Review Article

THE SIGNIFICANCE OF THE CESTODE *JOYEUXIELLA PASQUALEI* (CYCLOPHYLLIDEA: DIPYLIDIIDAE) FOR CLINICAL PRACTICE AND THE WELFARE OF CATS

Tamara ILIĆ¹^(D), Jelena PAVLOVIĆ²^(D), Nemanja M. JOVANOVIĆ¹^(D), Predrag STEPANOVIĆ³^(D), Katarina NENADOVIĆ^{4*}^(D)

1 – University of Belgrade, Faculty of Veterinary Medicine, Department of Parasitology, Belgrade, Serbia

2 - Veterinary Pharmacy Plus Plus Ltd., Serbia

3 – University of Belgrade, Faculty of Veterinary Medicine, Department of Equine, Small Animal, Poultry and Wild Animal Diseases, Belgrade, Serbia

4 – University of Belgrade, Faculty of Veterinary Medicine, Department of Animal Hygiene, Belgrade, Serbia

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Abstract

The cestode *Joyenxiella pasqualei* is a common parasite of cats in Southern European countries, and due to the increasingly pronounced effects of global warming, there is a tendency for the spread and appearance of this parasite among carnivores in other parts of the European continent. The adult forms of the parasite are localized in the small intestines of definitive hosts (cats, dogs, foxes, wolves, and other carnivores). Cats become infected by ingesting primary hosts (coprophagic insects) and secondary intermediate hosts (reptiles and small mammals), which harbor the infective larval forms of the parasite (cysticercoids). In most infected animals, the disease progresses asymptomatically. An exception occurs in cases of high-intensity infections, where the adhesion of adult parasites to the intestinal mucosa leads to necrosis of the intestinal villi, invagination, and partial obstruction of the intestine, significantly compromising the health and well-being of cats. Successful treatment is achieved through the administration of praziquantel, and for prevention, it is necessary to prevent contact

^{*}Corresponding author - e-mail: author@vet.bg.ac.rs

between cats and populations of intermediate hosts. Data on the etiopathogenesis, diagnosis, and control of this tapeworm are of particular importance for inexperienced diagnosticians, who, due to insufficient knowledge about *J. pasqualei* parasitism, can make significant errors in clinical diagnosis. Due to its significance for clinical practice and the welfare of cats, it is necessary to include this cestode in the differential diagnosis of intestinal invagination in cats and of other carnivore cestodes, which are species from the genera *Diplopylidium* and *Dipylidium*.

Key Words: cat, Joyeuxiella pasqualei, diagnostic, control, welfare

INTRODUCTION

Joyeuxiella pasqualei is a predominant cestode of cats, and in the indirect life cycle of this cestode, besides cats, the definitive host can be dogs, foxes, wolves, or other carnivores. The adult forms of this helminth parasite occur in these carnivores' intestines. Cats become infected by ingesting secondary intermediate hosts (lizards, occasionally small mammals), in which the infective larva cysticercoid forms in the peritoneal cavity, liver, and muscles (Soulsby, 1968; Bowman et al., 2002). This parasite is much less frequently recorded in dogs (than in cats) due to misdiagnosis and confusion with the more common, well-known, and expected cestode, *Dipylidium caninum*. The appearance of *J. pasqualei* proglottids in a dog from Italy living indoors indicates the need for greater attention to the biology of this parasite (Bezerra-Santos et al., 2022).

Although there is still no data on the zoonotic potential of this parasite in relevant world literature, due to its significant clinical importance, it is necessary to include it on the list of agents important for the differential diagnosis of intestinal invagination in cats and of other carnivore cestodes (especially species from the genera *Dipylidium* and *Diplopylidium*) (Blagburn and Todd, 1986; Papazoglou et al., 2003; Bezerra-Santos et al., 2022). Data on the etiopathogenesis, timely diagnosis, and control *J. pasqualei* are of particular importance for inexperienced diagnosticians, who, due to insufficient knowledge about this tapeworm's parasitism, could make significant errors in establishing a valid clinical diagnosis (Diakou et al., 2017; Schuster, 2020).

There are numerous reports from Serbia related to the issues of intestinal, cardiorespiratory, ocular, and urinary parasitic infections in owned dogs (Kulišić et al., 1992; Pavlović et al., 1997; Ilić et al., 2015; Stepanović et al., 2015; Hadži Milić et al., 2016; Ristić et al., 2020; Ilić et al., 2021a; Ilić et al., 2023), stray dogs (Ilić et al., 2021), and wild carnivores (Pavlović and Kulišić, 1994; Ilić et al., 2012; Lalošević et al., 2013; Ilić et al., 2016; Ilić et al., 2016a; Gajić et al., 2019; Ilić et al., 2020; Aleksić et al., 2020), while the number of reports on feline endoparasitoses is significantly lower (Lažetić et al., 2012; Pavlović and Terzin, 2012; Gajić et al., 2014; Ilić et al., 2017; Stepanović et al., 2020; Pavlović and Tasić, 2023).

Since previous research in Serbia has not paid sufficient attention to the study of cat parasitoses, the aim of this study is to provide new information on the etiopathogenesis

of *J. pasqualei* cestode and to indicate the need for investigation of the presence of this parasite in cats in Serbia.

In Serbia's epizootiological area, populations of intermediate hosts live, and climatic conditions are optimal for the appearance, maintenance, and spread of this cestode, which has already been established in Albania (Knaus et al., 2011) and Greece (Gianelli et al., 2017; Symeonidou et al., 2018), which is why *J. pasqualei* can be expected in cats in Serbia. Also, among exotic pets, various species of lizards are increasingly kept, in which finding cysticercoids would confirm the possible presence of adult forms of this cestode in cats. In research on the presence of parasites in Serbia, in addition to domestic cats, wild cats, and other wild carnivores should be examined as potential reservoirs of infection.

Etiopathogenesis of *Joyeuxiella pasqualei* (Cyclophyllidea: Dipylidiidae) cestode infection

The genus *Joyeuxia* was initially named by Lopez-Neira (1927) for all tapeworms possessing morphological characteristics similar to *Dipylidium*. Since this name was already in use for a sponge genus, Fuhrmann (1935) changed the name of the tapeworm genus to *Joyeuxiella*. Subsequently, Jones (1983) redescribed the genus and recognized three species: *Joyeuxiella pasqualei, Joyeuxiella fuhrmanni*, and *Joyeuxiella echinorhinchoides*. The species *Joyeuxiella domestica*, described in domestic cats in India (Deshmukh, 1990), was morphologically identical to the already established species, *J. pasqualei*.

Morphological characteristics of the parasite. *J. pasqualei* measures 3-10 cm in length (occasionally up to 30 cm) and 0.7-2.45 cm in width. The scolex bears a retractable rostellum with rows of curved, hook-like spines and four suckers resembling cups (Diamare, 1893; Fuhrmann, 1935; Hosseini et al., 2020). The genital pores are located on the lateral sides in the anterior part of the proglottid. Gravid proglottids contain eggs located laterally and medially to the excretory ducts. Egg capsules (capsula ovifera) contain individual eggs with an embryonated hexacanth embryo with three pairs of hooks (Blagburn and Todd, 1986).

Parasite life cycle. Adult tapeworms live in the small intestines of definitive hosts (cats, dogs, foxes, wolves, and other carnivores). The parasite's life cycle is indirect, and cats become infected by ingesting infected primary hosts (coprophagic insects) or secondary intermediate hosts (reptiles and small mammals) (Soulsby, 1968; Bowman et al., 2002), in whose peritoneal cavity and liver, or sometimes in muscles or beneath the skin, infective larval forms of the parasite (cysticercoids) are found (Witenberg, 1932). Secondary hosts can be domestic geckos (*Hemidactylus frenatus*), ground lizards (*Oblepharus boutoni*) (Talbot, 1970), small mammals, like shrews (*Crocidura suaveolens*), and rarely snakes (Schuster, 2020). The Etruscan shrew (*Suncus etruscus*) could also play a role as a secondary intermediate host or paratenic host through cannibalism (similar to the life cycle of *Mesocestoides* spp.) (Galán-Puchades et al., 2021) (Figure 1).



Figure 1. Life cycle of cestode Joyeuxiella pasqualei (Original)

Pathogenic action of the parasite. Adult forms of *J. pasqualei* are attached to the intestinal mucosa distally from the duodenum and can periodically be found along the entire length of the small intestine (Blagburn and Todd, 1986), causing vasodilation, congestion, hemorrhage, and necrosis with destruction of intestinal villi and degeneration of the lamina propria, as well as epithelial hyperplasia and diffuse infiltration by lymphocytes and other mononuclear cells (Hosseini et al., 2020). Subacute and chronic catarrhal enteritis accompany an increase in the number of active goblet cells and increased secretion of mucous exudate, as well as pronounced hyperplasia of the gastrointestinal-associated lymphoid tissue (GALT) accompanied by the formation of large lymphoid follicles in the intestinal submucosa (Mohamed et al., 2021).

Low-intensity infections with *J. pasqualei* mostly progress asymptomatically, with no significant impact on the health status of cats. In cases of high-intensity infections, the pathogenic action of the adult forms of the parasite in the digestive tract leads to poor food conversion with loss of body weight and poor coat quality, significantly compromising the health and welfare of cats (Hosseini et al., 2020). Diagnostic failures by clinicians and parasitologists can result in prolonged parasitism of this cestode in cats, with possible economic losses that could adversely affect cat breeding facilities in cases of more serious infections (Pavlović, 2023).

Geographic distribution of the cestode Joyeuxiella pasqualei

The larval stages and adult forms of *J. pasqualei* were initially discovered in Mediterranean countries. The disease has been diagnosed in cats in Southern European countries with varying prevalences ranging from individual cases in Berlin (Schuster and Montag, 2000) to 0.1% in Southern Germany (Barutzki and Schaper, 2003), 0.39% in Austria

(Supperer and Hinaidy, 1986), 3.4-39.8% (Papazoglou et al., 2006) and 1.2-10.2% (Gianelli et al., 2017; Symeonidou et al., 2018) in Greece, 7% in Cyprus (Diakou et al., 2017), 76% in wild cats (Hosseini et al., 2020), and 21-80.3% in domestic cats in Spain (Millan and Casanova, 2007, 2009; Santana-Hernández and Rodriguez-Ponce, 2019), with reported cases of infections in 11.1% of cats in Albania (Knaus et al., 2011), 2.7-50% in Turkey (Yaman et al., 2006; Öter et al., 2011), and 16.4% in Portugal (Waab et al., 2014).

On the Asian and African continents, this cestode has been discovered in Georgia, Uzbekistan, Kazakhstan, and Southern Russia (Kozlov, 1977), Iraq (Daoud et al., 1988; Al-Rammahi et al., 2014; Al-Rubaie et al., 2015), Iran (Borji et al., 2011), Kuwait (El-Azazy et al., 2016), India (Das et al., 2011), the United Arab Emirates (Schuster et al., 2009), and South Africa (Minnaar and Krecek, 2001), while in the USA, it has only been found as imported cases in cats that stayed in Nigeria (Linquist and Austin, 1981) or Saudi Arabia (Blagburn and Todd, 1986).

The prevalence of *J. pasqualei* in stray cats ranged from 10% in Iran (Changizi et al., 2007), 26-58.3% in Iraq (Al-Obaidi, 2012), 38.3% in Kuwait (El-Azazy et al., 2016), 55.2% in Spain (Calvete et al., 1998), and to 65.8% in Dubai (Schuster et al., 2009). It has also been diagnosed in 8.3% of dogs in Turkey (Aydenizoz, 1997) and in 27.3% of foxes, and 30% of jackals in Iran (Dalimi et al., 2006).

Knowledge of the geographical distribution of morphologically similar genera of cestodes (*Joyeuxiella* and *Diplopylidium*) is important for differential diagnosis. The causative agents from these genera are not always identified to the species level due to difficult interspecific differentiation, especially between *J. pasqualei* and *J. fubrmanni* in cases of fresh infections or when solely coprological diagnostics are performed (Diakou et al., 2017; Schuster, 2020). On the European continent, besides *J. pasqualei*, *Diplopylidium acanthotetra* (Italy, Spain) is also present, which is distributed in Tunisia, Algeria, and Palestine, as is *Diplopylidium nölleri* (Spain), which was discovered in Kazakhstan and later detected in Egypt and Palestine. Both species have been found in Turkmenistan in domestic cats and in Azerbaijan, Uzbekistan, Turkmenistan, and Kazakhstan in domestic and wild cats, dogs, wolves, and foxes (Kozlov, 1977). A poorly described species, *Diplopylidium genettae*, was found in a genet in the London Zoo, with no specific country of origin mentioned (Beddard, 1913; Schuster, 2020).

Joyeuxiella echinorhynchoides was first described in Fennec foxes in Egypt, after which it was detected in foxes in Georgia, Uzbekistan, and Tajikistan (Kozlov, 1977), in Corsica (Jordi et al., 2005), Spain (Sanchis Moronis, 2015), and in Saudi Arabia (Alagali et al., 2011), in foxes, wolves, jackals (Arbabi et al., 2004), dogs (Nabavi et al., 2014), and cats (Arbabi and Hooshyar, 2009) in Iran, as well as in jackals (South Africa), wolves (Palestine), Indian gerbils (Iran), and Fennec foxes (USA) (Hosseini et al., 2020). In the last 30 years, *J. fuhrmanni* has been found only in cats in South Africa (Baker et al., 1989) and in Dubai (Schuster et al., 2009; Schuster et al., 2016), while species such as *Joyeuxiella rossicum, Diplopylidium skrjabini, Diplopylidium monoophorum, Diplopylidium*

gervaisi, and *Diplopylidium zschokkei* have not been reported for more than three decades (Kozlov, 1977; Schuster, 2020).

Clinical and parasitological parameters important for diagnosing joyeuxiellosis in cats

Clinical suspicion of joyeuxiellosis in cats can be based on anamnestic data and clinical presentation. Anamnestic data on the cat's lifestyle acquired from the owner (diet, housing conditions, ability to roam unsupervised) can be particularly important for raising suspicion of this cestode infection (Pavlović, 2023).

Clinical examination is not a reliable diagnostic parameter for detecting this cestodiasis, as it often presents asymptomatically or with nonspecific symptoms in cats, but it can serve to raise justified suspicion of this condition. The severity of clinical symptoms and the harmful effects of the parasite depend on the degree of infection with adult tapeworms. In cases of high-intensity *J. pasqualei* infections in cats, intestinal invagination can occur (Agrawal and Pande, 1979).

Papazoglou et al. (2006) reported a clinical case in which a cat with respiratory and digestive issues underwent medial laparotomy under general anesthesia. Examination of the abdominal cavity revealed intestinal invagination, resulting from the ingestion of a linear foreign body, and parasites were observed upon opening the pylorus. Parasitological examination identified and determined the adult forms of *J. pasqualei*. Recovery lasted for 2 days, and the animal was orally treated with 25 mg praziquantel to eliminate residual parasites.

Since the parasites were fixed with rostellar hooks in the cranial part of the digestive tract, their free ends were oriented distally under the influence of peristaltic waves, causing the intestine to fold around the parasites. Radiographically and surgically, intestinal invagination caused by the presence of *J. pasqualei* was evident, without clinical signs of intestinal obstruction (Papazoglou et al., 2003). Native radiography usually cannot detect parasites, but the application of barium on the image easily reveals the characteristic defects caused by larger parasites (Farrow, 2003).

For these reasons, Papazoglou et al. (2006) suggest that the cestode *J. pasqualei* should be included on the list of causative agents of importance for the differential diagnosis of intestinal invagination in cats.

A reliable **ante-mortem diagnosis is** made by coprological examination, which always starts with a macroscopic examination of the cat's feces to detect excreted proglottids (Figure 2A) (Linquist and Austin, 1981). For detailed microscopic analysis, it is necessary to disintegrate gravid proglottids in a small amount of physiological saline or water to release characteristic eggs. Each proglottid of *J. pasqualei* has two genital openings and one egg in the capsule ovifera (Blagburn and Todd, 1986).

A **post-mortem diagnosis** is made by parasitological section, with the aims of finding adult forms of this cestode in the intestines, pathological changes caused by it, and typical findings on histopathological examination (Hosseini et al., 2020).

Since infections of cats with the cestode *J. pasqualei* are generally of low intensity, it happens that even resulting pathomorphological changes are not very pronounced or are completely absent. In cases of high-intensity infections, subacute and chronic catarrhal enteritis accompanied by necrosis and destruction of intestinal villi are observed at necropsy (Mohamed et al., 2021).

Adult forms of tapeworms collected at necropsy are identified and determined according to the characteristic appearance of the scolex with four hooks and a retractable rostellum (Blagburn and Todd, 1986). According to conventional helminthological techniques, cestodes are first fixed in 70% ethanol and stained for the next 24 hours. Then, they are partially degraded with acidic alcohol, dehydrated in an alcohol series of different dilutions, cleaned with xylene, and fixed in Canada balsam between a microscopic slide and a cover slip. Before staining the adult forms of cestodes, the last gravid proglottids are separated to carry out the morphological identification of cestode eggs, as the staining and dehydration process tends to change the morphology of the eggs. The last gravid proglottids are placed on a slide with a drop of lactophenol, then disintegrated to release the eggs (Galán-Puchades et al., 2021).

Differential diagnosis. The adult parasite *J. pasqualei* morphologically resembles the species *Dipylidium caninum*, making it easy to confuse them during diagnosis. Species from the genus *Joyeuxiella* differ from those from the genus *Dipylidium* in that each gravid proglottid of *Joyeuxiella* contains one embryo covered with uterine material (Figure 2B). They mainly differ from species of the genus *Diplopylidium* in the appearance of hooks, which in the genera *Joyeuxiella* and *Dipylidium* have a thorny shape, while in the genus *Diplopylidium*, they are hammer-shaped (Diamare, 1893; Fuhrmann, 1935).



Figure 2. A) Proglottids of *Joyeuxiella pasqualei*; B) Eggs of *Joyeuxiella pasqualei* (Photo by Nemanja M. Jovanovic)

Molecular genetic studies have shown that DNA sequences obtained from *J. pasqualei* have the highest similarity in nucleotides with species from the genera *Versteria* and *Echinococcus*, Raillietina sonini, Taenia polyacantha, and *D. caninum* (Bezerra-Santos et al., 2022).

In previous research on carnivore parasitosis in Serbia, attention has mainly been drawn to causative agents important for the differential diagnosis of certain cardiorespiratory and urinary nematodes in dogs (Ilić et al., 2015; Ilić et al., 2021; Jovanović et al., 2023; Ilić et al., 2023). Since the cestode *D. caninum* can parasitize both dogs and cats, while *J. pasqualei* only affects cats, special attention should be paid to detailed parasitological examinations, including macroscopic examination of feces and identification and determination of adult forms of intestinal parasites in cats.

Control of joyeuxiellosis in cats

Therapy. The efficacy of praziquantel at a dose of 25 mg/kg body weight at 6-week intervals has been proven for the treatment of infections caused by *J. pasqualei* in domestic cats (Blagburn and Todd, 1986; Schuster and Montag, 2000). Several consecutive treatments with praziquantel at a dose of 5 mg/kg body weight only lead to temporary cessation of proglottid shedding (Dorchies et al., 1980).

A high level of efficacy (>99%) against adult forms of *J. pasqualei* and *J. fuhrmanni* has been demonstrated by a formulation containing a combination of 8.3% w/v fipronil, 10% w/v (S)-methoprene, 0.4% w/v eprinomectin, and 8.3% w/v praziquantel, which is registered for the therapy and/or prevention of numerous cat parasitoses (Schuster et al., 2016). Initially, this formulation showed pronounced efficacy against most species of cestodes parasitizing cats, such as *D. caninum*, *Hydatigera taeniaeformis*, and *Echinococcus multilocularis* (Knaus et al., 2014; Tielemans et al., 2014; Rehbein et al., 2014).

Prevention. Animals at the highest risk of joyeuxiellosis include: (i) animals living in breeding facilities, shelters, or households with multiple cats; (ii) cats living outdoors or occasionally going outdoors, where they can come into contact with intermediate hosts (reptiles or small mammals); and (iii) cats with owners who take them when traveling to countries endemic for this helminthiasis or during transport through these regions (ESCCAP, 2021).

Since in infections caused by *J. pasqualei*, proglottids with eggs are excreted via feces into the external environment, controlling the developmental stages in the environment is essential to reduce the likelihood of infection in intermediate hosts and other animals. Wild cats and stray cats serve as reservoirs for this cestode, and infection of intermediate hosts (reptiles) contributes to the longer survival of developmental stages in the environment.

In order to prevent environmental contamination with parasites, it is necessary to implement comprehensive parasite control programs, including the following

measures: 1) daily and safe disposal of cat feces, which should not be disposed of in sewage or put into compost that will be used in vegetable gardens; 2) encourage the adoption of recommendations for safe disposal of feces in special containers or bags designated for this purpose; 3) conduct regular coprological examinations of owned cats 2-4 times a year; 4) based on the results of coprological examination, pay special attention to individual deworming of owned cats and planned deworming of stray cats (Figure 3); 5) assess the effectiveness of prevention measures and selected anthelmintic using quantitative coprological diagnostic methods (ESCCAP, 2021).



Figure 3. Scheme for individual deworming of cats (ESCCAP, 2021)

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Authors' contributions

IT wrote the manuscript with input from all authors. PJ prepared initial draft of the text and figures. NJ finalized the manuscript for submission. PJ, NJ, PS, KN critical revision.

Competing interests

The authors declare that they have no competing interests.

ORCID iDs

Tamara Ilić (D https://orcid.org/0000-0002-2813-6466 Jelena Pavlović (D https://orcid.org/0009-0000-4891-9073 Nemanja M. Jovanović (D https://orcid.org/0000-0003-1617-2862 Predrag Stepanović (D https://orcid.org/0000-0002-5351-7607 Katarina Nenadović (D https://orcid.org/0000-0003-4010-7964

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ZNAČAJ CESTODE *JOYEUXIELLA PASQUALEI* (CYCLOPHYLLIDEA: DIPYLIDIIDAE) ZA KLINIČKU PRAKSU I DOBROBIT MAČAKA

Tamara ILIĆ, Jelena PAVLOVIĆ, Nemanja M. JOVANOVIĆ, Predrag STEPANOVIĆ, Katarina NENADOVIĆ

Kratak sadržaj

Cestoda Joyeuxiella pasqualei je čest parazit mačaka u zemljama južne Evrope, a zbog sve izraženijih efekata globalnog zagrevanja postoji tendencija širenja i pojave ovog parazita i kod mesojeda u ostalim delovima evropskog kontinenta. U tankim crevima pravih domaćina (mačka, pas, lisica, vuk i drugi karnivori) lokalizovani su adultni oblici parazita. Mačka se inficira ingestijom primarnih (koprofagni insekti) i sekundarnih prelaznih domaćina (reptili i mali sisari), u kojima se nalaze infektivni larveni oblici parazita (cisticerkoidi). Kod većine inficiranih životinja oboljenje protiče asimptomatski. Izuzetak su infekcije visokog intenziteta, kada adulti parazita adhezijom za crevnu mukozu dovode do nekroze crevnih resica, invaginacije i parcijalne opstrukcije creva, značajno narušavajući zdravstveno stanje i dobrobit mačaka. Uspešan tretman se postiže primenom prazikvantela, a u cilju profilakse potrebno je sprečiti kontakt mačaka sa populacijama prelaznih domaćina. Podaci o etiopatogenezi, dijagnostici i suzbijanju ove pantljičare od posebnog su značaja za neiskusne dijagnostičare, koji zbog nedovoljne informisanosti o parazitizmu *J. pasqualei* mogu napraviti grube greške u postavljanju kliničke dijagnoze. Zbog značaja za kliničku praksu i dobrobit mačaka, neophodno je da se ova cestoda uvrsti u diferencijalnu dijagnozu crevne invaginacije kod mačaka i drugih cestoda mesojeda, koje prouzrokuju vrste iz rodova Diplopylidium i Dipylidium.

Ključne reči: mačka, Joyeuxiella pasqualei, dijagnostika, kontrola, dobrobit