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Spirocerca lupi - Fascinating new facts and research opportunities

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INTRODUCTION

Following the highly successful series of presentations on *Spirocerca lupi* at the James Hill Benefit Lectures, we have decided to collate this information, including additional material obtained following the open floor discussions at the lectures, to heighten awareness amongst the profession and industry players about this emerging serious threat to our canine population.

Spirocerca lupi is a common parasite of Canidae of the warm African continent, but is known to occur worldwide. Domestic dogs and other wild carnivores (fox, wolf, coyote and jackal) are most commonly affected, although natural infections have also been reported in domestic and wild felids, man, goats, horses and donkeys. Target organ systems are the oesophagus and aorta, resulting in gastrointestinal, respiratory and circulatory signs. Another species, *Spirocerca arctica*, occurs in northern Russia. Over the past decade there has been a significant increase in the incidence of spirocercosis in domestic dogs, particularly in urban areas. This could be attributed to an increasing awareness of the disease process, together with the introduction of greenbelts and lush gardens in suburbs and cities creating niches for the intermediate and transport hosts of the parasite. A study conducted in South Africa in 2000, suggested an apparent prevalence of 28%, with Gauteng and KwaZulu-Natal showing the highest incidence.

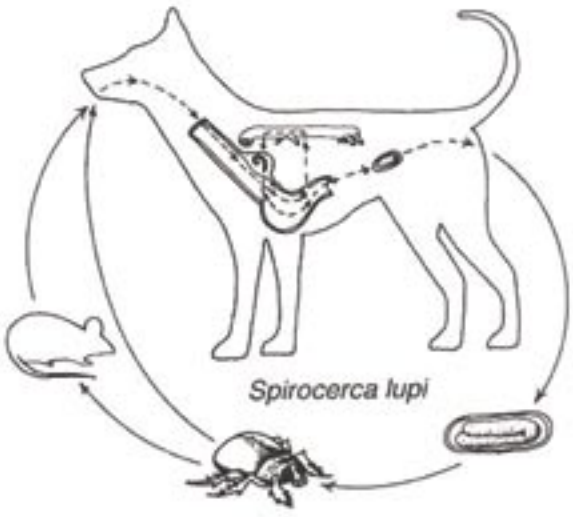

Fig.1: Life cycle of Spirocerca lupi. (Courtesy of Foreyt W J. 2001. Veterinary Parasitoloy Reference Manual 5th ed.)

LIFE CYCLE AND EPIDEMIOLOGY

Adult *S. lupi* worms reside within nodules in the wall of the dog's thoracic oesophagus. Females produce eggs containing larvae (embryonated eggs) which are transferred through a tract in the nodule into the oesophogeal lumen. Eggs are then passed in the faeces or vomitus of infected dogs and are ingested by coprophagous beetles (intermediate host) where they hatch and develop to infective L3 stage larvae within 2 months (Fig. 1). Dung beetles most commonly harbouring infective L3 are those which preferentially feed on omnivore (dogs, pigs and human) dung. Various genera of the Family Scarabaeidae (scarab beetles), Subfamilies Scarabaeinae (dung beetles) (Fig. 2) and Aphodiinae (Fig. 3) are widely distributed throughout South Africa in both urban and rural areas. Cornel du Toit and his team under the guidance of Prof Clarke H. Scholtz, Department of Zoology and Entomology, University of Pretoria, have been

Fig. 2: Scarabaeinae dung beetle.

Fig. 3: Aphodiinae dung beetle.

Fig 4: Histerid predator beetle.

Fig. 5: Staphylinid predator beetle (Rove beetle).

researching the host-parasite associations between dung beetles (Scarabaeinae) and *S. lupi* in the rural, peri-urban and urban areas around Pretoria. To date they have recovered infective L3 of *S. lupi* from five different dung beetle species. Dung beetles from urban areas had the highest prevalence of infection, followed by those in the rural areas, which may go a long way in explaining the noticeable increase in the incidence of spirocercosis in urban dogs over the past decade.

Carnivores (dogs) are infected by ingestion of a coprophagous beetle(s) containing infective L3 larvae. Alternatively a variety of transport (insectivorous) hosts including mice, hedgehogs, lizards, birds and rabbits, may ingest beetles and remain infected with encysted larvae (in various viscera) as paratenic hosts, which transmit the infection to carnivores when killed and ingested as prey. In addition, there are various predator beetles within the dung environment that prey on dung beetle and fly (Diptera) eggs and larvae, and these too could become potential paratenic hosts following predation upon infected dung beetles or *Spirocera* eggs. The Hister beetles (Histeridae, Fig. 4), Rove beetles (Staphylinidae, Fig. 5) and Hydrophilid beetles (Hydrophilidae, not illustrated) are commonly encountered in the same dung ecosystems as the dung beetles. Expansion of current research programs to include these and various other families of beetles associated with the dung environment is envisaged, although funding currently remains a stumbling block. Through determining the particle size range that dung beetles ingest, which is species specific and differs considerably within a genus, it would be possible to draw up an inventory of dung beetle species that are suitable as intermediate hosts. Identification of beetle species within a particular area would then give an indication of possible parasite presence in the area.

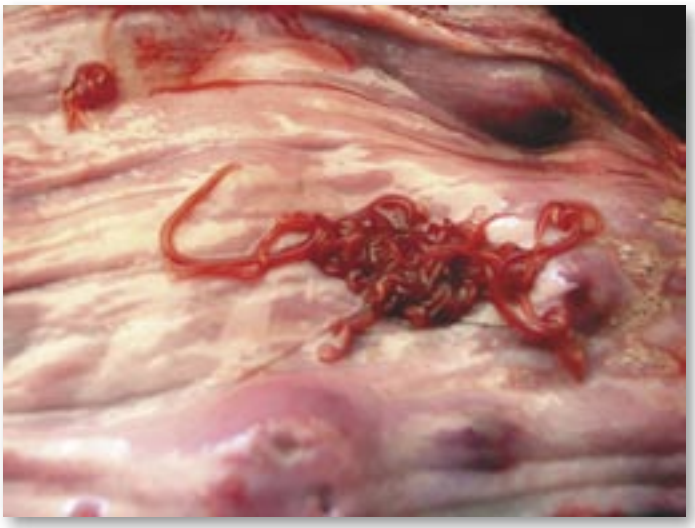

Fig. 6: Oesophagus which has been opened to reveal multiple intramural granulomas and adult Spirocerca lupi worms on the surface of the oesophageal mucosa.

In the carnivore, ingested L3 larvae of *S. lupi* penetrate the gastric mucosa, from where they migrate subintimally in the adventitia and media of the walls of arteries, reaching the cranial aorta within about 3 weeks. Following a final moult, the immature adults migrate to the oesophagus, typically at a point about midway between the diaphragm and aortic arch. Here they mature within nodules in the submucosa and adventitia of the oesophagus over the next 3 months (Fig. 1). The stimulus for the directional migration of the larvae is unknown and multiple reports exist of aberrant migration.

Pamela de Waal and her team of researchers from the Departments of Genetics and Paraveterinary Sciences (Pathology Section), University of Pretoria, are investigating genetic variation of *S. lupi* and matching this to geography. Through this information it may be possible to determine mobility of the nematode and hence the infective risk. Although the sample population of *S. lupi* worms analyzed thus far is small, there are clear genetic differences between worms. Initial data suggest that worms are capable of migrating over fairly significant distances. This group is desperately seeking worm submissions from across the country and any *S. lupi* worms found should be collected into absolute alcohol and submitted to Dr de Waal, together with a geographic location (ideally GPS data) of the canine host.

PATHOLOGY

Oesophageal granulomas, usually multiple in the distal oesophagus (Figs 6 & 7), and aortic scarring leading to aneurysms (Fig. 8) are

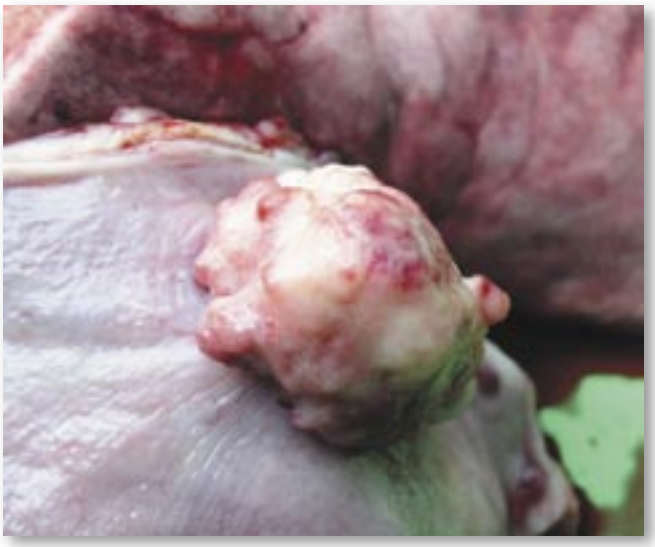

Fig. 7: Oesophagus: Cauliflower-like granulomas bulging into the lumen of the opened oesophagus.

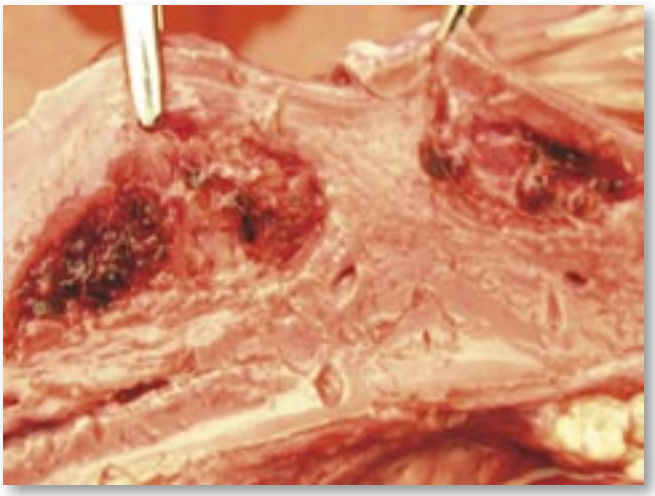

Fig. 8: Aorta: The aorta has been opened to reveal proliferative endarteritis and multiple developing aneurysms.

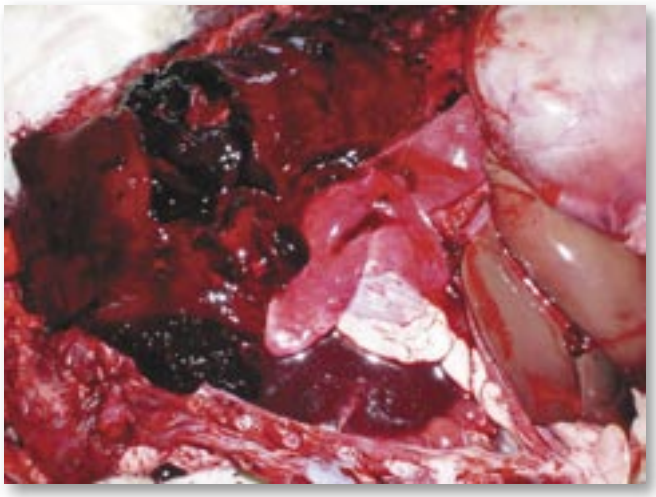

Fig. 9: Thoracic cavity opened to reveal a large amount of free-lying clotted blood, due to a ruptured aortic aneurysm

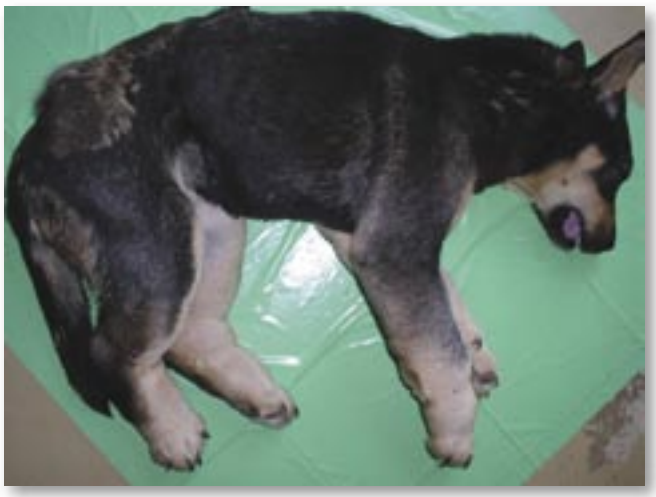

Fig. 10: Hypertrophic osteopathy (Marie's disease). Note the classic distribution in this case with thickening of the distal limbs of all 4 legs.

the most common lesions noted at autopsy. Adult worms can remain in the oesophagus for up to two years and neoplastic transformation at this site is well documented. In a recent survey, the incidence of *Spirocerca*-associated oesophageal sarcoma in South Africa was considered high, with an incidence of neoplastic transformation being reported at 26%. The exact mechanism by which neoplastic transformation occurs remains unknown, however.

Localized irritant effects of larval migration with endarteritis and periarteritis of intervertebral arteries are believed to be responsible for the vertebral spondylitis, which commonly develops on the ventral surface of thoracic vertebrae adjacent to the descending aorta. Other complications include: aortic mineralization, intervertebral arteritis with spinal cord damage, heterotopic bone formation, aortic rupture with fatal haemothorax (Fig. 9), oesophageal neoplasia (fibrosarcoma, osteosarcoma, squamous-cell carcinoma), mega-oesophagus and hypertrophic osteopathy of the distal limbs "Marie's disease" (Figs 10 & 11).

Aberrant larval migration can lead to nodule formation away from the oesophagus, including stomach, small intestine, lung, mediastinum, pleura, coronary arteries, vertebrae, urinary system, subcutaneous tissues, vertebral canal and salivary gland. The potential also exists that *S. lupi* worms may trigger immune-mediated mechanisms as has been documented with *Dirofilaria immitis* in heartworm cases.

Fig. 11: Metacarpals. The soft tissue has been boiled away to reveal the prominent periosteal exostoses which characterize hypertrophic osteopathy (Marie's disease). Lesions classically involve the metacarpals / metacarpals initially and then spread proximally, although phalanges, vetebrae and ribs may also be affected in rare instances.

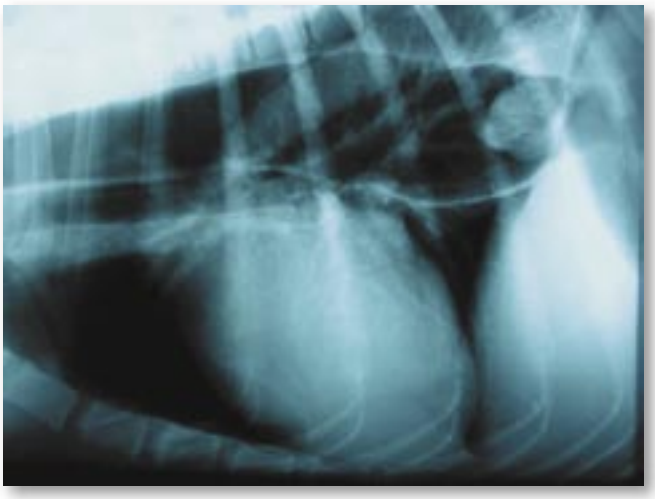

Fig. 12: Air oesophagram of thorax. Note how the introduction of air into the oesophagus has provided good contrast to delineate the nodule expanding into the lumen of the distal oesophagus.

CLINICAL MANIFESTATIONS

Clinical symptoms vary depending on the stage of the disease and whether any complications are present. Clinical signs directly attributed to spirocercosis are those associated with oesophageal disease and include vomiting, regurgitation, weight loss, salivation, dysphagia and odynophagia (painful swallowing).

Our experience is that the early symptoms are often very subtle and careful questioning of the owner and observing the dog immediately after eating is needed. Repeated swallowing movements and cranial extension of the neck after swallowing are often seen, in conjunction with shallow breathing. Even small nodules appear to have a marked affect on normal motility of the oesophagus.

Other common presentations include coughing, varying degrees of dyspnoea, symmetrical enlargement of parotid or mandibular salivary glands, pyrexia (often due to severe secondary bacterial infections), and chronic anaemia (blood loss). Unfortunately, 2-12% of cases still present as acute deaths following aortic aneurysm rupture. Aberrant migration can result in a wide variety of clinical presentations including a thoracolumbar-disc-like syndrome.

DIAGNOSIS

Early diagnosis is extremely challenging; unfortunately, most cases are diagnosed with advanced disease. Recovery of eggs from faecal material confirms the diagnosis and has a reported sensitivity in some studies of 80%. Our experience suggests a much lower sensitivity, as the eggs are shed intermittently and for short periods of time; requires either the use of a flotation fluid of higher specific gravity such as zinc sulphate or the use of faecal sedimentation techniques; and will only pick up the egg-producing adults in mature nodules with a patent passage to the oesophageal lumen, by which stage significant pathology may have already been produced by the migrating larval stages.

Endoscopy remains the ideal diagnostic tool for the diagnosis of the typical oesophageal nodules. Many practices may not have access to the equipment needed for this procedure, but do have radiographic facilities. In addition to the typical oesophageal nodules, thoracic vertebral spondylitis and aortic aneurysms and mineralization are regarded as diagnostic in endemic areas.

Large nodules can be seen on normal thoracic radiographs, particularly on the DV or VD view, but smaller and more cranially located nodules are difficult to see radiologically. Pneumo-oesophagography (introducing gas into the oesophagus) dramatically increases the visibility of the nodules (Fig. 12) due to the contrasting gas in the oesophagus and the surrounding lung and doesn't require any additional equipment aside from an endotracheal tube and general anaesthesia.

Secondary changes associated with spirocercosis such as pneumonia, pleural effusions, mediastinitis and neoplasia are also often visible on thoracic radiographs and may assist in the diagnosis. For this reason any thoracic radiograph taken in endemic regions should be examined carefully to allow for early diagnosis and treatment of non-clinical cases.

Endoscopic biopsies are often disappointing and successive biopsies from the same site are recommended to obtain reliable diagnostic material. Care must be taken not to perforate the oesophagus. Cases in which surgical excision of the mass is being considered should ideally have a CT scan.

TREATMENT AND CONTROL

Current knowledge on treatment of spirocercosis remains limited. It appears that no one remedy is effective in killing both adult and larval stages of *S. lupi* while not harming the host. The majority of drug trials have been limited in terms of numbers of animals included in these studies. With disophenol no longer available in RSA, the current recommended treatment is the extra-label use of doramectin (Dectomax® 1% m/v – Pfizer Animal Health).

Dosages and treatment intervals reported vary tremendously and highlight the fact that we know little about the pharmocodynamics of this drug in canines. Much is based on extrapolation from cattle, and further research is needed to determine the minimum inhibitory concentration needed to kill the worm and the partition co-efficient between the nodule and the blood. Anecdotal reports and clinical evidence have not supported ivermectin as the sole treatment, as an effective adulticide. A recent report suggested a combination of ivermectin with nitroxynil to be successful in treating 81.6% of cases.

In the author's experience, subcutaneous injection of doramectin at a dose of 400-500 μg/kg every 14 days for 3-6 treatments results in the resolution of the majority of pre-neoplastic nodules, with the majority of cases showing symptomatic cure within 14-21 days. Nodules persisting in asymptomatic animals after this time are either continued on monthly doramectin injections or are dosed orally at 500 μg/kg/day until resolution of the nodule has occurred.

Unfortunately, treatment efficacy against the larval stage remains

unknown and consequently no recognized prophylactic treatment protocol exists. Two common protocols used in private practice include: a single injection of doramectin every 3 months; or 3 treatments of doramectin at 14-day intervals given every 6 months. Further research is needed to determine minimum serum drug concentrations and maximum treatment intervals, particularly in endemic areas where continuous exposure to infective larvae exists.

It must be noted that in areas endemic for *Dirofilaria repens* (particularly the KZN coastal belt) care needs to be taken with the use of any of macrocyclic lactones (avermectins). These pharmacological agents can induce massive die-off of circulating microfilaria in animals that are microfilaraemic.

This microfilarial die-off is responsible for release of antigens from the degenerating parasites, which induces an endotoxic shock-like syndrome. In addition, dead and degenerating microfilaria form microemboli that can plug small-caliber capillaries, particularly in the lung and kidney. Therefore, in these endemic areas EDTA bood samples should ideally be screened for microfilaria before implementing the use of any macrocyclic lactone.

An extremely important and often overlooked facet of control is the education of veterinarians and dog owners alike about dung management. These simple yet highly effective management procedures may produce significant short- and long-term results. Ideally, dung should be removed from the garden on a daily basis, although weekly removal is better than nothing. Dung should be placed with the municipal waste to ensure removal from the property.

If garden compost heaps contain dung, they should be fenced; if not they can be left open. The reintroduction of *S. lupi* into a garden's soil via compost production and the potential of these infecting particularly young children also needs to be considered. This risk could be reduced via the provision of a sealed sandpit for young children's use.

CONCLUSION

From all of this information it is clear that there is still much to be learned about effective control and prevention of spirocercosis in domestic dogs. The current research teams should be lauded for their contribution to greater and better knowledge about this condition and providing the profession with more effective biological control procedures based on sound scientific information. Perhaps industry and the profession at large need to stand up and support these research initiatives as regards funding and provision of field material. The contact details of the research teams are included below for your convenience.

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QUESTIONS

Please select only ONE answer for each of the following questions.

QUESTION 1:

Which are the organ systems most commonly associated with *Spirocerca lupi* infection?

A. Oesophagus and aorta
B. Stomach and small intestine
C. Small intestine and large intestine
D. Aorta and coronary arteries
E. Heart

QUESTION 2:

How may domestic dogs become infected with *Spirocerca lupi*?

A. By ingestion of faecal-contaminated feed or water
B. By ingestion of infected coprophagous beetles
C. By ingestion of an infected transport host
D. All of the above
E. B & C

QUESTION 3:

What is currently proposed as the mechanism for the development of the vertebral spondylitis commonly associated with *Spirocerca lupi* infection?

A. Localised hypoxia of the thoracic vertebral periosteum.
B. Local irritant effects of larval migration with endarteritis and periarteritis of intervertebral arteries.
C. Release of cytokines from *Spirocerca*-associated oesophageal sarcomas.
D. None of the above.
E. A, B & C

QUESTION 4:

Over what period of time have adult *Spirocerca* parasites been reported to remain within the oesophagus?

A. Up to 6 months.
B. Up to 1 year
C. About a month
D. Up to 2 years.
E. More than 3 years

QUESTION 5:

What is the most common cause of acute death in clinical cases of spirocercosis?

A. Aortic aneurysm rupture.
B. Rupture of the oesophagus.
C. Metastatic neoplasia.
D. Acute congestive heart failure.
E. Aspiration pneumonia

QUESTION 6:

Which of the following diagnostic procedures are considered the most sensitive for the confirmation of clinical spirocercosis?

A. Recovery of eggs from faecal material.
B. Oesophageal endoscopy.
C. Routine X-ray
D. Pneumo-oesophagography
E. Faecal flotation.

QUESTION 7:

Which of the following secondary changes, visible on routine radiographs, should warrant further investigation into possible clinical spirocercosis?

A. Pneumonia
B. Pleural effusions
C. Mediastinitis
D. All of the above
E. B & C

QUESTION 8:

Which of the following pharmacological agents is currently considered the most effective therapeutic agent available in South Africa, against the adult stages of *Spirocerca lupi*?

A. Doramectin
B. Ivermectin
C. Nitroxynil
D. Disophenol
E. Albendazole

QUESTION 9:

Which of the following neoplasm or neoplasms have been associated with *Spirocerca* oesophageal parasitism?

A. Fibrosarcoma
B. Osteosarcoma
C. Myxosarcoma
D. Squamous-cell carcinoma
E. A, B & D.

QUESTION 10:

What is considered an important facet of *Spirocerca* control which is frequently overlooked?

A. Routine use of pharmacological agents effective against adult worms.
B. Regular use of broad-spectrum anthelmintics.
C. Dung management
D. Regular routine thoracic X-rays of dogs.
E. Routine oesophageal endoscopy.