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RANDOMIZED PLACEBO-CONTROLLED TRIAL OF THE EFFICACY OF MEBENDAZOLE POLYMORPHS IN THE TREATMENT OF HOOKWORM INFECTIONS

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Mebendazole has three polymorphic forms, identified as A, B and C. **It has been suggested that unlike polymorph C, A is ineffective in the treatment of hookworm and whipworm infections. A randomized double-**blind, placebo-controlled trial was carried out to compare the efficacy **of single dose 500 mg tablets of pure mebendazole Polymorph C with those containing a 1:1 mixture of Polymorphs A and C, for the treatment of hookworm infections. All eligible individuals living in 219 households were recruited after obtaining written, informed consent. A single fecal sample was obtained and examined the same day, using the Kato-Katz technique for intestinal nematode infections. Those who were found infected with hookworms were randomized to one of three treatment arms and requested to provide a second faecal sample 10 - 14 days after** treatment. This was examined in the same manner as the first. A total **of 892 individuals were recruited; 601 provided fecal samples; 214 were found positive for hookworm; 70, 74 and 70 individuals were randomized to treatment arms A (mixture of polymorphs A and C), B (pure polymorph C) and C (placebo) respectively. Follow-up samples were provided by 53, 48 and 49 persons respectively in each treatment arm. The cure rates in the three treatment arms were 28.3%, 18.8% and 16.3% respectively;** they were not significantly different from one another. Comparison **of fecal egg count reductions (FECR) in the 3 treatment arms (86.1%, 84.5% and -6.6% in Arms A, B and C respectively) showed that both** mebendazole formulations performed significantly better than placebo, but there was no statistically significant difference between FECR with **the two drug formulations. It is concluded that a single 500mg dose of mebendazole, either as Polymorph C alone, or as a mixture of Polymorphs** A and C, has little efficacy in curing hookworm infections. However, both formulations were significantly better than placebo in reducing the intensity of infection, with no statistically significant difference between **the two formulations.**

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MUCOSAL IMMUNE RESPONSES DURING HELMINTH TREATMENT FOR INFLAMMATORY BOWEL DISEASES

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Helminth treatment for inflammatory bowel diseases has support **from experiments in mouse models as well as clinical studies, but the mechanism of action is unclear. Based on a longitudinal analyses of an individual who self-infected with Trichuris trichiura to treat his symptoms of ulcerative colitis, we hypothesize that enhancement of mucosal barrier function by TH2 immunity and IL-22 may improve conditions of ulcerative colitis. In this patient, as well as additional other ulcerative colitis patients,** TH22 cells (IL-22+, IL-17-) were reduced in tissues with active inflammation **and induced in tissues colonized by worms. We then conducted a trial where we treated macaques suffering from idiopathic chronic diarrhea with Trichuris trichiura, collecting biopsies before and after treatment for FACS analyses. A TH2 response was induced and 4 out of the 5 treated macaques improved their symptoms. We also found reduced bacterial** attachment to the intestinal mucosa and identified changes to the **composition of microbial communities attached to the intestinal mucosa** post treatment. These findings suggest that helminth treatment may **restore mucosal barrier functions, reducing overall bacterial attachment to the epithelium, and also altering the communities of attached bacteria. We are currently enrolling patients in a double-blinded placebo controlled trial to further investigate these mechanisms in human subjects, treated with Trichuris suis ova (TSO). The trial is designed to characterize mucosal responses to TSO treatment and to distinguish between responders and non-responders to TSO treatment.**

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THE IMPORTANCE OF CONTEXT: HOW SOCIAL AND ENVIRONMENTAL FACTORS MODIFY THE EFFECT OF HEAVY RAINFALL ON DIARRHEA INCIDENCE

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The impact of heavy rainfall on water-borne diarrheal diseases is uncertain. This may be due to important biophysical and social factors that modify its effect. We aimed to estimate the effect of heavy rainfall on diarrhea incidence in northern coastal Ecuador, evaluating whether biophysical and social factors impact vulnerability to heavy rainfall events. Active surveillance for diarrhea was conducted weekly for 39 months in 19 villages. We defined heavy rainfall as one-day rainfall in a seven-day period **exceeding the 90th percentile value within the study period. Mixed effects Poisson regression was used to test the hypothesis that prior rainfall, water** and sanitation coverage and social cohesion modified the relationship **between heavy rainfall and diarrhea incidence. We found prior rainfall** and drinking water treatment modified the relationship between heavy **rainfall and diarrhea. Heavy rainfall was associated with increased diarrhea incidence following 8-week periods of low rainfall (IRR 1.39, 95% CI 1.03, 1.87) and decreased diarrhea incidence following 8-week periods of high rainfall (IRR 0.74, 95% CI 0.59, 0.92). Drinking water treatment reduced the deleterious impacts of heavy rainfall following dry periods. When 67% percent of households reported drinking water treatment, the risk of diarrhea due to heavy rainfall was null (IRR 1.04, 95% CI 0.70, 1.54). Sanitation, hygiene and community social cohesion did not modify the relationship between heavy rainfall and diarrhea. Heavy rainfall appears to cause diarrhea through contamination of drinking water, and presents the greatest health risk following periods of low rainfall. Interventions to increase drinking water treatment may reduce climate vulnerability.**

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MICROBIAL SOURCE TRACKING IN RURAL INDIA: UNDERSTANDING HUMAN AND ANIMAL CONTRIBUTIONS TO FECAL CONTAMINATION OF IMPROVED AND UNIMPROVED COMMUNITY WATER SOURCES, STORED DRINKING WATER AND HANDS

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To reduce the global diarrhea disease burden, the Millennium Development Goal (MDG) 7c aims to increase access to safe drinking water and basic sanitation. The MDG definition of improved drinking water, however, does **not include assessment of microbial safety. Several studies in low-income countries have shown improved drinking water sources are contaminated with feces, and household stored drinking water can have higher levels of fecal contamination than source water due to contact with dirty hands.** Identification of fecal pollution sources is necessary to better assess health **risks and protect drinking water from high risk sources, especially in areas like rural India where animal and open human defecation occur together. Microbial source tracking (MST) using Bacteroidales genetic markers is an emerging approach to determine host contributions to fecal pollution.**