water related activities of daily living and recreational play. Local primary school teachers had little to no training about the disease and no teaching tools or materials for students.

Conclusions: Conducting activities in open natural freshwater contaminated by *S. haematobium* larvae compromises the health of school-aged children in Zanzibar. The perception of urogenital schistosomiasis as a minor illness rather than a serious threat to a child's well-being contributes to the spread of disease. Understanding community perceptions of disease along with the barriers and facilitators to risk reduction behaviors among children can inform health promotion activities, campaigns, and programs for the prevention, control, and elimination of urogenital schistosomiasis in Zanzibar.

DOI: 10.1371/journal.pntd.0004814 / PMCID: PMC4939940 / PMID: 27399310 [PubMed - in process]

104.

J Biosoc Sci. 2016 Sep;48 Suppl 1:S56-73. doi: 10.1017/S0021932016000067.

Community co-designed schistosomiasis control interventions for school-aged children in Zanzibar.

Authors: Person B, Knopp S, Ali SM, A'kadir FM, Khamis AN, Ali JN, Lymo JH, Mohammed KA, Rollinson D.

Abstract: Top-down biomedical interventions to control schistosomiasis in sub-Saharan Africa have had limited success, primarily because they fail to engage with the social, political, economic and ecological contexts in which they are delivered. Despite the call to foster community engagement and to adapt interventions to local circumstances, programmes have rarely embraced such an approach. This article outlines a community co-designed process, based upon Human-Centered Design, to demonstrate how this approach works in practice. It is based on initial work undertaken by social science researchers, public health practitioners and community members from the Zanzibar Islands, Tanzania, between November 2011 and December 2013. During the process, 32 community members participated in a qualitative and quantitative data-driven workshop where they interpreted data on local infections from *S. haematobium* and co-designed interventions with the assistance of a facilitator trained in the social sciences. These interventions included the implementation of novel school-based education and training, the identification of relevant safe play activities and events at local schools, the installation of community-designed urinals for boys and girls and the installation of community-designed laundry-washing platforms to reduce exposure to cercariae-contaminated fresh water. It is suggested that the a community co-designed process, drawing from Human-Centered Design principles and techniques, enables the development of more sustainable and effective interventions for the control of schistosomiasis.

DOI: 10.1017/S0021932016000067 / PMID: 27428066 [PubMed - in process]

105.

Acta Trop. 2016 Nov;163:142-8. doi: 10.1016/j.actatropica.2016.08.004. Epub 2016 Aug 3.

Increasing the reach: Involving local Muslim religious teachers in a behavioral intervention to eliminate urogenital schistosomiasis in Zanzibar.

Authors: Celone M, Person B, Ali SM, Lymo JH, Mohammed UA, Khamis AN, Mohammed YS, Mohammed KA, Rollinson D, Knopp S.

Abstract: In Zanzibar, United Republic of Tanzania, Madrassa schools are influential institutions, where children and adults can learn about the interpretation of the Koran. We aimed to explore the involvement of Madrassa teachers for behavior change interventions in a randomized operational research trial designed to investigate the impact of multiple approaches to eliminate urogenital schistosomiasis transmission from Zanzibar. Madrassa teachers performing in the 30 communities of the behavior change study arm were trained in new interactive and participatory teaching methods by the local behavioral team and provided with schistosomiasis-teaching tools for teaching about transmission and prevention in their Madrassa. In July 2014, in a qualitative research study, we conducted 25 semi-structured interviews with Madrassa teachers to find out how they perceived their involvement in interventions against schistosomiasis. In 2014, 5926 among the 8497 registered Madrassa students in 30 communities on Unguja and Pemba islands received health education and participated in interactive behavior change exercises about schistosomiasis. Madrassa teachers reported that they valued their inclusion in the study and the opportunity to educate their students about schistosomiasis transmission, prevention, and treatment. They also perceived personal and community benefits as a result of their training and strongly supported the inclusion of additional Madrassa teachers in future intervention activities. Madrassa teachers are influential in the Zanzibari society, and hence are important change agents within our community-level behavioral intervention. They might constitute an untapped resource that can help to expand and increase acceptance of and participation in schistosomiasis and other neglected tropical disease control activities in African Muslim communities.

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DOI: 10.1016/j.actatropica.2016.08.004 / PMCID: PMC5019290 [Available on 2016-11-01] / PMID: 27498244 [PubMed - in process]

106.

J Biosoc Sci. 2016 Sep;48 Suppl 1:S56-73. doi: 10.1017/S0021932016000067.

Community co-designed schistosomiasis control interventions for school-aged children in Zanzibar.

Authors: Person B1, Knopp S2, Ali SM3, A'kadir FM4, Khamis AN4, Ali JN4, Lymo JH4, Mohammed KA4, Rollinson D2.

Abstract: Top-down biomedical interventions to control schistosomiasis in sub-Saharan Africa have had limited success, primarily because they fail to engage with the social, political, economic and ecological contexts in which they are delivered. Despite the call to foster community engagement and to adapt interventions to local circumstances, programmes have rarely embraced such an approach. This article outlines a community co-designed process, based upon Human-Centered Design, to demonstrate how this approach works in practice. It is based on initial work undertaken by social science researchers, public health practitioners and community

members from the Zanzibar Islands, Tanzania, between November 2011 and December 2013. During the process, 32 community members participated in a qualitative and quantitative data-driven workshop where they interpreted data on local infections from *S. haematobium* and co-designed interventions with the assistance of a facilitator trained in the social sciences. These interventions included the implementation of novel school-based education and training, the identification of relevant safe play activities and events at local schools, the installation of community-designed urinals for boys and girls and the installation of community-designed laundry-washing platforms to reduce exposure to cercariae-contaminated fresh water. It is suggested that the a community co-designed process, drawing from Human-Centered Design principles and techniques, enables the development of more sustainable and effective interventions for the control of schistosomiasis.

PMID:27428066 / DOI:[10.1017/S0021932016000067](https://doi.org/10.1017/S0021932016000067) [PubMed - in process]

107.

Ophthalmic Epidemiol. 2016 Dec;23(6):412-417. Epub 2016 Oct 24.

Baseline Trachoma Surveys in Kaskazini A and Micheweni Districts of Zanzibar: Results of Two Population-Based Prevalence Surveys Conducted with the Global Trachoma Mapping Project.

Authors: [Omar FJ](#), [Kabona G](#), [Abdalla KM](#), [Mohamed SJ](#), [Ali SM](#), [Ame SM](#), [Ngwalle A](#), [Mbise C](#), [Rotondo L](#), [Willis R](#), [Flueckiger RM](#), [Massae PA](#), [Bakhtiari A](#), [Solomon AW](#), [Ngondi JM](#).

Purpose: Based on health care records and trachoma rapid assessments, trachoma was suspected to be endemic in Kaskazini A and Micheweni districts of Zanzibar. This study aimed to investigate the prevalence of trachomatous inflammation-follicular (TF), and trachomatous trichiasis (TT) in each of those districts.

Methods: The survey was undertaken in Kaskazini A and Micheweni districts on Unguja and Pemba Islands, respectively. A multi-stage cluster random sampling design was applied, whereby 25 census enumeration areas (clusters) and 30 households per cluster were included. Consenting eligible participants (children aged 1-9 years and people aged 15 years and older) were examined for trachoma using the World Health Organization simplified grading system.

Results: A total of 1673 households were surveyed and 6407 participants (98.0% of those enumerated) were examined for trachoma. Examinees included a total of 2825 children aged 1-9 years and 3582 people aged 15 years and older. TF prevalence in 1-9-year-olds was 2.7% (95% confidence interval, CI, 2.7-4.1%) in Kaskazini A and 11.4% (95% CI 6.6-16.5%) in Micheweni. Among people aged 15 years and older, TT prevalence was 0.01% (95% CI 0.00-0.04%) in Kaskazini A and 0.21% (95% CI 0.08-0.39%) in Micheweni.

Conclusion: Trachoma is a public health problem in Micheweni district, where implementation of all four components of the SAFE strategy (surgery, antibiotics, facial cleanliness, and environmental improvement), including mass drug administration with azithromycin, is required. These findings will facilitate planning for trachoma elimination.

PMID:27775454 / DOI:[10.1080/09286586.2016.1235206](https://doi.org/10.1080/09286586.2016.1235206)[PubMed - in process]

108.

Lancet Glob Health. 2016 Nov;4(11):e837-e844. doi: [10.1016/S2214-109X\(16\)30223-6](https://doi.org/10.1016/S2214-109X(16)30223-6). Epub 2016 Sep 29.

Efficacy of chlorhexidine application to umbilical cord on neonatal mortality in Pemba, Tanzania: a community-based randomised controlled trial.

Authors: [Sazawal S](#), [Dhingra U](#), [Ali SM](#), [Dutta A](#), [Deb S](#), [Ame SM](#), [Mkasha MH](#), [Yadav A](#), [Black RE](#).

Background In low-income countries, including the east African region, a third of neonatal deaths are due to infections. A substantial proportion of these have been attributed to sepsis, which can result from umbilical cord infections. Evidence from Asia suggests that chlorhexidine application to the neonatal umbilical cord reduces mortality, but no data from Africa are available. We aimed to assess the effect of umbilical cord cleansing with 4% chlorhexidine solution on neonatal mortality and omphalitis in rural settings of sub-Saharan Africa.

Methods We did a community-based randomised controlled trial on Pemba Island, Zanzibar, Tanzania. All eligible babies (aged 1 h to 48 h, without congenital malformations) from hospital-based and community-based deliveries on Pemba Island were enrolled. Participants were randomly assigned to either 4% free chlorhexidine for cord care or to dry cord care using a computer-generated random sequence. For babies allocated to the chlorhexidine group, mothers or caretakers were advised to apply the solution to the cord every day until 3 days after the cord had dropped off. Cord stumps were examined for redness, pus, swelling, and foul odour on day 0, 1, 4, 10, and 28. The primary outcome for this study was mortality until day 28 on an intention-to-treat basis. The trial is registered with ClinicalTrials.gov, number [NCT01528852](https://clinicaltrials.gov/ct2/show/study/NCT01528852).

Findings Between May 19, 2011, and Aug 31, 2014, 36 911 newborn babies were enrolled into the chlorhexidine (n=18 015) and dry cord care study (n=18 896) groups. 17 468 (96·9%) of 18 015 neonates

in the chlorhexidine group were available for complete follow-up (28 days) compared with 18 384 (97.3%) of 18 896 neonates in the dry cord care group. Mortality rate in the chlorhexidine group (10.5 deaths per 1000 livebirths) was not significantly lower than that in the dry cord care group (11.7 per 1000 livebirths; relative risk 0.90, 0.74-1.09; $p=0.27$).

Interpretation Our findings do not support the use of chlorhexidine for reduction of neonatal mortality in this east African setting, which might not justify a change in the WHO policy. To inform global policy, a detailed meta-analysis and pooled analysis needs to be undertaken using data from both African and Asian settings.

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109.

Neonatal mortality within 24 hours of birth in six low- and lower-middle-income countries.

Authors: [Baqui AH](#), [Mitra DK](#), [Begum N](#), [Hurt L](#), [Soremekun S](#), [Edmond K](#), [Kirkwood B](#), [Bhandari N](#), [Taneja S](#), [Mazumder S](#), [Nisar MI](#), [Jehan F](#), [Ilyas M](#), [Ali M](#), [Ahmed I](#), [Ariff S](#), [Soofi SB](#), [Sazawal S](#), [Dhingra U](#), [Dutta A](#), [Ali SM](#), [Ame SM](#), [Semrau K](#), [Hamomba FM](#), [Grogan C](#), [Hamer DH](#), [Bahl R](#), [Yoshida S](#), [Manu A](#).

Objective: To estimate neonatal mortality, particularly within 24 hours of birth, in six low- and lower-middle-income countries.

Methods: We analysed epidemiological data on a total of 149 570 live births collected between 2007 and 2013 in six prospective randomized trials and a cohort study from predominantly rural areas of Bangladesh, Ghana, India, Pakistan, the United Republic of Tanzania and Zambia. The neonatal mortality rate and mortality within 24 hours of birth were estimated for all countries and mortality within 6 hours was estimated for four countries with available data. The findings were compared with published model-based estimates of neonatal mortality.

Findings: Overall, the neonatal mortality rate observed at study sites in the six countries was 30.5 per 1000 live births (range: 13.6 in Zambia to 47.4 in Pakistan). Mortality within 24 hours was 14.1 per 1000 live births overall (range: 5.1 in Zambia to 20.1 in India) and 46.3% of all neonatal deaths occurred within 24 hours (range: 36.2% in Pakistan to 65.5% in the United Republic of Tanzania). Mortality in the first 6 hours was 8.3 per 1000 live births, i.e. 31.9% of neonatal mortality.

Conclusions: Neonatal mortality within 24 hours of birth in predominantly rural areas of six low- and lower-middle-income countries was higher than model-based estimates for these countries. A little under half of all neonatal deaths occurred within 24 hours of birth and around one third occurred within 6 hours. Implementation of high-quality, effective obstetric and early newborn care should be a priority in these settings.

2017

110.

[Trans R Soc Trop Med Hyg](#). 2017 Jan 18. doi: 10.1093/trstmh/trw078. [Epub ahead of print]

The molecular speciation of soil-transmitted helminth eggs collected from school children across six endemic countries.

Authors: [George S](#), [Geldhof P](#), [Albonico M](#), [Ame SM](#), [Bethony JM](#), [Engels D](#), [Mekonnen Z](#), [Montresor A](#), [Hem S](#), [Tchuem-Tchuente LA](#), [Huong NT](#), [Kang G](#), [Vercruysse J](#), [Levecke B](#).

Abstract

Background: The diagnosis of soil-transmitted helminths (STHs; *Ascaris*, *Trichuris* and hookworms) is traditionally based on the demonstration of eggs in stool using microscopic techniques. While molecular techniques are more appropriate to speciate STH species they are seldom applied. In this study we speciated STH eggs from stool using molecular techniques to gain insights into the distribution of both human and animal STH species in the human host.

Methods: We speciated 207 STH egg isolates from stool collected during the baseline survey of six drug efficacy trials conducted in Brazil, Cambodia, Cameroon, Ethiopia, Tanzania and Vietnam applying a PCR - restriction fragment length polymorphisms based approach.

Results: DNA of *Ascaris* was detected in 71 (34.3%) samples, of which all were identified as the human roundworm *Ascaris lumbricoides*. In 87 (42.0%) samples, DNA of *Trichuris* spp. was found and further speciation demonstrated the presence of the human *Trichuris trichiura* (100%) and the canine *Trichuris vulpis* ($n=7$; 8.0%;

in Cameroon only). Hookworms were identified in 104 (50.2%) samples, with *Necator americanus* (n=73; 70.2%) being the predominant species followed by *Ancylostoma duodenale* (n=40; 38.5%).

Conclusions: Our study indicates that STH infections in humans are predominantly caused by human STH species. They also suggest that zoonotic transmission occurs on a local scale.

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Siglarlo/ Abbreviations

Acta Trop. : *Acta Tropica*

Adv Parasitol. : *Advances in Parasitology*

Am J Clin Nutr.: *American journal of Clinical Nutrition*

Ann Ig.: *Annali di igiene: Medicina preventiva e di comunità*

Ann Ist Super Sanita. : *Annali dell'istituto superiore di sanità*

Ann Trop Med Parasitol.: *Annals of tropical Medicine and Parasitology*

BMC Infect Dis: *British medical Journal Infectious Diseases*

BMC Pregnancy Childbirth.: *British medical Journal Pregnancy Childbirth*

BMC Public Health : *British medical Journal Public Health*

BMC Res Notes : *British medical Journal Research Notes*

BMJ.: *British Medical Journal*

Bull World Health Organ.: *Bulletin of the World Health Organization*

Early Hum Dev: *Early Human Development Journal*

East Afr Med J: *East African Medical Journal*

Eur J Clin Microbiol Infect Dis.: *European journal of Clinical Microbiology and Infectious Diseases*

Field phase Report

Hum Vaccin Immunother.: *Human vaccines and Immunotherapeutics Journal*

Int J Epidemiol.: *International Journal of Epidemiology*

Int J Parasitol Drugs Drug Resist.: *International Journal of Epidemiology Drugs and Drug Resistance*

Int J Parasitol.: *International Journal for Parasitology*

FIGO: *International Federation of Gynecology and Obstetrics*

J Biosoc Sci.: *Journal of Biosocial Science*

J Clin Microbiol.: *Journal of Clinical Microbiology*

J Health Popul Nutr.: *Journal of Health, Population and Nutrition*

J Helminthol.: *London School of Hygiene and Tropical Medicine*

J Nutr.: *Journal of Nutrition*

Lancet Infect Dis.: *the Lancet Infectious Diseases*

Lancet.: *the Lancet*

Malar Res Treat.: *Malaria research and treatment*

Matern Child Nutr.: *Maternal & child nutrition*

Mol Biochem Parasitol.: *Molecular and Biochemical Parasitology*

N Engl J Med.: *New England Journal of Medicine*

Ophthalmic Epidemiol.: *Ophthalmic Epidemiology*

Parasit Vectors.: *parasites and Vectors*

Parasitol Int. : *Parasitology International Journal*

PLoS Negl Trop Dis.: *PLOS Neglected Tropical Diseases*

PLoS One.

Trans R Soc Trop Med Hyg.: *Transactions of The Royal Society of Tropical Medicine and Hygiene*

Trop Doct.: *Tropical Doctor*

Trop Med Int Health. : *Tropical Medicine and International Health*