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CRYPTOSPORIDIUM CANIS AND *C. FELIS* AS A POTENTIAL RISK TO HUMANS

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K e y w o r d s: *Cryptosporidium* spp., dogs, cats, infectivity, diagnostics, treatment.

A b s t r a c t

Cryptosporidium spp. are protozoan parasites found in the respiratory and gastrointestinal tracts of many vertebrates. This paper aims to present information about *Cryptosporidium* spp. related to their biology, life cycle, pathogenesis, infectivity, diagnostic methods and the treatment of diseases caused by them. *C. canis* and *C. felis* are common parasites of dogs and cats, therefore contact with ill or asymptomatically infected animals could pose a risk of infection especially for children and people with immunodeficiency disorders. The diagnostic difficulties and inadequately developed methods to treat pets make an infection with *Cryptosporidium* worse, and this has been proven by many confirmed cases of the disease.

CRYPTOSPORIDIUM CANIS I *C. FELIS* JAKO POTENCJALNE ZAGROŻENIE DLA CZŁOWIEKA

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S ł o w a k l u c z o w e: *Cryptosporidium* spp., psy, koty, zarażenie, diagnozowanie, zwalczanie.

A b s t r a k t

Cryptosporidium spp. są to pierwotniaki znajdowane w układzie pokarmowym i oddechowym wielu kręgowców. Praca ta ma na celu przedstawienie wiadomości na temat biologii, rozwoju, patogenezy, inwazjologii, metod diagnostycznych oraz leczenia *Cryptosporidium* spp. z uwzględnieniem tych gatunków, które mogą być zagrożeniem dla człowieka. U psów i kotów często występują *C. canis* i *C. felis*, a skażenie środowiska oocystami lub kontakt ze chorym zwierzęciem może być szczególnie groźne dla dzieci i osób z immunosupresją. Trudności w diagnozowaniu i nie w pełni opracowane leczenie zwierząt towarzyszących pogłębiają problem zakażeń ludzi kryptosporydiozą, czego dowodem jest wiele potwierdzonych przypadków zachorowań.

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Cryptosporidium spp. is a genus of apicomplexan parasitic protozoans belonging to Eimeria suborder of the Cryptosporidiae family. They commonly exist in 280 species of vertebrates, reptiles and fish (UPTON et al. 1985, MORGAN et al. 1999, CAVALIER-SMITH 2003). The parasite was first described in 1907 by E. E. TYZZER, who found it in the gastric glands of mice and named it as *Cryptosporidium muris* (TYZZER 1910). These protozoans live within host epithelial cells inhabiting the surface of the brush border, usually of the distal intestine. They may attack the epithelium of the respiratory track and stomach of humans especially individuals with immunosuppression. So far, 26 species and 73 genotypes have been described, including 8 that are pathogenic to human: *C. hominis*, *C. parvum*, *C. meleagridis*, *C. felis*, *C. canis*, *C. suis*, *C. muris, C. cuniculus*, *C. ubiquitum*, *C. viatorum*, *C. fayeri*, *C. andersoni*, *C. bovis*, *C. scrofarum*, *C. tyzzeri*, *C. erinace* and *C. cervine* (RYAN and HIJJAWI 2015). Weakened, young and old organisms or those with immunosuppression are susceptible to invasion. The protozoa is transmitted through faeces, contaminated food, water and air. 1 g of human faeces may contain about 50,000 oocysts, which can enter the soil and water (WEBER et al. 1991). Theoretically, one oocyst is enough to infect an individual. The most known epidemic outbreak of cryptosporidiosis was reported in Milwaukee, USA, in 1993, when the water supply was contaminated with oocysts of *C. parvum* (MAC KENZIE et al., 1994). As a result, 100 people died, and the disease was confirmed in 403,000 cases. Pets, mainly dogs and cats, may be an important reservoir for the germs pathogenic for humans (CAUSAPE et al. 1996, THOMPSON et al. 2008, OVERGAAUW et al. 2009, PALMER et al. 2008, BOWMAN and LUCIO-FORSTER 2010). In Poland, the dog population is estimated at 11 million, and cat at 6 million. This indicates that every third Pole may be a dog owner, and every fifth may have a cat. Dogs are natural hosts to commonly occurring *C. canis* and cats to *C. felis*. Studies confirm that these animals are susceptible to infection with many other species/genotypes of *Cryptosporidium*, for example: *C. hominis, C. parvum, C. meleagridis, C. felis, C. andersoni, C. muris* (FITZ GERALD et al. 2011, XIAO and FAYER 2008).

Life cycle of *Cryptosporidium*

Cryptosporidium spp. is a homoxenic parasite, i.e. it completes its life cycle in a single host. The main place of residence for the parasite is villus epithelial cells in the small intestine or epithelial cells in the respiratory tract. Humans and animals acquire infection via the fecal-oral route and sporadically by inhalation. Following infection, each invasive oocyst releases four mobile sporozoites, which invade villus epithelial cells in the intestine (and/or in the respiratory tract). They locate extracytoplasmatically in host cells within

parasitophorus vacuoles, where they differentiate into spherical trophozoites. Trophozoites undergo asexual multiplication to form two types of meronts: type I meronts (containing 6 or 8 merozoites) leave the parasitophorus vacuole, enter villus epithelial cells next and undergo asexual multiplication or develop into type II meronts (containing 4 merozoites). The type II meronts undergo sexual multiplication to form gamonts. Following gametogony, micro- and macrogamont form a zygote, which develops into an oocyst. Two types of oocysts develop during the life cycle of *Cryptosporidium*: thin-walled oocysts, which initiate a new life cycle (autoinvasion), resulting in chronic infection of the host, and thick-walled oocysts, which are shed in faeces to the environment (BARR 1998). Oocysts are invasive immediately after excretion and very resistant to environmental conditions, so they may be rapidly transmitted to the next host. The incubation period of cryptosporidiosis varies and depends mainly on the species of the parasite and its host.

Pathogenesis of the disease – The course of the disease in humans and animals is similar. The parasites cause villous atrophy, leading to a decrease in absorption area, especially in the duodenum and distal intestine. The mechanism of diarrhoea induction has not been fully described, but it is supposed that it is a result of secretion disorder or poor absorption. These processes are based on abnormal secretion of prostaglandin (PGE), which stimulates the contraction of smooth muscles of the gastrointestinal tract, substance P, responsible for an increase in the vascular permeability of endothelial cells in the intestine and inflammations, and tumour necrosis factor (TNF), which is involved in inflammation processes as well. Disorders of the active transport of sodium and H2O dependent on glucose have been proven, too. It is supposed that toxins produced during the life cycle of the parasite negatively influence the absorption of chloride ions. Disorders of secretion of the abovementioned components and a negative influence on the absorption mechanism lead to villous atrophy caused by inflammation and to diarrhoea caused by poor absorption. Inflammations in particularly chronic cases result in severe damage of villus and their enterocytes. Diarrhoea is caused by disorders of the balance of water and electrolytes. Depending on the condition of the organism, the disease caused by *Cryptosporidium* spp. may be symptomless, acute or chronic. The symptomless disease occurs in young individuals more often than older ones. It is characterized by a lack of symptoms during pre-patent and patent periods. These individuals are a reservoir for the parasite. While there are no symptoms, the individual is theoretically considered as healthy. The disease self-cures after several cycles of parasite multiplication. The chronic disease lasts up to 21 days and is particularly dangerous for young individuals. The patent period, i.e. the stage in which parasites enter the intestine wall, lasts up to 7 days. Lack of appetite, slightly increased body temperature and nausea were observed. The patent period is characterized by profuse, self-

limited diarrhoea. Following the given period, the physical condition suddenly improves, and the disease self-cures. The chronic disease may even last several months. It occurs in cachectic organisms or those with immunosuppression. Symptoms include coughing, dyspnoea, increased body temperature, vomiting, frequent diarrhoea and, as a consequence, cachexia, body weight loss and bloody diarrhoea. It may lead to death. Factors predisposing to the development of the disease are, in particular, acquired immunodeficiency syndrome and diseases causing immunosuppression, e.g. leukaemia (CLARK and SEARS 1996, LAURENT et al. 1999, KOSEK et al. 2001, TZIPORI and WARD 2002, DOMENECH et al. 2011).

Infectivity – Animals under 90 days old are most often affected (JIAN et al., 2014). Studies carried out in many countries showed a different number of infected animals, e.g. 2.3–26.2% of dogs and 2.3–26.2% of cats in Brazil, 7.4–9.3% of dogs and 7.3% of cats in Canada, 3.9% and 3.8%, respectively, in Japan, 3.8% and 4% in the USA, 3.8% of dogs in China, 3.3% in Italy and 8.1% of cats in Great Britain (ARAI et al. 1990, EL-AHRAF et al. 1991, MTAMBO et al. 1991, GENNARI et al. 1999, SHUKLA et al. 2006, GIANGASPERO et al. 2007, MUNDIM et al. 2007, BALASSIANO et al. 2009, COELHO et al. 2009, YOSHIUCHI et al. 2010, UEHLINGER et al. 2013, JIAN et al., 2014). An animal with cryptosporidiosis excretes in faeces invasive oocysts to the environment. They constitute a reservoir for the animals using the waterhole. Isolation of the parasite from water in rivers, where their number was from 2 to 112 oocysts per litre of H2O, can cause infection at a considerable distance from the source of contamination (ONGERTH et al., 1987). Incorrect manure storage, drainage leakage and absence of hygienic precautions in farms or other animal communities promote water contamination. It was shown that wild animals, e.g. foxes, can constitute a serious hazard (SMITH et al., 2006). An important transmission route is contaminated food of plant origin and gardens in playgrounds for children. For example, it was stated in Peru that a 3-year-old boy and his siblings were infected by a pet dog (XIAO et al. 2007). It was indicated that an increased incidence rate of cryptosporidiosis in people occurs in spring and autumn during abundant rainfalls and in the summertime, when recreation and water sports are more frequent (MAJEWSKA 2003, LAL et al. 2012). Usage of water reservoirs containing oocysts promotes infection. It was specified that 20.5% of wild animals were infected with *Cryptosporidium*, so they constitute a dangerous reservoir to the environment, animals and humans. The parasites represented 21 genotypes, and 11 of them were in water (FENG et al. 2007). Dogs and cats infected with cryptosporidia are a source of infection to household members, in particular to children attending public institutions, such as nursery schools or schools, and to elderly people living in nursing homes, etc. An outbreak of cryptosporidiosis in children attending a nursery school in Georgia, USA, was described, where 49% of children were

infected and as many as 70% of them suffered from diarrhoea. It should be noted that the parasite was identified in 13% of adults who were there, too, but the course of infection implied that children were more susceptible to infection with the parasite (TANGERMANN et al. 1991). When elderly people are concerned, cryptosporidiosis has been described in 36% of patients hospitalized in the USA (NEILL et al. 1996). The occurrence of cryptosporidiosis has been documented in paediatric hospitals as well, e.g. above 20 such invasions were mentioned in 1980 in China. It has been demonstrated that 1.62% of infected patients had 6 genotypes of *C. hominis* and 4 genera of *Cryptosporidium*, including *C. canis* and *C. felis* (FENG et al. 2012). 159 children of 533 children under 4 years of age examined in Peru were infected with *Cryptosporidium* spp., and approx. 7% of cases were caused by cryptosporidiosis in dogs and cats. *C. canis* and *C. felis* are a specific threat to people with immunosuppression, in particular patients infected with HIV, which is caused by CD+ lymphocytes deficiency. There are many indications that *Cryptosporidium* is a significant pathogen that might cause death from cachexia through dehydration and diarrhoea (BLANSHARD et al. 1992, TIANGTIP and JONGWUTIWES 2002). In different countries, *C. felis* was found in 6% of people with immunosuppression (TIANGTIP et al. 2002). Studies carried out in Brazil showed that as many as 18.5% of people infected with HIV were carriers of *C. felis*, and 3.7% of *C. canis* (LUCCA et al. 2009). There is the possibility that one individual is infected with various species of *Cryptosporidium* spp., e.g. a patient of Jamaica with immunosuppression was infected with *C. felis* and *C. hominis* (GATEI et al. 2008). Another example is a Peruvian infected with three types of protozoan: *C. felis, C. hominis* and *C. meleagridis* (CAMA et al. 2006). Studies by MEINHARDT et al. (1996) showed that there were no preferences for sex of the host regardless of parasite species or genotype. Throughout history, there have been many mass invasions of *Cryptosporidium* spp. Examples given below confirm that cryptosporidiosis poses a common threat and is a serious problem that can affect highly developed countries, too. In 1987, 13,000 residents of the state of Georgia, USA, were affected by an outbreak of cryptosporidiosis. Oocysts were found in drinking water (HAYES et al. 1989). During an agricultural fair in 1993, it was stated that cider was the main source of oocysts of *Cryptosporidium*. 89% of individuals exposed to contact with the protozoan were infected. This is the first description of the spread of this parasite in the population through contaminated food (MILLARD et al. 1994). In 1997, contamination of borehole water in the area in the northern part of the River Thames in England was recorded; 746,000 inhabitants were exposed to the infection, and 345 with documented diagnosis of cryptosporidiosis were hospitalized (WILLOCKS et al. 1998). Other large outbreaks of cryptosporidiosis caused by water contaminated with oocysts were described by TAYLOR et al. 1985,

RICHARDSON et al. 1991, BRIDGMAN et al. 1995, YOKOI et al. 2005, CAUSER et al. 2006, VANDENBERG et al. 2012.

Diagnostic methods – Diagnostics of cryptosporidiosis in dogs and cats depends on the severity of symptoms and place of residence of the parasite in the organism. A stool examination should be performed if there are symptoms from the gastrointestinal tract, and sputum is the material to test if respiratory cryptosporidiosis is considered. It is hard to find oocysts in stool, so it should be collected over a few days. In exceptional circumstances, oocysts can be found in bile. Biopsy of the duodenum, distal intestine or lung is undertaken in severe cases. Microscopic examination of a stool smear stained with the use of the acid-fast procedure (Ziehl-Neelsen), i.e. the method of Kinyouna, Gram and Giemsa, is the simplest, but not always accurate, method for detection of *Cryptosporidium* spp. (O'DONOGHUE, 1995). Specialised laboratories use immunological methods, i.e. western blotting, detection of antibodies in stool or identification of oocysts by the direct immunofluorescence method (ARROWOOD et al., 1991). PCR is the most sensitive method, as it allows to identify particular species of *Cryptosporidium*, what is very useful in determining the source of infection. An autofluorescence method can be applied in diagnostics, too (VAREA et al. 1998).

Treatment – Methods to treat cryptosporidiosis in dogs and cats have not been fully developed. There is no effective medication for animals with *Cryptosporidium* spp. Therapy against the protozoan has been much better developed for humans. Macrolide antibiotics azithromycin and paramycin are applied (ARMITAGE et al. 1992, BLANSHARD et al., 1997). Their use has permitted the cure of pulmonary cryptosporidiosis in an AIDS patient (PALMIERI et al. 2005). Therapy with the use of spiramycin had no desired effects, because there was no clinical improvement (WITTENBERG et al. 1989). Nitazoxanide, applied to cure children with diarrhoea, can become a future treatment of cryptosporidiosis (SMITH and CORCORAN 2004, FOX and SARAVOLATZ 2005). Halofuginone is considered to be of some significance for the control of oocysts. It was proven in *in vitro* studies that use of monensin and halofuginone can cause a decrease in the number of the oocysts by as much as 90% (MCDONALD et al. 1990, NACIRI et al. 1993). *Cryptosporidium spp*. oocysts are resistant to external factors, and therefore the treatment of water supply or food can often be unreliable. Water chlorination is unreliable too. Filters applied to intake water for humans should have pores of a size smaller than 1 ,m to protect against oocysts.

Summation – *Cryptosporidium canis* and *felis* are important and underestimated human's pathogen. Many scientific works cited in article confirms, that this protozoan are a serious threat to young people, elders and with immunosuppression. Illness which is caused by *Cryptosporidium* spp. depends

on health status and may be symptomless, acute or chronic. *Cryptosporidium* spp. that occurs in dogs and cats are able to contaminate gardens, parks and water reservoirs. Due to high resistance of the oocysts, contamination of the environment can take several months. There is lack of information about prevalence of *C. canis* and *C. felis* in dogs and cats in Poland have a negative impact on the prevention aimed against this parasite. These protozoa can cause diarrhoea in puppies or kittens which often lead to increased mortality. Pet animals are an important vector of the parasite due to its proximity with humans. The exposed persons should examine their animals for the presence of this protozoan. Early diagnosis of cryptosporidiosis prevent the spread of *Cryptosporidium* spp. The aim of the veterinarian in the protection of public health should be to minimize environmental pollution with oocysts by rapid identification of sick animals, as well raising awareness of animal owners to ensure hygiene which will reduce the the chance of infection to humans.

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