REVIEW OF SARCOCYSTOSIS IN MALAYSIA

SP Kan and R Pathmanathan

Departments of Parasitology and Pathology, Faculty of Medicine,
University of Malaya, 59100 Kuala Lumpur, Malaysia.

Abstract. *Sarcocystis* is a tissue coccidian with an obligatory two-host life cycle. The sexual generations of gametogony and sporogony occur in the lamina propria of the small intestine of definitive hosts which shed infective sporocysts in their stools and present with intestinal sarcocystosis. Asexual multiplication occurs in the skeletal and cardiac muscles of intermediate hosts which harbor *Sarcocystis* cysts in their muscles and present with muscular sarcocystosis. In Malaysia, *Sarcocystis* cysts have been reported from many domestic and wild animals, including domestic and field rats, moonrats, bandicoots, slow loris, buffalo, and monkey, and man. The known definitive hosts for some species of *Sarcocystis* are the domestic cat, dog and the reticulated python. Human muscular sarcocystosis in Malaysia is a zoonotic infection acquired by contamination of food or drink with sporocysts shed by definitive hosts. The cysts reported in human muscle resembled those seen in the moonrat, *Echinosorex gymnurus*, and the long-tailed monkey, *Macaca fascicularis*. While human intestinal sarcocystosis has not been reported in Malaysia so far, it can be assumed that such cases may not be infrequent in view of the occurrence of *Sarcocystis* cysts in meat animals, such as buffalo. The overall seroprevalence of 19.8% reported among the main racial groups in Malaysia indicates that sarcocystosis (both the intestinal and muscular forms) may be emerging as a significant food-borne zoonotic infection in the country.

INTRODUCTION

Sarcocystosis is caused by the tissue parasite of the genus *Sarcocystis* belonging to the family Sarcocystidae. The other medically important tissue protozoan in this family is *Toxoplasma gondii*. Members of the family Sarcocystidae are characterised by an alteration of sexual and asexual generations in their respective definitive and intermediate hosts. The two forms of sarcocystosis affecting man are intestinal and muscular sarcocystosis.

LIFE CYCLE

Among *Sarcocystis* species, sexual generations of gametogony and sporogony occur in the lamina propria of the intestine of definitive hosts which are flesh-eating carnivores or omnivores, while asexual generations occur in the muscles (both skeletal and cardiac muscles) of intermediate hosts which are usually herbivorous or prey animals. Thus, *Sarcocystis* has an obligatory two-host life cycle in which definitive hosts present with intestinal sarcocystosis and intermediate hosts present with muscular sarcocystosis. Definitive hosts shed sporocysts with their stool. These are immediately infective when ingested by intermediate hosts. Rupture of sporocysts in the intestine of intermediate hosts releases sporozoites, which undergo an initial phase of schizogony in the vascular endothelium of internal organs. Rupture of schizonts releases merozoites which develop into cysts in skeletal or cardiac muscles. These cysts, known as sarcocysts, are usually spindle-shaped and contain thousands of zoites. Ingestion of raw or undercooked meat containing sarcocysts results in the initiation of gametogony and sporogony in the intestinal epithelium with the appearance of sporocysts in the stool.

TAXONOMIC RELATIONSHIPS

Ultrastructural features, such as the thickness of the cyst wall, the absence or presence of cytophaneres/projections and septa, and the size and appearance of zoites, together with information on the definitive and intermediate hosts,

are of importance in deciding the taxonomic relationships of Sarcocystis parasites. A total of 93 species of *Sarcocystis* species have been reported from a wide range of domestic and wild animals, but the final and intermediate hosts of only 29 species are known (Levine and Tadros, 1980). Man is unique in that he can serve both as definitive and intermediate host for several known as well as unknown species of *Sarcocystis*. Among those species where man is the known definitive host are *Sarcocystis hominis* and *S. suihominis* (Rommel and Heydorn, 1972), whereas, among those cases of human muscular sarcocystosis reported so far, neither the original definitive hosts nor the natural intermediate hosts are known.

SARCOCYSTOSIS AMONG ANIMALS IN MALAYSIA

In Malaysia, the complete life cycles (with known definitive and intermediate hosts) of only five species of *Sarcocystis* are known. These include *Sarcocystis levinei* with a cat-buffalo cycle, *S. fusiformis* with a dog-buffalo cycle (Dissanaike *et al*, 1977; Dissanaike and Kan, 1978) and *S. singaporensis, S. villivillosus* and *S. zamani* with a ratpython cycle (Beaver and Malecker, 1978). The ultrastructural features of these five species have been studied under the electron microscope and the characteristics of the sporocysts shed by the definitive hosts are known.

In addition, *Sarcocystis* cysts have been reported from a wide range of domestic and wild animals in Malaysia, including domestic rats such as *Rattus norvigecus* (Zaman and Colley, 1975) and *Rattus rattus diardii* (Kan and Dissanaike, 1977); field rats such as *R. annandalei, R. exulans* and *R. jolorensis* (Lai, 1977; Kan, 1979); the bandicoot, *Bandicota indica* (Kan, 1979); the moon rat *Echinosorex gymnurus* (Dissanaike and Poopalachelvam, 1975; Kan and Dissanaike, 1976); the slow loris, *Nycticebus coucang* (Zaman, 1970); the buffalo, *Bubalus bubalis* (Zaman and Colley, 1972; Dissanaike and Kan, 1978; Kan and Dissanaike, 1978) and the Malaysian long-tailed macaque, *Macaca fascicularis* (Prathap, 1973; Kan *et al*, 1979). Except for the parasites found in *R. norvegicus* and *B. babalis*, the definitive hosts of all these species of *Sarcocystis* are unknown.

HUMAN SARCOCYSTOSIS IN MALAYSIA

Muscular sarcocystosis

Only the muscular form of human sarcocystosis has been reported in Malaysia with a total of 11 cases documented from both males and females, ranging from 12–67 years of age, among the main ethnic groups (Malays, Chinese, Indians and aborigines) from both East and West Malaysia since 1975 (Pathmanathan and Kan, inpress.). As all these 11 cases were seen in paraffin sections of autopsied or biopsied materials, ultrastructural studies of these human cases could not be carried out. Thus, the exact species of *Sarcocystis* causing human muscular sarcocystosis in Malaysia are unknown. However, the light microscopic features of these human sarcocysts resembled those seen in the moon rat and the Malaysian long-tailed macaque. As none of the subjects had ever left the country, it was assumed that these cases of muscular sarcocystosis were acquired locally and the disease was endemic in the country, with perhaps isolated, but local, foci of infection. In view of the occurrence of *Sarcocystis* in a relatively wide range of domestic and wild animals in Malaysia, human muscular sarcocystosis is considered a zoonotic infection and probably a sylvatic zoonosis.

Despite the apparent zoonotic nature of these infections in Malaysia, human muscular sarcocystosis has not been characterised by any significant cellular infiltration or inflammatory responses, as were cases of human muscular sarcocystosis reported in other parts of the world (Jeffrey, 1974; Beaver *et al*, 1979). Among the 11 cases reported in Malaysia, eight were associated with malignancies, four of which had carcinoma of the tongue. All the cases of lingual sarcocystosis associated with carcinoma were reported in elderly Indian patients who had common histories of chewing betal nut, a well-accepted risk factor for oral cancer. However, the apparent frequent association of muscular sarcocystosis with malignancies may also be due to the fact that excised malignant tissues were generally more frequently and thoroughly examined than other types of tissues, thus increasing the chances of detection of *Sarcocystis* cysts in these tissues. While the inital phase of schizogony in the vascular endothelium preceding the later phase of

cyst formation in skeletal muscles was reported to cause massive tissue destruction and even abortions and death in naturally and experimentally-infected animal intermediate hosts (Heydorn and Mehlhorn, 1978; Leek and Fayer, 1978; Zaman and Colley, 1975), all the cases of human muscular sarcocystosis were not accompanied by or associated with any history of past or recent episodes of severe illness. This was probably due to the fact that *Sarcocystis* cysts were able to survive for many years in the muscles of intermediate hosts; it was observed that some wild-caught, naturally-infected monkeys still harbored sarcocysts after several years in captivity (Karr and Wong, 1975). Thus, due to the apparent mildness of muscular sarcocystosis, as well as the persistence of sarcocysts in intermediate hosts, it might be impossible for human subjects to recall or relate an earlier episode of illness (if any) during the acute phase of schizogony, with the much later and milder, chronic phase of muscular involvement when the latter was detected. Neither might these subjects recall retrospectively the causes or sources of infection, even if the onset of infection had been characterised by an episode of acute or severe illness.

While the exact sources of muscular sarcocystosis is unknown, it is highly possible that this condition could be caused by the contamination of food or drink with sporocysts shed with the feces of domestic or wild animal definitive hosts, such as cats, dogs or pythons. These immediately infective sporocysts could easily contaminate the environment (soil and water) and serve as a readily source of infection to suitable immediate hosts, including man. *Sarcocystis* sporocysts found in dog feces have been shown to be transported in nature by flies (Markus, 1980), whereas several species of cockroaches were experimentally demonstrated to be able to serve as transport hosts of a murine *Sarcocystis* (Smith and Frenkel, 1978). As dogs and cats are known definitive hosts of several species of *Sarcocystis* in Malaysia, sporocysts shed by these animal definitive hosts could easily contaminate the environment which they share with their human hosts. *Toxoplasma* oocysts shed by domestic cats were shown to be able to survive for several months in shady, moist soil (Ruiz *et al*, 1973; Coutinho *et al*, 1982), and it is expected that *Sarcocystis* sporocysts shed by canine or feline definitive hosts would be likewise viable in similarly moist and shaded soil conditions. A study in South Germany revealed that approximately two-thirds of Sarcocystis infections in cattle were due to *S. hominis* caused by human fecal contamination, another two-thirds were due to *S. bovicanis* infections acquired from dog feces, and about one third was due to *S. bovifelis* infections acquired from cat feces (Boch *et al*, 1978).

Intestinal sarcocystosis

While muscular sarcocystosis has been reported from the main ethnic groups in Malaysia, intestinal sarcocystosis is not yet documented in the country. It is likely that such cases of intestinal involvement may have been missed or misdiagnosed rather than absent. *Sarcocystis* cysts have been demonstrated in buffaloes and other herbivorous meat animals, such as cattle, goats and sheep (Kan, personal observation). While the exact prevalence rates and severity of human intestinal sarcocystosis caused by eating undercooked meat is not known among the human population in Malaysia, workers elsewhere have shown that experimental infections among human volunteers were mild or subclinical (Rommel and Heydorn, 1972). Human subjects ingesting raw beef infected with cysts of *S. hominis* complained of nausea, abdominal pain, and diarrhea 3–6 hours after ingestion, whereas ingestion of raw pork infected with cysts of *S. suihominis* gave rise to more pronounced nausea, bloating, anorexia, marked abdominal pain, unproductive retching, and diarrhea 6–8 hours after ingestion. Six other cases of intestinal sarcocystosis acquired naturally from ingestion of undercooked beef were accompanied by fever, acute abdominal pain, nausea, vomiting, and diarrhea (Bunyaratvej *et al*, 1982). In view of the lack of specificity and the transient nature of the symptoms in most cases of experimentally-induced or naturally-acquired human infection, it would be expected that the majority of cases would have been missed if there were no deliberate effort to specifically detect sporocysts in the feces of human subjects.

Seroprevalence of *Sarcocystis* in Malaysia

A serological survey of 243 Malay, Chinese, Indian and aboriginal subjects in West Malaysia

revealed an overall seroprevalence rate of 19.7% (Thomas and Dissanaike, 1978), with the highest prevalence rate reported among aborigines (39.7%), followed by Malays (17%), Indians (8.7%) and Chinese (3.6%). While seropositivity for *Sarcocystis* antibodies could not differentiate betwen muscular or intestinal sarcocystosis, this survey indicated that at least one in five individuals examined had been exposed to *Sarcocystis* parasites. The higher seroprevalence rates among certain racial groups did not reflect any genetic predisposition or racial susceptibility to infection, but was an indication of the life-styles, pastimes and socioeconomic status of a particular community. Aborigines who lived in conditions of poor environmental sanitation and had close contact with domestic animals (pets or beasts of burden) and wild animals which they hunted for meat or hide would have greater exposure to the sources of infection, compared to other ethnic groups who lived in highly urbanized communities with better environmental sanitation and little or minimal contact with either domestic or wild animals.

PUBLIC HEALTH SIGNIFICANCE OF SARCOCYSTOSIS IN MALAYSIA

Sarcocystis has been reported from domestic and wild animals and humans in Malaysia. So far, human sarcocystosis reported in Malaysia consists of the muscular form only, with man serving as an accidental intermediate host. This infection is probably zoonotic, acquired by the ingestion of sporocysts shed by known and unknown definitive hosts. It is highly possible that the environment, especially soil and water, may be contaminated by sporocysts shed by definitive hosts, as reflected by an overall seroprevalence rate of almost 20% among the main ethnic groups in the country. Because of the mildness and chronicity of muscular sarcocystosis and the non-specificity and transient nature of intestinal sarcocystosis, however, may such cases among the human population may have been missed or misdiagnosed.

However, both forms of sarcocystosis, especially intestinal sarcocystosis, can become a potentailly serious public health problem if the sources of infection (sporocysts and sarcocysts) are not controlled or monitored. This is particularly so in view of the fact that seemingly harmless or innocuous zoonotic infections caused by *Toxoplasma gondii, Pneumocystis carinii*, and the intestinal protozoan, *Cryptosporidium* spp., have been shown to be severe and even fatal among immunosuppressed patients, especially those with the acquired immunodeficiency syndrome (AIDS). It is highly possible for the mild and transient form of intestinal sarcocystosis to become protracted, prolonged, and disseminated among immunosuppressed individuals who may not necessarily have AIDS but may have been subjected to immunosuppressive therapy for other disease conditions. Similarly, the initial acute phase of schizogony in the vascular endothelial cells that preceded the later chronic phase of cyst formation in the muscle cells also has the potential to cause widespread and massive tissue damage if this phase is protracted or prolonged in immunocompromised hosts. In view of the current frequent use of immunosuppressive therapy, it becomes mandatory to thoroughly screen all patients for sarcocysts in muscles or sporocysts in the feces before initiating such chemotherapeutic regimes.

In addition to detection and surveillance of human infection, it would be prudent to adopt measures to detect and prevent sarcocystosis among domestic and wild animals. All animals, especially pets and livestock, should be periodically screened for sarcocystosis, and infected animals should be treated. Animals slaughtered in abattoirs should be inspected for sarcocysts before being approved for human consumption. Both human and animal waste should be safely disposed of to avoid contamination of the environment and infection of intermediate hosts. Health education should be given regarding proper food hygiene and the necessity of thoroughly cooking meat.

While most of the above measures would, to some extent, prevent exposure to and transmission of infection among domestic animals and man, very little can be done to reduce the sources of infection maintained by semi-domestic and wild animals. Public awareness of the existence of this sylvatic zoonosis would reduce the risk of exposure to infection, especially among those people whose livelihood or pastimes (timber-logging, hunting, camping) predispose them to infection with sylvatic parasites.

The occurrence of *Sarcocystis* among both domestic and wild animals poses a threat to both rural and urban communities. Furthermore, intestinal sarcocystosis could easily occur wherever there is unsanitary disposal of human and animal waste. Such conditions of poor environmental sanitation prevails in all socioeconomically disadvantaged communities in both rural and urban areas, including among aborigines living within or at the fringes of jungle settlements of Malaysia. Lastly, man is capable of serving as a definitive or intermediate host for both domestic or sylvatic species of *Sarcocystis*, thereby increasing his chances of acquiring the infection from either domestic or wild animals in urban or rural environments. The ease of transmission of infection, especially the muscular form (by contamination of food or drink with immediately infective sporocysts), together with exotic culinary practices (such as eating raw or undercooked meat) further enhances the potential of sarcocystosis to be a major food-borne zoonotic infection in Malaysia.

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