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EDITORIAL COMMENTARY

The Silent Reservoir of Cryptosporidiosis

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(See the Major Article by Krumkamp et al on pages 1358–66.)

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Cryptosporidiosis is a leading cause of moderate-to-severe diarrhea in children under 5 worldwide, second only to rotavirus [1]. Unlike rotavirus, for which there exists an effective vaccine, there is no available vaccine for cryptosporidiosis, and there are limited therapeutic options to prevent morbidity and mortality in young children [2]. Recent estimates suggest that each year, *Cryptosporidium* species are responsible for >200 000 deaths in children aged <2 years in South Asia and sub-Saharan Africa and associated with morbidity in >7 million children in these regions [3]. *Cryptosporidium* infection in young children, even in the absence of diarrheal disease, has been associated with damaging long-term sequelae including linear growth faltering and cognitive deficits [4–7]. In 2016, *Cryptosporidium* diarrhea was associated with >4.2 million disability-adjusted life-years (DALYs) lost, and after accounting for the parasite's effect on growth faltering, an additional 7.85 million DALYs were attributable to *Cryptosporidium* infection [8].

In this issue of the journal, Krumkamp et al describe the largest multicenter study of *Cryptosporidium* transmission in sub-Saharan Africa to date [9]. Taking place in 4 countries (Gabon, Ghana, Madagascar, and Tanzania), this study identified children <5 years of age presenting to outpatient care centers with *Cryptosporidium* diarrhea, and then returned to their homes to track household contacts, neighbors, and most notably, animal contacts, making it the first study of cryptosporidiosis in children to evaluate animal and human contacts to describe transmission of the parasite. Overall, 1363 children with diarrhea were enrolled, and 184 (13%) were found to be *Cryptosporidium* positive. Subsequently, 108 contact networks from positive children, consisting of household contacts, neighboring children, and animals contacts, were sampled, and 68 *Cryptosporidium*-negative contact networks were sampled.

Krumkamp et al found that neighboring children <5 years of age had the highest prevalence of cryptosporidiosis (23%), even greater than the rate seen in initial cases presenting with diarrhea. This is not surprising, as we know that there is a high rate of asymptomatic carriage of *Cryptosporidium,* especially among children under 5 [5, 6]. Animal sources played a smaller role in spread of infection than did anthroponotic spread. This is a significant finding, considering at most sites, families did keep domesticated animals. Interestingly, there was no significant difference in the rate of positive animal contacts between *Cryptosporidium*-positive and -negative initial cases. In contrast, there were higher rates of *Cryptosporidium*-positive family and neighborhood contacts in the *Cryptosporidium*-positive cases than negative initial cases. Based on genotyping, there was low concordance between the species found in initial cases and animal contacts. The *gp60* subtype analysis demonstrated that among individuals within transmission clusters, 71% were infected with the subtype defining the cluster, and of the individuals infected, neighboring children and household contacts had highest concordance with the cluster-defining *gp60* subtype.

The significance of these findings cannot be overstated. Anthroponotic spread of cryptosporidiosis appears to be the largest driver of infection in children under 5. And more specifically, child-to-child transmission is likely the largest contributor to spread of infection.

The authors suggest that neighborhood outbreaks are likely. However, perhaps there is always a baseline-level cryptosporidiosis circulating within these communities, likely in school-aged children, serving as a silent reservoir. These asymptomatic carriers then serve to infect younger children, who then are more likely to develop symptomatic diarrheal disease and suffer further consequences

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in terms of growth faltering and cognitive outcomes [4–8].

This raises the question: should the focus be on targeting asymptomatic carriers of cryptosporidiosis? If this is where the reservoir exists, perhaps intervention at this point could save infants from suffering from infection. How would such an intervention look? Obviously, water, sanitation, and hygiene (WASH) interventions would be most logical. A focus on elimination of household contamination of *Cryptosporidium* (as well as other diarrheal pathogens) by improving hand hygiene, storage of water, and perhaps most importantly, safe disposal of fecal matter would presumably reduce transmission of infection. However, studies of low-cost WASH interventions, involving improvement in access to clean water and access to improved latrines, have yet to demonstrate reduction in *Cryptosporidium* infection rates [10, 11]. We do not yet have clear indications about which WASH interventions would be most effective; more studies are needed [10, 11].

What about mass treatment of children to target colonization? The mass treatment approach has been effectively applied toward helminth infection [12, 13]. If we believe that colonization in some individuals can lead to infection in vulnerable children, then decolonization must be considered an option. The issue would be identifying an effective drug for decolonization. Nitazoxanide is the only US Food and Drug Administration–approved drug for cryptosporidiosis, but data are lacking on whether it would reduce asymptomatic shedding.

The study by Krumkamp et al adds an important piece to the puzzle of cryptosporidiosis. Asymptomatic infection in children is not only hazardous for their health but also poses a threat to children around them. Now the question is, how can we mitigate this threat? With millions of children affected each year, we urgently need data on effective interventions for stopping transmission.

Note

Potential conflicts of interest. P. S. K. reports no potential conflicts of interest. The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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