Research in Veterinary Science 136 (2021) 151–157

Contents lists available at ScienceDirect

Research in Veterinary Science

journal homepage: www.elsevier.com/locate/rvsc

Zoonotic Sarcocystis

Benjamin M. Rosenthal *

Animal Parasitic Disease Laboratory, United States Department of Agriculture- Agricultural Research Service, 10300, Baltimore Avenue, Beltsville, MD 20705, United States of America

ARTICLE INFO

Keywords:
Enteritis
Zoonoses
Sarcocystis
Sarcocystosis
Myositis
Food-borne illness

ABSTRACT

Apicomplexan species in the genus *Sarcocystis* form tissue cysts, in their intermediate hosts, similar to those established in chronic toxoplasmosis. More than 200 species are known, but just a few are known to threaten human health owing to infection in livestock species. Intestinal sarcocystosis occurs when people consume raw or undercooked beef contaminated with *Sarcocystis hominis* or *S. heydorni* or undercooked pork contaminated with *S. suihominis*. Those infections may cause mild enteritis, but most infections are thought to be asymptomatic. People also become dead-end (intermediate) hosts for non-human *Sarcocystis* spp. after accidentally ingesting sporocysts, leading to extraintestinal sarcocystosis. The clinical spectrum may range from asymptomatic muscle cysts to a severe, acute, eosinophilic myositis associated with systemic symptoms with peripheral eosinophilia. Most human cases have been described from Southeast Asia, but *Sarcocystis* parasites have a worldwide distribution, especially where livestock is raised, and human infections in other areas have been described but may be underrecognized.

1. Introduction

Apicomplexan parasites in the genus *Sarcocystis* cycle between predators and prey. Predators (and scavengers) become infected by consuming tissues harboring intracellular tissue cysts (sarcocysts). Such predators experience gastrointestinal (GI) infections and the development of sexual stages which mate and produce oocysts which the host then excretes. In so doing, these carnivores serve as "definitive hosts." Herbivorous "intermediate hosts" acquire infection by ingesting food or water contaminated with the excreted oocysts. They support asexual parasite reproduction, culminating in the formation of tissue cysts (sarcocysts). More than 200 known species of *Sarcocystis* cycle in non-human hosts (Dubey et al., 2016). Some cycle efficiently between domesticated livestock (intermediate) hosts and in domestic canine or feline (definitive) hosts. Only three are known to cycle between livestock intermediate hosts and human definitive hosts: *Sarcocystis hominis, Sarcocystis heydorni,* and *Sarcocystis suihominis*. Human beings also sustain infections with parasites capable of causing tissue cysts, though the range of species capable of doing so (and the cycles that sustain them) remain less well understood. This review focuses on those species of *Sarcocystis* established or suspected of causing human disease.

When people consume undercooked beef containing sarcocysts they can become definitive hosts of *Sarcocystis hominis* (Ahmadi et al., 2015; Chen et al., 1999; Chen et al., 2003; Domenis et al., 2011; Dubey et al., 1988; Dubey et al., 1989; Hajimohammadi et al., 2014; Heydorn et al., 1975; Lian et al., 1990; Nimri, 2014; Nourani et al., 2010; Saito et al., 1999; Vangeel et al., 2007; Wouda et al., 2006) or *S. heydorni* (Fig. 1). The former produces thick-walled cysts in cattle tissue and has a predilection for heart muscle, whereas the latter forms thin-walled cysts that express distinctive, short protrusions from the cyst wall (Dubey et al., 2015a; Hu et al., 2016). Consuming undercooked pork can cause human infections with *S. suihominis* (Calero-Bernal et al., 2016; Chauhan et al., 2020; Coelho et al., 2015; Fayer et al., 1979; Gazzonis et al., 2019; Heydorn, 1977; Heydorn and Mehlhorn, 1978; Heydorn and Weniger, 1988; Huang et al., 2019; Li et al., 2007; Li et al., 2004; Mehlhorn and Heydorn, 1977, 1979; Saito et al., 1998). These generally result in transient infections restricted to the gastrointestinal tract. Light microscopy suffices to differentiate thick from thin-walled sarcocysts in a given host, but further differential diagnosis relies on ultrastructural differences in the sarcocyst wall only discernable at the greater magnification afforded by electron microscopy (exemplified for two species occurring in pork in Fig. 3) or using genetic differentiation (discussed further, below).

Although parasites in the genus *Sarcocystis* have a worldwide distribution, our understanding of the epidemiology of human sarcocystosis relies primarily on case reports and occasional outbreaks from

* Corresponding author.
E-mail address: benjamin.rosenthal@usda.gov.

https://doi.org/10.1016/j.rvsc.2021.02.008
Received 10 June 2020; Received in revised form 25 January 2021; Accepted 4 February 2021
Available online 19 February 2021
0034-5288/Published by Elsevier Ltd.

Southeast Asia. Malaysia and Thailand are known foci of transmission; there, limited seroprevalence studies and stool surveys confirm widespread distribution and exposures, and suggest human infections are underreported (Wilairatana et al., 1996; Wong and Pathmanathan, 1992). Incidental findings at autopsy suggest widespread infection in endemic areas. In one study of routine autopsy material, infection prevalence was estimated at more than 20% (Wong and Pathmanathan, 1992). In Iran, sporocysts of *Sarcocystis* were identified (alone or in conjunction with other parasites) in 4 of over 2000 undiagnosed cases of abdominal distress (Agholi et al., 2016). This underscores the effort that may need to be devoted to truly defining prevalence in a population.

Sarcocystis nesbitti, a parasite initially described from tissue cysts in rhesus macaques (Mandour, 1969; Yang et al., 2005), was suspected on phylogenetic grounds as having a predatory snake as its definitive hosts (Tian et al., 2012). That suggestion proved helpful when seeking the source of large outbreaks of human infections attributed to *S. nesbitti* (Abubakar et al., 2013; Lau et al., 2014; Shahari et al., 2016). A toxin isolated from *S. fayeri* appears responsible for food poisoning in people who have consumed raw horsemeat (Kamata et al., 2014). Fig. 4 depicts sarcocysts obtained from biopsies from three human subjects infected with parasites attributed to *S. nesbitti*.

By domesticating livestock, human beings have created conditions that favor the evolution of parasites exploiting our proximity to cattle and pigs and our consumption of their meat. The likeliest sources of exposure to tissue cysts of other, as-yet undiscovered species of *Sarcocystis* would seem to be other domesticated livestock (such as poultry, goats, sheep, and reindeer). People do eat a wide range of other animals; wildlife, too, may harbor as-yet undiscovered zoonotic species for which people might serve as definitive hosts. Accidental human infection with parasites that naturally cycle between our prey and their natural

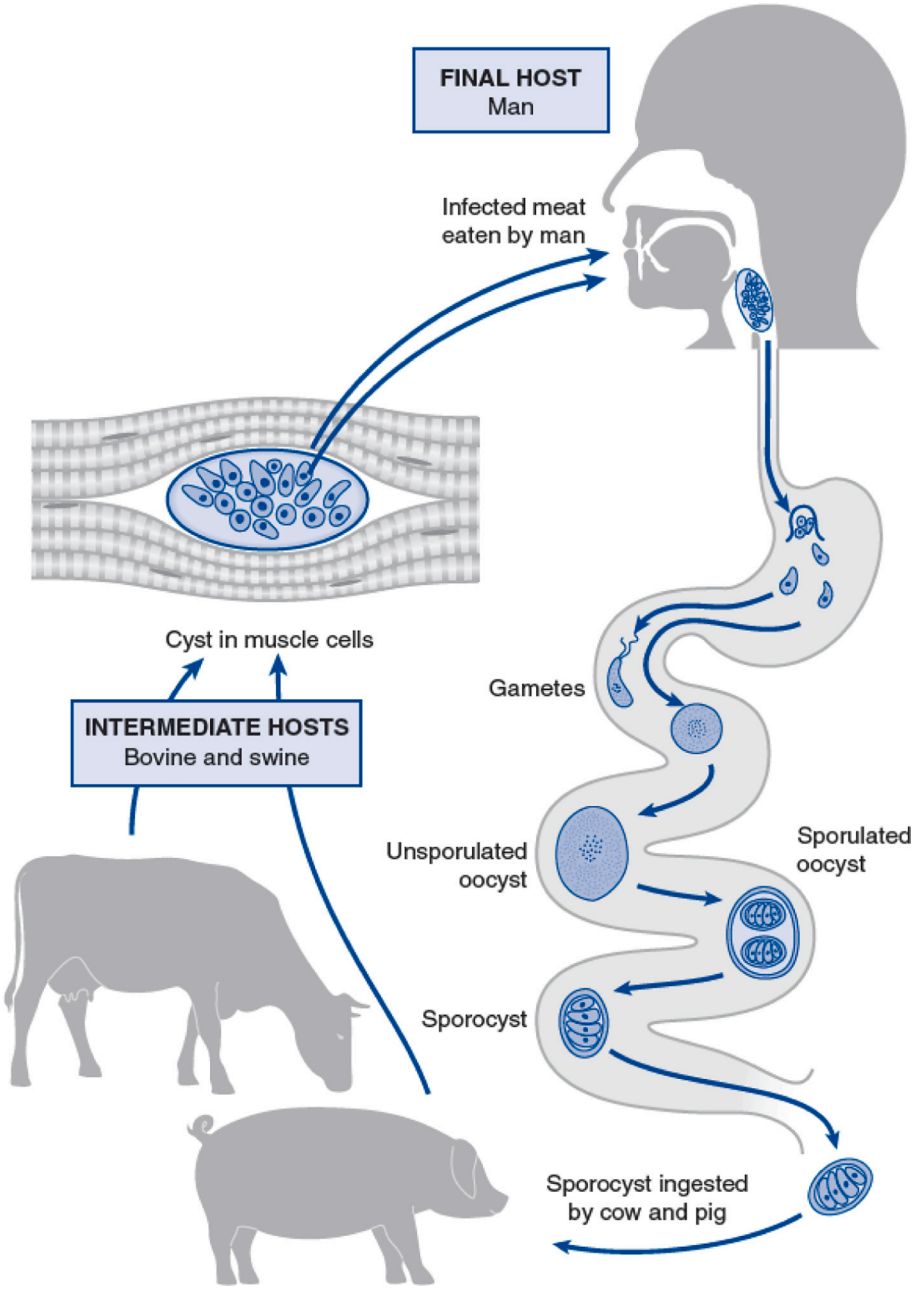

Fig. 1. Schematic representation of the life cycle of *Sarcocystis hominis* and *S. suihominis*. (Reproduced with permission from Murrell KD, Fayer R, Dubey JP. Parasitic organisms. Advances in meat research. West Port, CT: AVI Publishing Co. 1986.) Like *S. hominis, S. heydorni* cycles between people and cattle. Predatory snakes are definitive hosts for *S. nesbitti*, excreting oocysts that engender sarcocysts in human tissues.

predators cannot be ruled out. Nor can we rule out the possibility that other forms of *Sarcocystis* may imperil human health when we ingest sporcysts excreted by other carnivores. Such concern is underscored by documented illness suffered by aberrant infections in hosts believed not to naturally sustain cycles of a given parasite's transmission (for example, equine parasitic myeloencephalitis, which horses contract by grazing on pastures contaminated with sporocysts of *Sarcocyistis neurona* excreted by opossums; disease in horses can be severe, but raccoons, armadillos, and other naturally-infected mammals more typically harbor tissue cysts infectious for opossums).

2. Pathogenesis

Sarcocystis parasites are intra-cellular coccidian parasites. *S. hominis, S. heydorni,* and *S. suihominis* use humans as definitive hosts and are responsible for intestinal sarcocystosis in the human host. Humans may also become dead-end hosts for non-human *Sarcocystis* spp. after the accidental ingestion of oocysts.

Individual sporocysts, and sporulated oocysts (each containing two sporocysts) are excreted. Each sporocyst contains four sporozoites and a refractile residual body. Sporocysts ingested by the intermediate host (cattle for *S. hominis* and *S. heydorni* and pigs for *S. suihominis*) rupture, releasing sporozoites. Sporozoites enter endothelial cells of blood vessels and undergo schizogony, resulting in first-generation schizonts. Merozoites derived from the first generation invade small capillaries and blood vessels, becoming second-generation schizonts. Second-generation merozoites invade skeletal and heart myocytes, as well as neurons, and develop into metrocytes and undergo a series of internal mitotic divisions (a process termed endodyogeny). When filled with bradyzoites, the metrocytes becomes a sarcocyst which can withstand digestion (Fig. 2).

Pathogenesis of intestinal human infections has been described in human volunteers who were infected by arguably abnormally large numbers of sarcocysts. After several days, and for several days thereafter, infected persons excreted oocysts and infective sporocysts. Although people can experience lengthy, indeed lifelong, infection with tissue stages (sarcocysts), the identity and origins of those parasites is unclear. Excellent, illustrated reviews of zoonotic sarcocystosis are available (Dubey et al., 2016; Dubey and Fayer, 1983; Fayer, 2004; Fayer et al., 2015). The complete genome of a single enzootic species (*S. neurona*) serves as a model to explore biology and pathogenesis (Blazejewski et al., 2015; Murungi and Kariithi, 2017).

3. Clinical manifestations

3.1. Enteric infection

Most individuals with intestinal sarcocystosis remain asymptomatic. Symptoms induced by experimental infections include nausea, abdominal discomfort, and self-limited diarrhea, with symptom severity varying with the amount of meat consumed (Beaver et al., 1979; Fayer, 2004; Jeffrey, 1974). The onset of diarrhea is typically sudden (in some subjects 3–6 h post-ingestion; usually within 48 h). Symptoms usually resolve within 36 h. Segmental, eosinophilic, necrotizing enteritis attributed to sexual forms of *Sarcocystis* has been reported; however, *Sarcocystis* was not definitely established as the cause for these symptoms (Bunyaratvej et al., 2007).

3.2. Muscle infection

As with gastrointestinal infection, cases of extraintestinal sarcocystosis typically lack symptoms. When people ingest sporocysts, the release of meronts to the endothelium and subsequent merozoite invasion of striated muscle can induce vasculitic and/or musculoskeletal symptoms. In an outbreak of eosinophilic myositis in a U.S. military unit operating in Malaysia, 7 of 10 exposed personnel reported an acute illness consisting of fever, myalgia, bronchospasm, fleeting pruritic rashes, transient lymphadenopathy, and subcutaneous nodules associated with eosinophilia, elevated erythrocyte sedimentation rate, and elevated hepatic enzymes and muscle creatinine kinase (Arness et al., 1999). One patient had serious, chronic sequelae; the other team members had milder, self-limited illnesses. A muscle biopsy of the index case showed an unidentified *Sarcocystis* species. In a recent outbreak in Tioman Island, Malaysia involving 93 suspected cases, including 2 cases confirmed as harboring tissue cysts of *S. nesbitti*, the most frequent symptoms were fever, myalgia, headache, and cough (Abubakar et al., 2013; Lau et al., 2014; Shahari et al., 2016).

Symptomatic cases can experience painful muscle swelling, measuring 1 to 3 cm in diameter and initially associated with erythema of the overlying skin; these occur episodically and last from 2 days to 4 weeks. Sometimes, lesions are accompanied by fever, diffuse myalgia, muscle tenderness, weakness, eosinophilia, and bronchospasm. A discharging sinus, painful swelling with erythema, an ill-defined mass, and chronic pain with ulceration have been reported from New Zealand (Mehrotra et al., 1996).

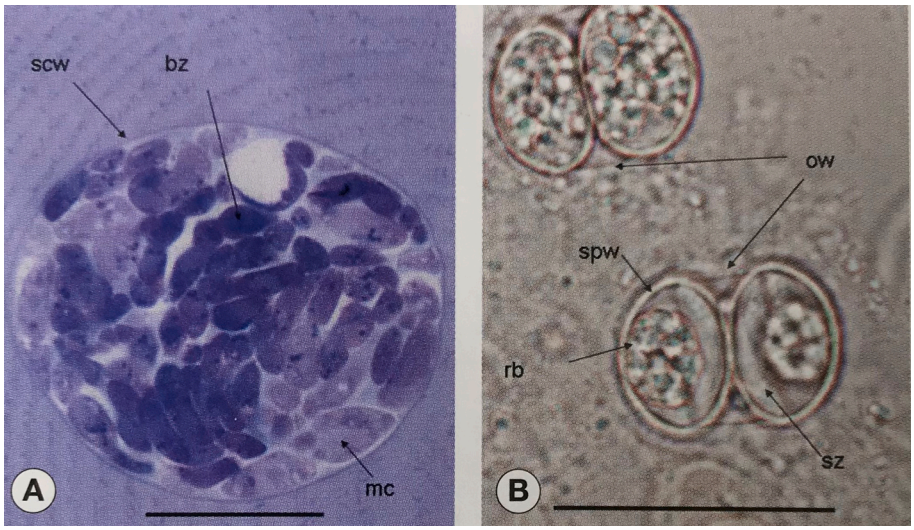

Fig. 2. Photomicrographs of *Sarcocystis muris,* an enzootic species of *Sarcocystis* that exemplifies features also found in zoonotic forms. (A) Developing sarcocyst in muscle tissue. Immature metrocytes (mc) and mature bradyzoites (bz) are enclosed by the sarcocyst wall (scw). (B) Two unsporulated oocysts (top left) and two sporulated oocysts (bottom right). In sporulated oocysts, sporozoites (sz) and residuum bodies (rb) are enclosed by the prominent sporocysts wall (spw), which, in turn, are paired within the oocyst wall (ow). In many instances, unpaired sporocysts will be recovered from ruptured oocysts. The scale bar denotes 20 μm.

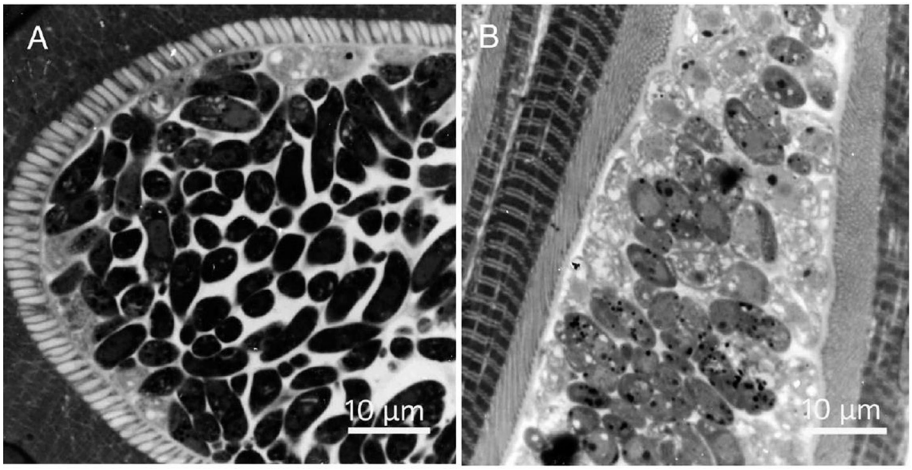

Fig. 3. The structure of the sarcocyst wall aids differential diagnosis of co-infecting species. Here, two sarcocysts in pig muscles are depicted. On the left, *S. miescheriana* for which dogs serve as the definitive host. On the right, *S. suihominis* for which people serve as the definitive host. Note the villar protrusions on the sarcocyst wall are thinner and longer for *S. suihominis*. (Dubey et al., 2016).

3.3. Diagnosis

Visible spooocysts (each containing four sporozoites) and sporulated oocysts (each containing two sporocysts) appear in microscopically in freshly voided stool specimens with the aid of flotation procedures. The acid-fast oocysts of *Sarcocystis* resemble those of *Isospora*. Oocysts lack features enabling their differential diagnosis via microscopy; they typically measure 15 × 20 µm, and sporocysts measure 12 × 6 µm. Visible trophozoites or bradyzoites in biopsy tissue also confirm diagnosis.

Genetic variation provides a basis to discriminate among excreted parasites (Xiang et al., 2009). The 18S rDNA was the first locus sequenced for species in the genus and affords modest resolution for differentially diagnosing members of the genus and for reconstructing their phylogeny. More recently, more variable markers such as ribosomal ITS-1 and mitochondrial cytochrome oxidase have enriched the understanding of parasite diversity, relationships, and transmission cycles (Abe et al., 2019; Antunes Murata et al., 2018; Cerqueira-Cezar et al., 2018; Cerqueira-Cezar et al., 2017; Dahlgren et al., 2008; Dubey et al., 2015b; Gjerde, 2012, 2013; Gjerde et al., 2020; Gjerde et al., 2017a; Gjerde et al., 2017b; Rubiola et al., 2018; Valadas et al., 2016; Zeng et al., 2018).

Muscle biopsy can definitively attribute myositis to *Sarcocystis* infection after excluding other muscle cyst-forming organisms, such as *Toxoplasma gondii* and *Trypanosoma cruzi*. Sarcocysts are septate and contain ultrastructurally distinct cyst walls. Bradyzoites of *Sarcocystis* and *T. gondii* stain with periodic acid–Schiff, but *T. cruzi* does not. Intact sarcocysts can measure up to 100 µm in diameter and 325 µm in length, but are more often in the 20 to 60 µm range and are do not generally induce inflammatory reactions in the surrounding tissue. However, mild inflammatory reactions can cause pain (Mehrotra et al., 1996). In the absence of muscle biopsy, eosinophilia in the presence of a compatible clinical syndrome and epidemiologic exposure support a probable diagnosis, especially if other diagnoses can be excluded. The chronic nature of sarcocyst infections and the cross-reactivity of sarcocyst antigens with those of related species renders serology of uncertain diagnostic value (Garcia-Lunar et al., 2015; Gondim et al., 2017; O'Donoghue and Weyreter, 1984; Weber et al., 1983; Weyreter and O'Donoghue, 1982). Studies of adults in rural areas of Laos and Tibet document seroprevalence of 10% - 20% (Xiang et al., 2009).

3.4. Treatment

The terminally differentiated organisms in muscle sarcocysts do not spread to new cells; treatments directed toward replicating stages do not harm these mature stages. Although various treatments have been used for symptomatic muscular infection, none have demonstrated efficacy, and no specific treatment for *Sarcocystis* infection has been described. Palliative treatment for symptoms can include corticosteroids, to reduce episodic allergic inflammatory reactions after cyst rupture or to alleviate more chronic, systemic symptoms. Cotrimoxazole treatment, especially when initiated early, shortened the duration of symptoms in a small cohort (Slesak et al., 2015). Because the intra-cystic bradyzoites do not spread, there seems no risk of recrudescence.

3.5. Prevention

Presumably, muscle infections could be prevented by avoiding food contaminated with feces of predatory carnivores and boiling water so contaminated. Avoiding raw or undercooked beef and pork prevents enteric infection with any of the three known species for which people serve as definitive hosts. Sarcocysts in pork can be destroyed at 60 °C for 20 min, 70 °C for 15 min or 100 °C for 5 min, or by freezing it at −4 °C for 2 days or − 20 °C for 24 h. This is in keeping with general CDC guidelines which recommend cooking all non-poultry meat to an internal temperature of 71 °C. Sporocysts and oocysts die when heated to 60 °C for 1 min, 55 °C for 15 min, or 50 °C for one hour, but can survive freezing. Commonly used disinfectants (e.g., 1% iodine, 10% formalin, 12% phenol, 2% chlorhexidine) fail to kill *S. neurona* sporocysts, but 5.25% sodium hydroxide (bleach) suffices (Dubey et al., 2002).

4. Public health burden

The full extent of the public health burden of human sarcocystosis remains unclear. Although veterinary data implicate immune suppression as a clinical risk factor for sarcocystosis, and although pregnancy and AIDS markedly exacerbate toxoplasmosis (caused by a closely related zoonotic parasite), less is known about how vulnerability to sarcocystosis may vary in human populations. A clinical report described marked symptoms and documented various life stages of a 31 year old AIDS patient, recommending sarcocystosis be considered as an opportunistic pathogen in such persons (Velasquez et al., 2008).

Those who routinely consume uncooked meat and reside where untreated human waste contaminates pastures are at greatest risk (Bunyaratvej et al., 2007). However, the burden of these infectious in such impoverished populations has remains ill-defined. Surprisingly prevalent *S. hominis* in European cattle (Vangeel et al., 2007), but not in American cattle (Pritt et al., 2008), suggests that even among developed countries, variation in risk may occur. The true extent of infection

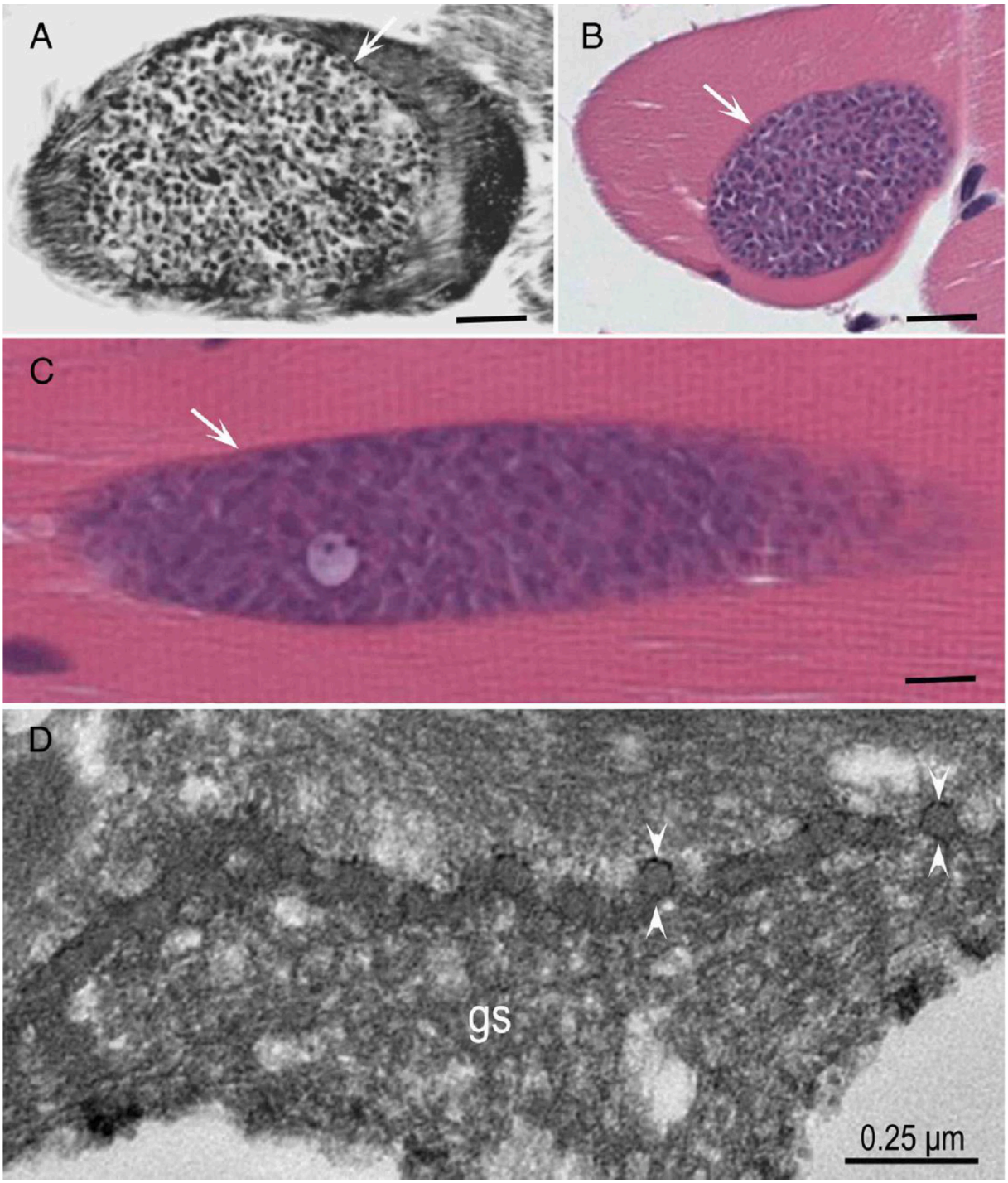

Fig. 4. Human muscular sarcocystosis attributable to *S. nesbitti*. A-C: light microscopy of cysts stained with hematoxalin and eosin; arrows indicate the thin sarcocyst wall. D: transmission electron micrograph illustrating small blebs and thin ground substance comprising the sarcocyst wall. (Dubey, 2015).

anywhere remains unclear, in part owing to the ubiquity of enzootic infections that pose no known risk to human health. Veterinary and human infections may exceed, in prevalence and consequence, that which is presently recognize, but the actual extent of public health burden remains ill-defined (Harris et al., 2015).

Declaration of Competing Interest

I have prepared this manuscript in the public interest with scientific integrity and effective open communication as my governing values. I have performed this work as a public servant and have no competing financial interests that influence what I have written or what I have omitted.

Acknowledgements

This work was funded by USDA Project "Detection and Control of Foodborne Parasites for Food Safety" 8042-32420-007-00-D.

References

Abe, N., Matsuo, K., Moribe, J., Takashima, Y., Baba, T., Gjerde, B., 2019. Molecular differentiation of five Sarcocystis species in sika deer (Cervus nippon centralis) in Japan based on mitochondrial cytochrome c oxidase subunit I gene (cox1) sequences. Parasitol. Res. 118, 1975–1979.

Abubakar, S., Teoh, B.T., Sam, S.S., Chang, L.Y., Johari, J., Hooi, P.S., Lakhbeer-Singh, H. K., Italiano, C.M., Omar, S.F., Wong, K.T., Ramli, N., Tan, C.T., 2013. Outbreak of human infection with Sarcocystis nesbitti, Malaysia, 2012. Emerg. Infect. Dis. 19, 1989–1991.

Agholi, M., Taghadosi, Z., Mehrabani, D., Zahabiun, F., Sharafi, Z., Motazedian, M.H., Hatam, G.R., Naderi Shahabadi, S., 2016. Human intestinal sarcocystosis in Iran: there but not seen. Parasitol. Res. 115, 4527–4533.

Ahmadi, M.M., Hajimohammadi, B., Eslami, G., Oryan, A., Yasini Ardakani, S.A., Zohourtabar, A., Zare, S., 2015. First identification of Sarcocystis hominis in Iranian traditional hamburger. J. Parasit. Dis. 39, 770–772.

Antunes Murata, F.H., Cerqueira-Cezar, C.K., Thompson, P.C., Tiwari, K., Mowery, J.D., Verma, S.K., Rosenthal, B.M., Sharma, R.N., Dubey, J.P., 2018. Sarcocystis cymruensis: discovery in Western hemisphere in the Brown rat (Rattus norvegicus) from Grenada, West Indies: redescription, molecular characterization, and transmission to IFN-gamma gene knockout mice via sporocysts from experimentally infected domestic cat (Felis catus). Parasitol. Res. 117, 1195–1204.

Arness, M.K., Brown, J.D., Dubey, J.P., Neafie, R.C., Granstrom, D.E., 1999. An outbreak of acute eosinophilic myositis attributed to human Sarcocystis parasitism. Am J Trop Med Hyg 61, 548–553.

Beaver, P.C., Gadgil, K., Morera, P., 1979. Sarcocystis in man: a review and report of five cases. Am J Trop Med Hyg 28, 819–844.

Blazejewski, T., Nursimulu, N., Pszenny, V., Dangoudoubiyam, S., Namasivayam, S., Chiasson, M.A., Chessman, K., Tonkin, M., Swapna, L.S., Hung, S.S., Bridgers, J., Ricklefs, S.M., Boulanger, M.J., Dubey, J.P., Porcella, S.F., Kissinger, J.C., Howe, D. K., Grigg, M.E., Parkinson, J., 2015. Systems-based analysis of the Sarcocystis neurona genome identifies pathways that contribute to a heteroxenous life cycle. mBio 6.

Bunyaratvej, S., Unpunyo, P., Pongtippan, A., 2007. The Sarcocystis-cyst containing beef and pork as the sources of natural intestinal sarcocystosis in Thai people. J. Med. Assoc. Thail. 90, 2128–2135.

Calero-Bernal, R., Perez-Martin, J.E., Reina, D., Serrano, F.J., Frontera, E., Fuentes, I., Dubey, J.P., 2016. Detection of zoonotic Protozoa toxoplasma gondii and Sarcocystis suihominis in wild boars from Spain. Zoonoses Public Health 63, 346–350.

Cerqueira-Cezar, C.K., Thompson, P.C., Verma, S.K., Mowery, J., Calero-Bernal, R., Antunes Murata, F.H., Sinnett, D.R., Van Hemert, C., Rosenthal, B.M., Dubey, J.P., 2017. Morphological and molecular characterization of Sarcocystis arctica-like sarcocysts from the Arctic fox (Vulpes lagopus) from Alaska, USA. Parasitol. Res. 116, 1871–1878.

Cerqueira-Cezar, C.K., Thompson, P.C., Murata, F.H.A., Mowery, J., Brown, J.D., Banfield, J., Rosenthal, B.M., Dubey, J.P., 2018. Histopathological, morphological, and molecular characterization of Sarcocystis species in elk (Cervus elaphus) from Pennsylvania, USA. Parasitol. Res. 117, 3245–3255.

Chauhan, R.P., Kumari, A., Nehra, A.K., Ram, H., Garg, R., Banerjee, P.S., Karikalan, M., Sharma, A.K., 2020. Genetic characterization and phylogenetic analysis of Sarcocystis suihominis infecting domestic pigs (sus scrofa) in India. Parasitol. Res. 119, 3347–3357.

Chen, X., Zuo, Y., Zuo, W., 1999. Observation on the clinical symptoms and sporocyst excretion in human volunteers experimentally infected with Sarcocystis hominis. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 17, 25–27.

Chen, X.W., Zuo, Y.X., Hu, J.J., 2003. Experimental Sarcocystis hominis infection in a water buffalo (Bubalus bubalis). J. Parasitol. 89, 393–394.

Coelho, C., Gomes, J., Inacio, J., Amaro, A., Mesquita, J.R., Pires, I., Lopes, A.P., Vieira-Pinto, M., 2015. Unraveling Sarcocystis miescheriana and Sarcocystis suihominis infections in wild boar. Vet. Parasitol. 212, 100–104.

Dahlgren, S.S., Gouveia-Oliveira, R., Gjerde, B., 2008. Phylogenetic relationships between Sarcocystis species from reindeer and other Sarcocystidae deduced from ssu rRNA gene sequences. Vet. Parasitol. 151, 27–35.

Domenis, L., Peletto, S., Sacchi, L., Clementi, E., Genchi, M., Felisari, L., Felisari, C., Mo, P., Modesto, P., Zuccon, F., Campanella, C., Maurella, C., Guidetti, C., Acutis, P. L., 2011. Detection of a morphogenetically novel Sarcocystis hominis-like in the context of a prevalence study in semi-intensively bred cattle in Italy. Parasitol. Res. 109, 1677–1687.

Dubey, J.P., 2015. Foodborne and waterborne zoonotic sarcocystis. Food Waterborne Parasitol. 1, 2–11.

Dubey, J.P., Fayer, R., 1983. Sarcocystosis. Br Vet J 139, 371–377.

Dubey, J.P., Fayer, R., Speer, C.A., 1988. Experimental Sarcocystis hominis infection in cattle: lesions and ultrastructure of sarcocysts. J. Parasitol. 74, 875–879.

Dubey, J.P., Speer, C.A., Charleston, W.A., 1989. Ultrastructural differentiation between sarcocysts of Sarcocystis hirsuta and Sarcocystis hominis. Vet. Parasitol. 34, 153–157.

Dubey, J.P., Saville, W.J., Sreekumar, C., Shen, S.K., Lindsay, O.S., Pena, H.F., Vianna, M. C., Gennari, S.M., Reed, S.M., 2002. Effects of high temperature and disinfectants on the viability of Sarcocystis neurona sporocysts. J. Parasitol. 88, 1252–1254.

Dubey, J.P., van Wilpe, E., Calero-Bernal, R., Verma, S.K., Fayer, R., 2015a. Sarcocystis heydorni, n. sp. (Apicomplexa: Sarcocystidae) with cattle (Bos taurus) and human (Homo sapiens) cycle. Parasitol. Res. 114, 4143–4147.

Dubey, J.P., Verma, S.K., Dunams, D., Calero-Bernal, R., Rosenthal, B.M., 2015b. Molecular characterization and development of Sarcocystis speeri sarcocysts in gamma interferon gene knockout mice. Parasitology 142, 1555–1562.

Dubey, J.P., Calero-Bernal, R., Rosenthal, B., Speer, C.A., Fayer, R., 2016. Sarcocystosis of Animals and Humans, 2 ed. Taylor & Francis, Boca Raton.

Fayer, R., 2004. Sarcocystis spp. in human infections. Clin. Microbiol. Rev. 17, 894–902 table of contents.

Fayer, R., Heydorn, A.O., Johnson, A.J., Leek, R.G., 1979. Transmission of Sarcocystis suihominis from humans to swine to nonhuman primates (pan troglodytes, Macaca mulatta, Macaca irus). Z Parasitenkd 59, 15–20.

Fayer, R., Esposito, D.H., Dubey, J.P., 2015. Human infections with Sarcocystis species. Clin. Microbiol. Rev. 28, 295–311.

Garcia-Lunar, P., More, G., Campero, L., Ortega-Mora, L.M., Alvarez-Garcia, G., 2015. Anti-Neospora caninum and anti-Sarcocystis spp. specific antibodies cross-react with Besnoitia besnoiti and influence the serological diagnosis of bovine besnoitiosis. Vet. Parasitol. 214, 49–54.

Gazzonis, A.L., Gjerde, B., Villa, L., Minazzi, S., Zanzani, S.A., Riccaboni, P., Sironi, G., Manfredi, M.T., 2019. Prevalence and molecular characterisation of Sarcocystis miescheriana and Sarcocystis suihominis in wild boars (sus scrofa) in Italy. Parasitol. Res. 118, 1271–1287.

Gjerde, B., 2012. Morphological and molecular characterization and phylogenetic placement of Sarcocystis capreolicanis and Sarcocystis silva n. sp. from roe deer (Capreolus capreolus) in Norway. Parasitol. Res. 110, 1225–1237.

Gjerde, B., 2013. Phylogenetic relationships among Sarcocystis species in cervids, cattle and sheep inferred from the mitochondrial cytochrome c oxidase subunit I gene. Int. J. Parasitol. 43, 579–591.

Gjerde, B., Giacomelli, S., Bianchi, A., Bertoletti, I., Mondani, H., Gibelli, L.R., 2017a. Morphological and molecular characterization of four Sarcocystis spp., including Sarcocystis linearis n. sp., from roe deer (Capreolus capreolus) in Italy. Parasitol. Res. 116, 1317–1338.

Gjerde, B., Luzon, M., Alunda, J.M., de la Fuente, C., 2017b. Morphological and molecular characteristics of six Sarcocystis spp. from red deer (Cervus elaphus) in Spain, including Sarcocystis cervicanis and three new species. Parasitol. Res. 116, 2795–2811.

Gjerde, B., de la Fuente, C., Alunda, J.M., Luzon, M., 2020. Molecular characterisation of five Sarcocystis species in domestic sheep (Ovis aries) from Spain. Parasitol. Res. 119, 215–231.

Gondim, L.F.P., Mineo, J.R., Schares, G., 2017. Importance of serological cross-reactivity among toxoplasma gondii, Hammondia spp., Neospora spp., Sarcocystis spp. and Besnoitia besnoiti. Parasitology 144, 851–868.

Hajimohammadi, B., Eslami, G., Oryan, A., Zohourtabar, A., Pourmirzaei Tafti, H., Moghaddam Ahmadi, M., 2014. Molecular identification of Sarcocystis hominis in native cattle of central Iran: a case report. Trop. Biomed. 31, 183–186.

Harris, V.C., van Vugt, M., Aronica, E., de Bree, G.J., Stijnis, C., Goorhuis, A., Grobusch, M.P., 2015. Human Extraintestinal Sarcocystosis: what we know, and what we don't know. Curr. Infect. Dis. Rep. 17, 495.

Heydorn, A.O., 1977. Life-cycle of Sarcosporidia. IX. Developmental cyclus of Sarcocystis suihominis n. spec. Berl. Munch. Tierarztl. Wochenschr. 90, 218–224.

Heydorn, A.O., Mehlhorn, H., 1978. Light and electron microscopic studies on sarcocystis suihominis. 2. The schizogony preceding cyst formation. Zentralbl Bakteriol Orig A 240, 123–134.

Heydorn, A.O., Weniger, J.H., 1988. The effect of an acute Sarcocystis suihominis infection on the fattening weight of market piglets. Berl. Munch. Tierarztl. Wochenschr. 101, 307–310.

Heydorn, A.O., Mehlhorn, H., Gestrich, R., 1975. Light and electron microscope studies on cysts of Sarcocystis fusiformis in the muscles of calves infected experimentally with oocysts and sporocysts of Isospora hominis Railliet et Lucet, 1891. 2. Fine structure of metrocytes and merozoites (author's transl). Zentralbl Bakteriol Orig A 232, 373–391.

Hu, J.J., Wen, T., Chen, X.W., Liu, T.T., Esch, G.W., Huang, S., 2016. Prevalance, morphology, and molecular characterization of Sarcocystis heydorni Sarcocysts from cattle (Bos Taurus) in China. J. Parasitol. 102, 545–548.

Huang, Z., Ye, Y., Zhang, H., Deng, S., Tao, J., Hu, J., Yang, Y., 2019. Morphological and molecular characterizations of Sarcocystis miescheriana and Sarcocystis suihominis in domestic pigs (Sus scrofa) in China. Parasitol. Res. 118, 3491–3496.

Jeffrey, H.C., 1974. Sarcosporidiosis in man. Trans. R. Soc. Trop. Med. Hyg. 68, 17–29.

Kamata, Y., Saito, M., Irikura, D., Yahata, Y., Ohnishi, T., Bessho, T., Inui, T., Watanabe, M., Sugita-Konishi, Y., 2014. A toxin isolated from Sarcocystis fayeri in raw horsemeat may be responsible for food poisoning. J. Food Prot. 77, 814–819.

Lau, Y.L., Chang, P.Y., Tan, C.T., Fong, M.Y., Mahmud, R., Wong, K.T., 2014. Sarcocystis nesbitti infection in human skeletal muscle: possible transmission from snakes. Am J Trop Med Hyg 90, 361–364.

Li, J.H., Lin, Z., Qin, Y.X., Du, J., 2004. Sarcocystis suihominis infection in human and pig population in Guangxi. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 22, 82.

Li, J.H., Lin, Z., Du, J.F., Qin, Y.X., 2007. Experimental infection of Sarcocystis suihominis in pig and human volunteer in Guangxi. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 25, 466–468.

Lian, Z., Ma, J., Wang, Z., Fu, L., Zhou, Z., Li, W., Wang, X., 1990. Studies on man-cattle-man infection cycle of Sarcocystis hominis in Yunnan. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 8, 50–53.

Mandour, A.M., 1969. Sarcocystis nesbitti n. sp. from the rhesus monkey. J Protozool 16, 353–354.

Mehlhorn, H., Heydorn, A.O., 1977. Light and electron microscopic studies of Sarcocystis suihominis. 1. The development of cysts in experimentally infected pigs. Zentralbl Bakteriol Orig A 239, 124–139.

Mehlhorn, H., Heydorn, A.O., 1979. Electron microscopical study on gamogony of Sarcocystis suihominis in human tissue cultures. Z Parasitenkd 58, 97–113.

Mehrotra, R., Bisht, D., Singh, P.A., Gupta, S.C., Gupta, R.K., 1996. Diagnosis of human sarcocystis infection from biopsies of the skeletal muscle. Pathology 28, 281–282.
Murungi, E.K., Kariithi, H.M., 2017. Genome-wide identification and evolutionary analysis of Sarcocystis neurona protein kinases. Pathogens 6.
Nimri, L., 2014. Unusual case presentation of intestinal Sarcocystis hominis infection in a healthy adult. JMM Case Rep 1, e004069.
Nourani, H., Matin, S., Nouri, A., Azizi, H., 2010. Prevalence of thin-walled Sarcocystis cruzi and thick-walled Sarcocystis hirsuta or Sarcocystis hominis from cattle in Iran. Trop. Anim. Health Prod. 42, 1225–1227.
O'Donoghue, P.J., Weyreter, H., 1984. Examinations on the serodiagnosis of Sarcocystis infections. II. Class-specific immunoglobulin responses in mice, pigs, and sheep. Zentralbl Bakteriol Mikrobiol Hyg A 257, 168–184.
Pritt, B., Trainer, T., Simmons-Arnold, L., Evans, M., Dunams, D., Rosenthal, B.M., 2008. Detection of sarcocystis parasites in retail beef: a regional survey combining histological and genetic detection methods. J. Food Prot. 71, 2144–2147.
Rubiola, S., Chiesa, F., Zanet, S., Civera, T., 2018. Molecular identification of Sarcocystis spp. in cattle: partial sequencing of cytochrome C oxidase subunit 1 (COI). Ital. J. Food Saf. 7, 7725.
Saito, M., Shibata, Y., Ohno, A., Kubo, M., Shimura, K., Itagaki, H., 1998. Sarcocystis suihominis detected for the first time from pigs in Japan. J. Vet. Med. Sci. 60, 307–309.
Saito, M., Shibata, Y., Kubo, M., Sakakibara, I., Yamada, A., Itagaki, H., 1999. First isolation of Sarcocystis hominis from cattle in Japan. J. Vet. Med. Sci. 61, 307–309.
Shahari, S., Tengku-Idris, T.I., Fong, M.Y., Lau, Y.L., 2016. Molecular evidence of Sarcocystis nesbitti in water samples of Tioman Island, Malaysia. Parasit. Vectors 9, 598.
Slesak, G., Schafer, J., Langeheinecke, A., Tappe, D., 2015. Prolonged clinical course of muscular sarcocystosis and effectiveness of cotrimoxazole among travelers to Tioman Island, Malaysia, 2011-2014. Clin. Infect. Dis. 60, 329.
Tian, M., Chen, Y., Wu, L., Rosenthal, B.M., Liu, X., He, Y., Dunams, D.B., Cui, L., Yang, Z., 2012. Phylogenetic analysis of Sarcocystis nesbitti (Coccidia: Sarcocystidae) suggests a snake as its probable definitive host. Vet. Parasitol. 183, 373–376.
Valadas, S.Y., da Silva, J.I., Lopes, E.G., Keid, L.B., Zwarg, T., de Oliveira, A.S., Sanches, T.C., Joppert, A.M., Pena, H.F., Oliveira, T.M., Ferreira, H.L., Soares, R.M., 2016. Diversity of Sarcocystis spp shed by opossums in Brazil inferred with phylogenetic analysis of DNA coding ITS1, cytochrome B, and surface antigens. Exp. Parasitol. 164, 71–78.
Vangeel, L., Houf, K., Chiers, K., Vercruysse, J., D'Herde, K., Ducatelle, R., 2007. Molecular-based identification of Sarcocystis hominis in Belgian minced beef. J. Food Prot. 70, 1523–1526.
Velasquez, J.N., Di Risio, C., Etchart, C.B., Chertcoff, A.V., Mendez, N., Cabrera, M.G., Labbe, J.H., Carnevale, S., 2008. Systemic sarcocystosis in a patient with acquired immune deficiency syndrome. Hum. Pathol. 39, 1263–1267.
Weber, M., Weyreter, H., O'Donoghue, P.J., Rommel, M., Trautwein, G., 1983. Persistence of acquired immunity to Sarcocystis miescheriana infection in growing pigs. Vet. Parasitol. 13, 287–297.
Weyreter, H., O'Donoghue, P.J., 1982. Serodiagnosis of Sarcocystis infection. I. Antibody formation in the mouse and the pig. Zentralbl Bakteriol Mikrobiol Hyg A 253, 407–416.
Wilairatana, P., Radomyos, P., Radomyos, B., Phraevanich, R., Plooksawasdi, W., Chanthavanich, P., Viravan, C., Looareesuwan, S., 1996. Intestinal sarcocystosis in Thai laborers. Southeast Asian J Trop Med Public Health 27, 43–46.
Wong, K.T., Pathmanathan, R., 1992. High prevalence of human skeletal muscle sarcocystosis in south-East Asia. Trans. R. Soc. Trop. Med. Hyg. 86, 631–632.
Wouda, W., Snoep, J.J., Dubey, J.P., 2006. Eosinophilic myositis due to Sarcocystis hominis in a beef cow. J. Comp. Pathol. 135, 249–253.
Xiang, Z., Chen, X., Yang, L., He, Y., Jiang, R., Rosenthal, B.M., Luan, P., Attwood, S.W., Zuo, Y., Zhang, Y.P., Yang, Z., 2009. Non-invasive methods for identifying oocysts of Sarcocystis spp. Parasitol Int 58, 293–296.
Yang, Z.Q., Wei, C.G., Zen, J.S., Song, J.L., Zuo, Y.X., He, Y.S., Zhang, H.F., Attwood, S. W., Chen, X.W., Yang, G.C., Zhou, X., Quan, X., Li, C.Y., Han, D., Liu, A.W., Lin, P., 2005. A taxonomic re-appraisal of Sarcocystis nesbitti (Protozoa: Sarcocystidae) from the monkey Macaca fascicularis in Yunnan, PR China. Parasitol. Int. 54, 75–81.
Zeng, W., Sun, L., Xiang, Z., Li, N., Zhang, J., He, Y., Li, Q., Yang, F., Song, J., Morris, J., Rosenthal, B.M., Sun, L., Liu, H., Yang, Z., 2018. Morphological and molecular characteristics of Sarcocystis bertrami from horses and donkeys in China. Vet. Parasitol. 252, 89–94.