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The Need for a Better Understanding of the Transmission of *Cryptosporidium* in Urban Areas

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Cryptosporidium is an intracellular protozoan parasite that infects the small intestine causing damage to the intestinal epithelium and disrupts absorption and barrier function, leading to mild-to-severe diarrhea [1]. *Cryptosporidium* has a worldwide distribution infecting humans and animals but in low and middle income countries, cryptosporidiosis is much more prevalent [2]. However, the burden of this parasitosis is underrated. According to Khalil et al (2018), *Cryptosporidium* infection was the fifth leading cause of diarrheal mortality in children younger than 5 years in 2016 and the estimation of the burden of *Cryptosporidium* is 2.5 times higher than previously reported by accounting childhood health beyond acute illness by decreasing growth. In addition, the co-infection of *Cryptosporidium* with other intestinal pathogens and respiratory cryptosporidiosis are other neglected topics [3]. There is currently no vaccine available, and the only approved treatment, the drug nitazoxanide, is not highly effective in immunocompromised individuals [4].

Characteristics of the biology of *Cryptosporidium* such as life-cycle completion within an individual host, zoonotic transmission, prolonged survival in environments, high probability of infection at low doses coupled with high excretion rate, substantial transmission through water and resistance to traditional water treatment technique are determinant to understand how environmental and social factors interact favoring the transmission of this parasite [5]. Among the factors that affect the incidence of *Cryptosporidium*, low socioeconomic status, crowded living conditions, presence of animals (pigs, cats, dogs, rodents, etc.), food storage, non-potable water consumption and rainy season are mentioned [2,6]. A model-based inventory of Cryptosporodium emissions to surface water developed by Hofstra et al [7] proposed large cities in China, India and Latin America, principally, as hot-spot areas. The authors suggested a more in-depth research attention regarding oocyst inactivation, specification for different genotypes, human and livestock emissions, the role of wildlife, wastewater treatment efficiency and runoff fraction for a better understanding of the causes of *Cryptosporidium*-related health problems.

Cities represent artificial ecosystems that are in constant transformation. According to reports from United Nations (UN), more than half of the world's population lives in urban areas and the higher urbanization rates take place in less developed regions [8]. Uncontrolled urban growth result in large health inequities and several rural pathogens have adapted to urban environments [9]. The most problematic areas with regards to safe disposal of human faeces, and thus to *Cryptosporidium* emission to the environment, are likely to be urban slums [10]. Studies conducted in urban slums worldwide have shown that the main responsible of cryptosporidiosis cases were *C. hominis* and the IIc subtype of *C. parvum*, revealing that anthroponotic transmission dominate in this type of informal settlements [11–14]. These results are in concordance with a recent review performed by King et al demonstrating that anthroponotic transmission of *Cryptosporidium* predominates primarily in lower-income countries with poor sanitation, highlighting that the need of improving sanitation provision may be the most important

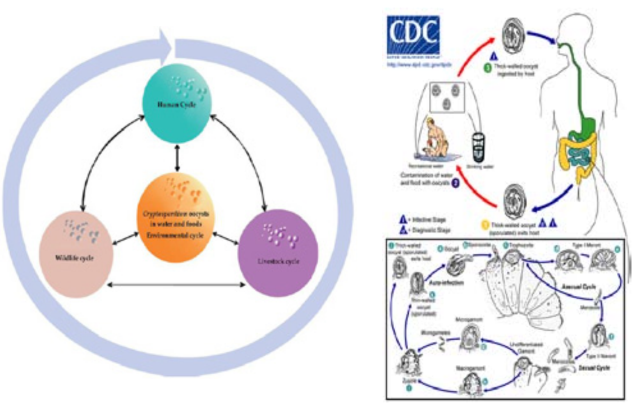

Figure 1: Life Cycle of *Cryptosporidium*: (a) *Cryptosporidium* spp. has a worldwide distribution and the ability to infect a wide range of hosts, including humans, and a broad variety of vertebrate. Humans can acquire cryptosporidiosis through several transmission routes, such as direct contact with infected persons or animals and consumption of contaminated water (drinking or recreational) or food (extracted from [25]). (b) Sporulated oocysts, containing 4 sporozoites, are excreted by the infected host through feces and possibly other routes such as respiratory secretions. Zoonotic and anthroponotic transmission occur through exposure to infected animals or exposure to water contaminated by feces of infected animals. Following ingestion (and possibly inhalation) by a suitable host, excystation (a) occurs and sporozoites are released and parasitize epithelial cells (b, c) of the gastrointestinal tract or other tissues such as the respiratory tract. In these cells, the parasites undergo asexual multiplication (d, e, f) and then sexual multiplication (g, h). Upon fertilization (i), oocysts (j, k) develop in the infected host. Two different types of oocysts are produced, the thick-walled, which is commonly excreted from the host (j), and the thin-walled oocyst (k), which is primarily involved in autoinfection. Oocysts are infective upon excretion, thus permitting direct and immediate fecal-oral transmission (extracted from Center of Disease Control: https://www.cdc.gov/parasites/crypto/pathogen.html)

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intervention to reduce the burden of the disease [15]. However, zoonotic transmission should not be neglected, since zoonotic species and genotypes of *Cryptosporidium* (*C. parvum* (not IIc), *C. felis, C. meleagridis, C. muris, C. canis*) were detected in human stool samples [11,14,16] and urban raw water samples [17,18]. Additionally, different genotypes of *Cryptosporidium* were detected in rats, dogs and cats, suggesting that urban pest and pet animals could be reservoirs for human cryptosporidiosis and potential sources of urban water contamination [19–22]. But studies involving a holistic approach considering the environment, animal reservoirs and human being in the transmission of *Cryptosporidium* in urban ecosystems are still lacking (Figure 1).

To recommend strategies to predict, prevent, respond to, and mitigate infectious diseases, it is necessary to understand the link among human beings, animals and environment [23]. A One Health approach promises a better understanding of how to prevent and control emerging infectious diseases at the human-animal-ecosystem interface, requiring therefore a genuine cross-sectoral integration and sustained social and political willingness to achieve control [24]. Cryptosporidiosis is a globally neglected public health issue, particularly in large cities in the developing world. More information under an integrated vision about molecular characterization of the pathogen, zoonotic emissions and environmental drivers in urban areas are required to develop strategies to reduce the transmission of *Cryptosporidium*. In addition, consensus and updated methodologies that are compatible across countries are required to make the information more comparable and permit future collaborations.

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