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Clinical Commentary

Fasciolosis in horses: A neglected, re-emerging disease

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Fasciola hepatica (F. hepatica), the common liver fluke, is a trematode parasite that can infect many different mammalian hosts and is found throughout the world. In the UK, the fluke is most commonly associated with disease in sheep and cattle. It is a highly pathogenic parasite, heavy infections in the autumn lead to the death of sheep and subclinical infections are a major source of production losses in cattle, costing the livestock industry an estimated £300 million per year. Traditionally, liver fluke has been considered to be uncommon in horses; based on the failure to establish infection following experimental exposure, it was said that horses are resistant to infection and infections rarely reach patency (Nansen *et al.* 1975; Alves *et al.* 1988). However, fasciolosis has been previously described in horses: a report nearly half a century ago, following the very wet summer of 1968, found infections in horses grazed on pasture also used for sheep and cattle. A range of clinical signs was observed and fluke eggs detected in faeces. In total, 38 cases were described in one practice in south-west England in a 12-month period; moreover, 4 out of 20 ponies bought at a Welsh market had mature flukes in their livers at *post mortem* examination (Owen 1977). Similarly, a study in the west of Ireland described fluke prevalence by faecal egg count in horses of 77% (Kearney 1974). However, since the mid-70s, fluke has become rather neglected as a potential cause of disease in horses, yet liver disease as a syndrome is common and often idiopathic (Pearson 1999).

Outside the UK, fluke infections in horses have been fairly extensively described. In mainland Europe, prevalence based on faecal egg detection has been found to range from 0.07% in Poland to 60% in Northern Spain (Sadzikowski *et al.* 2009; Arias *et al.* 2012). Infections have been described in horses in Australia and a study in Western Australia found infection in 23 yearlings all previously treated with triclabendazole on 2 occasions. This indicates that horses are susceptible to infection and can carry fluke burdens which are triclabendazole resistant (Palmer *et al.* 2014).

In contrast to horses, donkeys appear to be a much more permissive host and infection appears to be highly prevalent in working donkeys in Ethiopia, for example Getachew *et al.* (2010), and donkeys have been implicated as a reservoir of human infection in Bolivia and Egypt (Valero and Mas-Coma 2000; Haridy *et al.* 2002). A recent study in donkeys from the Donkey Sanctuary in the UK suggested that prevalence in donkeys admitted between 2011–2013 was 10.2% and was most commonly seen in donkeys coming from Northern Ireland (F. Burden, personal communication).

Fasciola hepatica has an indirect life cycle involving an amphibious mud snail, *Galba truncatula*. The snail and free living stages of the parasite (egg, miracidium, cercaria and metacercaria) are all dependent on water and a temperature above 10°C for development. Hence, high summer rainfall is the leading risk factor for fluke (McCann *et al.* 2010) which is most prevalent in the wetter west of the UK with hot spots in South Wales, north-west England, south-west Scotland and Northern Ireland.

There has been a rise in prevalence of *F. hepatica* in sheep and cattle over the past 15–20 years which has been attributed to changing weather patterns, with milder winters and wetter summers (Williams *et al.* 2014). Other factors which have contributed to this increase include changes to environmental/countryside stewardship schemes that encourage farmers to maintain wetlands and other wildlife habitats. In addition, stock are moved around the country more frequently and there is evidence that fluke has been introduced into parts of the country where it was previously rare or nonexistent (Pritchard *et al.* 2005). Climate change is likely to foster the life cycle of the parasite and changes in the epidemiology are predicted (Fox *et al.* 2011; Caminade *et al.* 2015). Whilst these factors will affect ruminant health and productivity most significantly, the knock-on effects on horses cannot be ignored.

The summer of 2012 was the wettest since 1912 (Anon 2012b) and by the end of that year the level of fluke-associated disease, particularly in sheep, was huge (Anon 2012a). Associated with the increase in occurrence of fasciolosis, there appeared to be a much greater awareness of fluke amongst farmers and veterinarians. As a consequence, the diagnostic services of the University of Liverpool were approached by a number of veterinary practitioners requesting diagnostic tests for fluke infections in horses grazing pasture used for sheep or cattle.

Diagnosis of *F. hepatica* infections in sheep and cattle is based on clinical signs, farm history, season and specific diagnostic tests. Faecal egg counts (FEC) using the sedimentation method are widely used to detect infection, particularly in cattle. Fluke FEC are time-consuming, only detect the presence of egg laying adults and have a low sensitivity of approximately 60% in cattle (Charlier *et al.* 2014). Eggs are shed by adult parasites in the bile ducts and in ruminants the eggs are often trapped in the gall bladder and released sporadically in faeces. Increasing the volume of faeces analysed up to 40 g can increase the sensitivity of a FEC (Charlier *et al.* 2008) but may also create difficulties in actually seeing the eggs because of the density of the faecal material in the dish.

Antibody detection ELISAs are available using either serum or milk; they are highly sensitive, detect early infection but because antibodies persist for several weeks after treatment, antibody positive animals may not carry active infection (Salimi-Bejestani *et al.* 2005). More recently, an ELISA that detects fluke antigen in the faeces of infected animals has been evaluated for sheep, cattle and horses. A study in Australia showed that whilst the copro-antigen ELISA is over

80% sensitive when detecting infection in sheep and cattle, it performed very poorly in horses, detecting only 9% of infected horses compared with faecal egg counts (Palmer *et al.* 2014).

Diagnosis of fluke infection in horses is problematic. Faecal egg counts are regarded as the gold standard diagnostic method but it is claimed that fluke infections in horses rarely reach patency (Nansen *et al.* 1975). Yet, clearly patent infections do occur in horses, since numerous studies have used FEC to estimate regional and national prevalence. Several studies have used antibody detection to diagnose infection in horses (Gorman *et al.* 1997; Arias *et al.* 2012; Acici *et al.* 2013) but none of these methods are commercially available. Efforts to modify and evaluate antibody detection ELISAs are underway in Liverpool and Dublin (M. Sekiya, personal communication), but although the Liverpool test is offered commercially by LVPD (http://www.liv.ac.uk/testapet/), the diagnostic sensitivity and specificity of both tests is yet to be published.

One of the problems of diagnosing fluke in horses, in addition to the lack of specific, sensitive, diagnostic tests, is the lack of pathognomic clinical signs as highlighted by Raftery *et al.* (2015). These authors suspected a parasitic cause of disease based on an eosinophilia in blood and peritoneal fluid together with an eosinophilic cholangiohepatitis identified from liver biopsies but the initial presenting signs, once PPID had been diagnosed and the associated laminitis controlled, were weight loss, inappetence and ventral oedema. Interestingly, no eggs were detected in the faeces of this animal despite the presence of hundreds of adult parasites in the biliary system.

The most common reason for samples from horses to be submitted for fluke testing at Liverpool has been weight loss and inappetence, together with changes in blood biochemistry and enzyme levels, including lower haemoglobin, packed cell volume, albumin, total protein and globulin levels and raised ALP, GLDH, GGT, fibrinogen and eosinophil counts. Frequently, horses had a history of grazing on poor or water-logged land, previously used for grazing ruminants and predominantly came from west Wales and north-west England, where fluke is known to be endemic and awareness of fluke is high. Of samples submitted to Liverpool in the past 2 years, approximately 16% were fluke positive, either by FEC and/or serum antibody detection.

In the case described by Raftery *et al.* (2015), the patient was treated with triclabendazole (TCBZ) at a dose rate of 12 mg/kg bwt which has been shown to be effective against TCBZ-susceptible parasites in horses. However, in this case and those reported in Australia (Palmer *et al.* 2014), TCBZ was found to be ineffective. Triclabendazole resistance is thought to be widespread in fluke populations affecting sheep in the UK (Williams *et al.* 2014); if horses are acquiring infection from pasture grazed by sheep and cattle, it is highly likely that resistance will become problematic in horses. Closantel, in combination with TCBZ, was used in horses with TCBZ-resistant parasites (Palmer *et al.* 2014) and nitroxynil at 7 mg/kg bwt was less effective at removing the fluke burden (Rubilar *et al.* 1988). However, none of these drugs are licensed for use in horses.

Conclusions

Our experience suggests that liver fluke infection in horses is more common than we realise and *F. hepatica* should be considered as a differential diagnosis in cases of weight loss or other indicators of liver disease, particularly if there is a history of grazing pasture used previously for sheep or cattle. There is a desperate need for a fully evaluated diagnostic test. Faecal egg counts appear to have low sensitivity and we lack an understanding of the dynamics of fluke infection in horses, the proportion of flukes which reach maturity, why egg output appears to be so sporadic and if the lack of a gall bladder in horses contributes to the irregular shedding of eggs. Similarly, we do not know if different breeds differ in terms of their susceptibility to infection and disease. Much more research on equine fasciolosis is urgently needed to address some of these questions.

Authors' declaration of interests

No conflicts of interest have been declared.

Authorship

Both authors contributed to the preparation of the manuscript and gave their final approval.

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