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# Infections of *Cryptosporidium* spp. in the context of climate change and urbanization

## Zakażenia *Cryptosporidium* spp. w kontekście zmian klimatycznych i urbanizacji

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## Abstract

**Introduction and Objective**. *Cryptosporidium* spp. are protozoans which are responsible for one of the most common waterborne disease, cryptosporidiosis. This disease is dangerous for children, immunocompromised individuals, and the residents of regions with limited access to sanitation infrastructure. Current climate change and urbanization significantly affect the transmission of these pathogens, increasing the risk of infection and causing challenges for public health. Our study analyzes the impact of urbanization and current climate changes on cryptosporidium epidemiology, with special focus on health consequences and current wastewater treatment methods.

**Brief description of the state of knowledge**. Heavy rainfall, rising temperatures and extreme weather events, such as floods, promote the survival of *Cryptosporidium* spp. oocysts, which may spread in the surface waters. The risk of transmission is significantly exacerbated in areas with a high population density and inadequate sanitation infrastructure, leading to heightened exposure and vulnerability. Oocysts, which are highly resistant to traditional disinfection methods, such as chlorination, are able to complicate prevention efforts. Current wastewater treatment methods are physical methods – filtration and sedimentation, biological processes – activated sludge and biofiltration, and chemical methods – disinfection of contaminated water.

**Summary**. Climate change and urbanization significantly increase the risk of *Cryptosporidium* spp. infections. Developing more effective wastewater treatment, new therapies and vaccines remain priorities, especially for protecting high-risk groups, such as young children, the elderly, and immunocompromised individuals.

### Key words

climate change, urbanization, *Cryptosporidium*, waterborne diseases

## Streszczenie

**Wprowadzenie i cel pracy.** *Cryptosporidium* spp. są pierwotniakami wywołującymi jedną z najczęstszych chorób wodnopochodnych – kryptosporydiozę. Choroba ta jest szczególnie niebezpieczna dla dzieci, osób z obniżoną odpornością, a także mieszkańców regionów o ograniczonym dostępie do infrastruktury sanitarnej. Zmiany klimatyczne i urbanizacja mają wpływ na transmisję patogenów, zwiększając ryzyko zakażeń, będących znaczącym wyzwaniem dla zdrowia publicznego. Celem pracy jest analiza wpływu procesów urbanizacyjnych i zmian klimatycznych na epidemiologię kryptosporydiozy, a także omówienie konsekwencji zdrowotnych zakażenia oraz współczesnych metod oczyszczania ścieków.

**Opis stanu wiedzy.** Intensywne opady, wzrost temperatury oraz ekstremalne zjawiska pogodowe, takie jak powodzie, sprzyjają przeżywalności oocyst *Cryptosporidium* spp. i ich rozprzestrzenianiu w wodach powierzchniowych. W regionach o dużej gęstości zaludnienia oraz niedostatecznej infrastrukturze sanitarnej rośnie ryzyko transmisji, co prowadzi do zwiększonej liczby zakażeń. Oocysty są wysoce odporne na tradycyjne metody dezynfekcji, takie jak chlorowanie. Obecnie do oczyszczania ścieków stosowane są różnorodne metody: fizyczne, takie jak filtracja i sedymentacja, biologiczne, w tym procesy z udziałem osadu czynnego, biologicznej filtracji czy stawów stabilizacyjnych, oraz chemiczne, polegające na dezynfekcji skażonej wody.

**Podsumowanie.** Zmiany klimatyczne i procesy urbanizacyjne mają istotny wpływ na wzrost ryzyka zakażeń *Cryptosporidium* spp. Prace nad skuteczniejszymi metodami oczyszczania wody oraz nowymi terapiami i szczepionkami pozostają priorytetem, zwłaszcza w ochronie grup wysokiego ryzyka.

### Słowa kluczowe

urbanizacja, zmiany klimatyczne, *Cryptosporidium*, choroby przenoszone przez wodę

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## INTRODUCTION

Parasites are common causes of gastrointestinal diseases, especially in developing countries [1]. About 22.67% of infectious diarrhea in children are caused by parasites [2]. Alongside rotaviruses, cryptosporidiosis is a leading cause of diarrhea and diarrhea-related mortality in young children in developing countries, and represents a significant etiological factor in waterborne disease outbreaks in industrialized nations [3].

*Cryptosporidium* maintains its life cycle via the faecal-oral route, therefore both waterborne and foodborne transmission play a key role in the epidemiology of this pathogen. The parasite has usually been recorded in drinking water, but it is increasingly being detected in recreational waters. Cryptosporidiosis poses a significant threat due to ongoing climate changes, as the increased frequency of floods elevates the risk of water contamination by *Cryptosporidium* spp. Higher temperatures enhance the survival of *Cryptosporidium* oocysts. Moreover, intensified rainfall events lead to the contamination of drinking water sources with *Cryptosporidium* oocysts, which results in an increase in the incidence of cryptosporidiosis [4, 5, 6].

Current methods for the removal and de-activation of infectious *Cryptosporidium* oocysts are based on secondary and tertiary wastewater treatment processes which use physical, biological, and chemical methods [7]. Developing more effective wastewater treatment, new therapies and vaccines remain priorities, especially for protecting high-risk groups.

## OBJECTIVE

The aim of this study is to discuss the impact of climate change and urbanization on the prevalence and increase in *Cryptosporidium* spp. infections, with particular emphasis on epidemiological factors, health consequences of infections, clinical manifestations, and risk roups susceptible to infection. Additionally, the study focuses on developing methods to reduce the number of infections caused by *Cryptosporidium*.

## DESCRIPTION OF THE STATE OF KNOWLEDGE

**Species description.** *Cryptosporidium* is an intracellular parasite that infects the epithelial cells of the gastrointestinal and respiratory tracts [8]. Currently, about 40 species of *Cryptosporidium* have been recognized, and they differ in their clinical significance. However more than 20 species of *Cryptosporidium* have been identified in humans [9], the most important from the point of view of the occurrence of cryptosporidiosis in humans are *C. parvum* and *C. hominis*. Based on sequence analysis of the locus encoding the 60kDa glycoprotein, about 20 subtype families have been distinguished in *C. parvum*. Some of these, such as IIc and IIe, are adapted to humans, whereas IIa (preferentially infecting cattle) and IId (preferentially infecting sheep and goats) are zoonotic. The gp60 locus is one of the most polymorphic regions in the entire *Cryptosporidium* genome. Whereas sequence analysis of the gp60 gene in *C. hominis* has identified over ten subtype families. *C. hominis* exhibits a narrower host range than *C. parvum*, which may be associated with its lower gp60 diversity [9, 10]. In livestock, such as cattle, the most commonly detected species are *C. parvum, C. andersoni, C. bovis,* and *C. ryanae*. In sheep and goats prevail *C. parvum, C. xiaoi and C. ubiquitum* [9]. *C. bovis* and *C. ryanae* are found in fish. *C. baileyi* is the species that mainly infects chickens [11].

**Life cycle and transmission of *Cryptosporidium*.** The life cycle of *Cryptosporidium* spp. begins with the ingestion of an infectious material, which is oocysts. Once in the gastrointestinal tract, sporozoites are released through the process of excystation. The released sporozoites infect enterocytes, primarily within the ileum. Within the host cell, the sporozoite transforms into a trophozoite, which undergoes asexual proliferation via merogony, forming meronts. Two types of meronts have been described. Meronts type I produce eight merozoites type I, which, upon maturation, form meronts type II, each containing four merozoites type II. Under appropriate environmental conditions, merozoites type I are also capable of autoinfection. Once released, merozoites type II initiate the sexual phase of the life cycle. Some of them differentiate into macrogametes, while others form microgametes. Subsequently, macrogametes and microgametes fuse to form a zygote. A cyst wall then forms around the zygote, resulting in the formation of an oocyst. Two types of oocysts can be distinguished: thick-walled (80%) and thin-walled (20%). Thick-walled oocysts are released with the faeces of the host, while thin-walled oocysts participate in autoinfection by releasing sporozoites [8, 12] (Fig. 1).

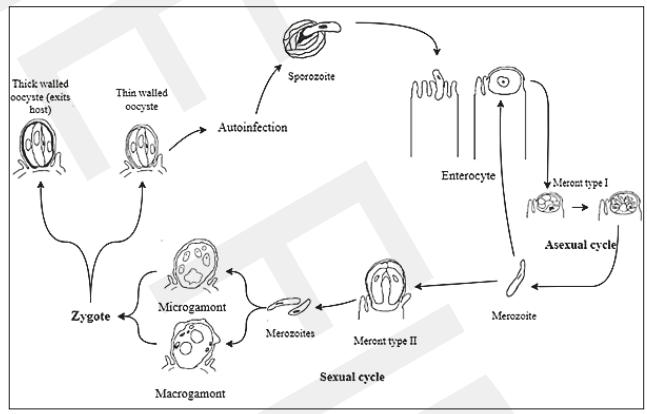


**Figure 1.** Life cycle of *Cryptosporidium* [8, 12]

When the life cycle is completed, thick-walled oocysts are released with the host›s faeces. These oocysts do not require sporulation and are immediately infectious [8, 12].

**Clinical manifestations of infections and risk groups for *Cryptosporidium* spp..** According to the Centers for Disease Control and Prevention (CDC), 823,000 cases of cryptosporidiosis are diagnosed annually in the United States [13]. According to a study conducted by Golan-Shopshnik, children under the age of five are the group vulnerable to cryptosporidiosis [14]. Research by Alali et al. identifies that cryptosporidiosis as the second most common cause of death due to severe diarrhea in children under four years, following rotavirus infection [3]. Complications of *Cryptosporidium* infection have also been observed in paediatric liver transplant recipients, with some cases resulting in fibrotic changes within the transplanted liver [15].

Humans can become infected through several routes: direct contact with infected people or animals, or indirectly through the ingestion of contaminated water or food. The most common modes of transmission of *Cryptosporidium* are person-to-person and waterborne transmission [16]. Water is the main route of transmission of *Cryptosporidium*, which is a serious public health problem. Livestock and wildlife are sources of infectious *Cryptosporidium* oocysts in water intended for human consumption. In recent years, larger outbreaks of cryptosporidiosis in humans have been documented, resulting in an increased need to monitor for the presence of *Cryptosporidium* oocysts in water and food products, such as lettuce, fruits and cilantro [11].

The first symptoms of *Cryptosporidium* infection can appear within two weeks of exposure and include diarrhea, fever, weight loss, nausea, and vomiting [17]. Children living in rural areas are the group vulnerable to cryptosporidiosis [3, 14]. Research by Shahrokh Izadi et al. demonstrated that individuals with weakened immune systems are at increased risk, such as those with acquired immunodeficiency syndrome (AIDS) – 4.6% of infected patients – and those with haematologic diseases, such as leukemia or lymphoma – 3.6% of infected patients [18]. In severe cases, *Cryptosporidium* may spread beyond the gastrointestinal tract and affect other organs (liver, gallbladder, pancreas, respiratory system) [14].

Infected farm animals are a significant reservoir for the transmission of *Cryptosporidium* and pose considerable challenges to agricultural productivity and economic stability. Cryptosporidiosis in ruminants is characterized by diarrhea, which contributes to increased morbidity and mortality rates. These outcomes result in escalated veterinary care expenditures and higher costs associated with the management and rearing of affected animals [19]. *Cryptosporidium* infections in dairy cattle can also be linked to decreased milk production, further exacerbating economic losses [20].

**Impact of climate change on the epidemiology of *Cryptosporidium*.** Research has demonstrated that climatic factors, such as temperature, precipitation, humidity, extreme weather events, and solar radiation, significantly influence the transmission of *Cryptosporidium* spp. The seasonal peaks of cryptosporidiosis incidence are closely linked to periods characterized by warm and humid conditions [4, 5].

Temperature increases have been shown to enhance the proliferation of *Cryptosporidium* spp. oocysts, attributable to both higher concentrations and improved survival rates in warm, moist environments. However, elevated temperatures may also contribute to the inactivation of oocysts, serving as a critical abiotic factor affecting their persistence and infectivity in the environment. As such, temperature emerges as a pivotal driver in the epidemiology of *Cryptosporidium* spp., promoting greater oocyst infectivity, intensifying host-pathogen interactions, and increasing oocyst excretion by animal hosts [5].

Intense precipitation events are associated with the contamination of water reservoirs, facilitating the transport of *Cryptosporidium* spp. oocysts into drinking water sources. Consequently, seasonal peaks of cryptosporidiosis cases, particularly in countries such as England, Wales, New Zealand, Scotland, and the United States, are strongly correlated with spring weather patterns characterized by increased rainfall and elevated temperatures [4, 5, 6].

Ultraviolet (UV) radiation from sunlight is a critical factor influencing the survival of *Cryptosporidium* spp. oocysts in the environment, significantly contributing to their inactivation in aquatic systems. Moreover, research has demonstrated a negative correlation between wind and the presence of *Cryptosporidium* spp., suggesting that wind may inhibit the dispersion of oocysts [4].

Flooding events further exacerbate the risk of waterborne *Cryptosporidium* spp. transmission. For instance, floods in the United Kingdom during the 1990s led to the contamination of drinking water sources through the runoff of *Cryptosporidium* spp. oocysts from soil surfaces. Moreover, secondary transmission occurred via cattle grazing on pastures contaminated by floodwaters. Heavy rainfall also facilitated the spread of infected manure across grazing areas [6]. Similar scenarios were documented in the United States between 1996–2018, where tropical cyclones triggered widespread flooding, resulting in the contamination of drinking and recreational water sources. Damage to water treatment facilities during these events frequently led to outbreaks of cryptosporidiosis [21]. A notable example of *Cryptosporidium* spp. contamination during flooding occurred in Nowshera, Pakistan. In 2010, severe monsoon rains inundated large parts of the region, causing significant contamination of local drinking water sources [22, 23].

**Urbanization as a factor in the rise of *Cryptosporidium* infections.** Human activities and economic conditions are intricately linked with environmental factors that influence the risk of cryptosporidiosis transmission. Regions characterized by high population density and low socio-economic development are particularly susceptible to this disease, primarily due to inadequate sanitation infrastructure, poor water quality, suboptimal hygiene practices, and insufficient health education [4, 24].

Agricultural expansion, deforestation, and habitat fragmentation further exacerbate the risk of zoonotic transmission [4]. Farmers face heightened exposure risks due to the presence of *Cryptosporidium* spp. oocysts in soil, which can serve as a source of infection [4].

The infiltration of *Cryptosporidium* spp. oocysts into drinking water systems – both filtered and unfiltered – plays a critical role in the epidemiology of cryptosporidiosis. Contamination of sewage systems supplying water to urban and rural populations amplifies this risk. Between 1946–2016, a total of 936 outbreaks of waterborne protozoan diseases were reported, of which 58% were attributed to *Cryptosporidium*, underscoring its resilience to conventional disinfectants, including chlorine, commonly used in traditional water treatment processes [5, 16].

The largest recorded waterborne cryptosporidiosis outbreak occurred in Milwaukee, Wisconsin (USA) in 1993. This event resulted in approximately 403,000 cases, with 4,400 hospitalizations and 100 fatalities [16, 25].

**Methods of control and prevention of *Cryptosporidium* spp. infections.** Current knowledge on the mechanisms of *Cryptosporidium* infection and effective treatment of cryptosporidiosis is limited. Strategies for the removal and deactivation of *Cryptosporidium* oocysts have focused on secondary and tertiary wastewater treatment. These strategies include: physical methods (e.g., sedimentation and filtration), biological methods (e.g., activated sludge, biological filtration, and stabilization ponds), and chemical methods (e.g.,

disinfection of contaminated water). For wastewater intended for agricultural purposes (not for potable use), a multi-barrier treatment approach is recommended, combining all the aforementioned methods [7].

Filtration involves the separation of liquids from solids using porous barriers (filters and membranes), while sedimentation relies on the natural settling of solids in liquids. Both methods play a significant role in removing *Cryptosporidium* from water sources. However, traditional filtration methods have proven ineffective due to the high resistance of oocysts to chemical agents like chlorine [16]. Nonetheless, studies by Folasade Esther Adeyemo et al. have shown that high chlorine exposure, combined with UV treatment, effectively eliminates *Cryptosporidium* [26]. Given the lack of effective techniques for managing this protozoan, new approaches to water monitoring and treatment are necessary to prevent *Cryptosporidium* infections.

Natural systems for wastewater treatment involve waste stabilization ponds (WSP) or constructed wetlands (CWL). Constructed wetlands are categorized into two main types: free-surface flow (FSF) and subsurface flow (SSF) systems. Factors such as predation, microbial activity, oxidation-reduction reactions, and exposure to plant- and bacteria-derived toxins contribute to oocyst inactivation. WSPs with retention times exceeding 20 days, along with SSF, have demonstrated significant effectiveness in removing *Cryptosporidium* oocysts from wastewater [7].

Studies by Graczyk et al. comparing subsurface-flow and free-flow ponds revealed that only subsurface-flow ponds were highly effective in wastewater treatment. No reduction in *Cryptosporidium* oocysts was observed in free-flow ponds [27]. Stabilization ponds use artificial water bodies where natural processes treat wastewater. Anaerobic, facultative, and aerobic ponds can be used, with sunlight exposure identified as a critical factor for reducing pathogenic parasites. Research by Roberto Reinoso demonstrated that facultative ponds were the most effective for oocyst inactivation [28].

Modern tertiary wastewater treatment methods include membrane ultrafiltration and ultraviolet (UV) irradiation, which has shown high efficacy even at low doses. Replacing chlorine with ozone has also proven effective for oocyst inactivation [27]. Another promising disinfection technique is ultrasonic radiation. Continuous ultrasonic exposure at 80W effectively eliminates oocysts without altering the chemical composition of the water or generating toxic byproducts [29]. Effective wastewater treatment plays a crucial role in preventing the spread of *Cryptosporidium*.

**Future directions for control and prevention of *Cryptosporidium* spp. infections.** Antimicrobial therapy is typically unnecessary in immunocompetent individuals, as *Cryptosporidium* infections are self-limiting. Proper hydration is crucial for preventing dehydration. For persistent diarrhea, a three-day course of nitazoxanide (500 mg twice daily) can be administered [30, 31]. Nitazoxanide is currently the only medication approved by the United States Food and Drug Administration (FDA) for treating cryptosporidiosis in immunocompetent individuals [19, 32]. In immunocompromised patients, its efficacy is limited without concurrent immune function improvement. For patients with HIV/AIDS, initiating highly antiretroviral therapy (ART) is necessary for symptom resolution [31].

The development of effective drugs and vaccines is crucial in mitigating the impact of cryptosporidiosis, particularly in groups such as immunocompromised individuals and children. Future drugs must have a safe pharmacological profile, minimal toxicity and low potential for drug-drug interactions. Promising drug targets include parasite-specific biochemical pathways: lipid kinase – Phosphatidylinositol 4-kinase PI(4) K, calcium-dependent protein kinases and aminoacyl-tRNA synthetases [19]. Vaccines could significantly reduce *Cryptosporidium* infections. Immunogenic *Cryptosporidium* proteins, such as gp15, Cp15 and Cp23, are promising candidates for vaccine development. However, a limited understanding of the immune response to *Cryptosporidium* infections continues to hinder progress in vaccine development [33].

## CONCLUSIONS

From the public health perspective, the presence of infectious *Cryptosporidium* oocysts in drinking water is a serious threat to human health and safety. This is due to the high pathogenic potential of *Cryptosporidium*, especially for people in high-risk groups such as children and immunocompromised individuals [10K].

The observed increase in Cryptosporidiosis cases in European countries, such as Ireland, The Netherlands, Spain and Norway [34, 35, 36], is due to several factors. Studies have shown that climatic factors, including temperature, precipitation, humidity, extreme weather events, and solar radiation, play a significant role in the transmission of *Cryptosporidium* spp. Regions with a high population density and low socio-economic development are especially vulnerable to this disease, due to inadequate sanitation, poor water quality, limited hygiene practices, and insufficient health education [4, 24].

One possible route of cryptosporidiosis infection is the consumption of water contaminated with *Cryptosporidium*. Current methods for removing infectious oocysts from wastewater include physical techniques, such as sedimentation and filtration, biological methods utilizing activated sludge, and chemical disinfection of contaminated water [37].

With the increasing number of *Cryptosporidium* infections, there is an urgent need to develop new prevention strategies for this protozoan, more effective treatment options, and acceleration of research into potential vaccination.

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