Treatment and Control of liver fluke in Sheep and Cattle

Technical Note

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Key Recommendations

Due to the increased risk of liver fluke disease it is essential that stockowners investigate any unexplained losses or disease entities particularly:

Investigate

- Sudden death.
- Ill thrift
- Reduced lambing percentage.
- Increase in barrenness.
- Condemnation of livers
- Unexplained metabolic disease in dairy cattle

Monitor

In addition the impact of the disease and the effectiveness of control measures should be regularly monitored using

- Blood samples
- Faecal egg counts,
- Post-mortem material
- Abattoir information.

Health Plan

Based on monitoring information a fluke control plan should be drawn up with the local vet as part of the veterinary health plan for the farm.

This technical note provides information on liver fluke under the following categories

- The Disease
- Life Cycle & Epidemiology
- Diagnosis and diagnostic tests
- Treatment and Control
- Forecasting

The Disease

The number of outbreaks of disease caused by the liver fluke *Fasciola hepatica* (fasciolosis) in cattle and sheep in Scotland has increased dramatically in recent years, with unprecedented numbers of animals affected in 2002, as illustrated below. The disease poses a threat to animal welfare and may also cause major economic losses through mortality, ill-thrift, condemnation of livers at the abattoir, predisposition to other diseases, treatment and associated veterinary costs.

The risk of liver fluke disease is closely linked to summer rainfall which favours fluke development and provides an optimum habitat for the intermediate host, the dwarf pond snail *Lymnaea truncatula*. The disease has long been associated with high mortality in sheep flocks, and anaemia and poor production in beef and dairy cattle. In the past few years, fluke-related deaths have also been reported in adult cattle and the parasite has been linked with outbreaks of salmonellosis and metabolic disease in dairy cattle.

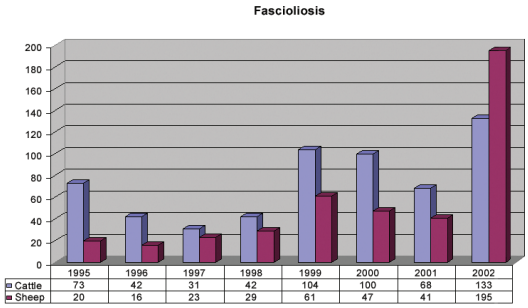

Figure 1 : *Outbreaks of fasciolosis in Scotland 1995-2002*

Life Cycle (fig 2, overleaf)

Fluke eggs passed in the faeces of a mammalian host develop and hatch into motile ciliated miracidia. This takes nine days at the optimal temperature of 22 to 26°C. Development at lower temperatures takes longer and will not occur below 10°C. The liberated miracidia have a short life-span and must come into contact with their intermediate host, *L truncatula*, within three hours if successful penetration is to occur. In infected snails, development proceeds through the sporocyst and redial stages to the final snail stage, the cercaria. These are shed from the snail as motile forms and attach themselves to firm surfaces, such as grass blades, where they encyst to form the infective metacercariae. It takes a minimum of six to seven weeks to complete development from miracidia to metacercariae, although under unfavourable circumstances a period of several months is required. Multiplication within the snail allows one miracidium to produce over 600 metacercariae.

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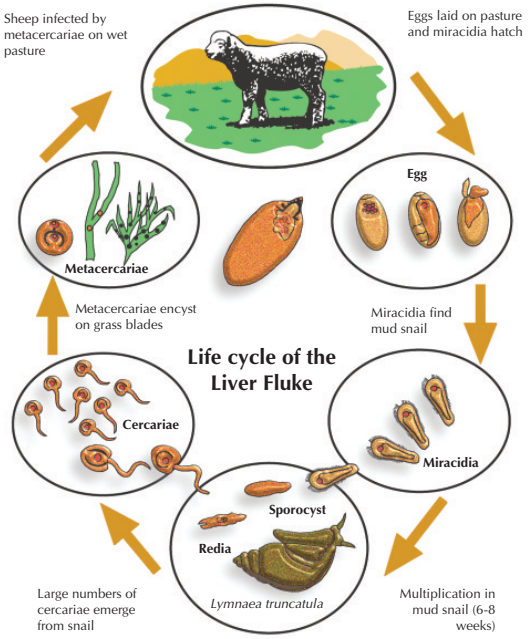
Metacercariae ingested by the final host excyst in the small intestine, migrate through the gut wall, cross the peritoneum and penetrate the liver capsule. The young flukes tunnel through the liver parenchyma for six to eight weeks and then enter the small bile ducts where they mature in about four weeks; during this period they migrate to the larger ducts and, occasionally, to the gall-bladder. The period from uptake of metacercariae to the presence of fluke eggs in the faeces is 10 to 12 weeks and so the minimum period for completion of one entire life cycle of *F hepatica* is 17 to 19 weeks.



Life Cycle takes 4-5 months to complete

Figure 2 : *Life Cycle of F hepatica*

Epidemiology

The extent of the habitat of the dwarf pond snail *L truncatula* which feeds mainly on algae relates to climatic conditions and soil hydrology. Ideal conditions for survival and multiplication of snails include a slightly acidic environment and a slow moving water medium to carry away waste products. Permanent habitats therefore, include the banks of ditches or streams and the edges of small ponds. Following heavy rainfall or flooding, temporary habitats may be provided by hoofmarks, wheel ruts or rain ponds. Fields with clumps of rushes are common sites as these have a slightly acidic pH. The wet conditions required for snail breeding and also for *F hepatica* development within the snails are achieved when rainfall exceeds transpiration. Such conditions also facilitate the development and hatching of *Fasciola* eggs, the search for snails by miracidia and the dispersal of cercariae after shedding from snails. A mean day/night temperature of 10°C or above is necessary for snail breeding, the development of *F hepatica* within the snail, and the development and hatching of fluke eggs. As the mean day/night temperature increases during late spring and early summer, the development time for the stages of the liver fluke outside of the final host (the suprapopulation), become shorter, reaching a minimum of five weeks in midsummer.

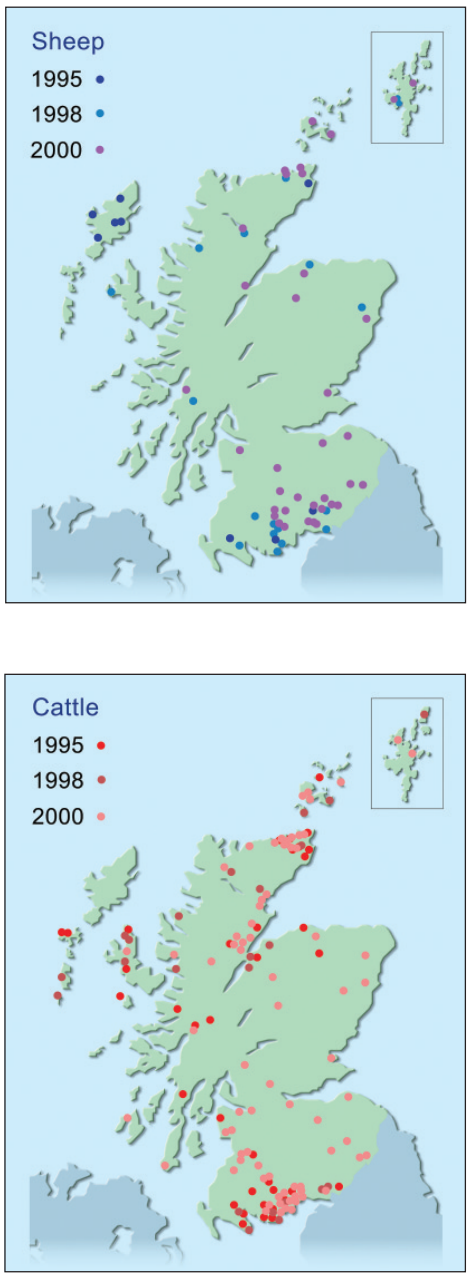


Figure 3 : *Fasciolosis Outbreaks Sheep and Cattle 1995, 1998 and 2000*

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The minimum temperature requirements for the development of a suprapopulation of *F hepatica* normally only prevail in the United Kingdom from April to October, with relatively minor variations. As a result, the main factor influencing the magnitude of the snail populations, and therefore the prevalence of fasciolosis, is summer rainfall. These climatic factors dictate that, in the UK, the majority of snails become infected in the summer by miracidia developed from eggs deposited in the spring and early summer; these take a minimum of five weeks to develop to cercariae, resulting in increased pasture levels of metacercariae from late August onwards. Uptake of the infective stages results in clinical disease in sheep and cattle normally from September onwards. Recent economic difficulties experienced by the sheep industry have resulted in an overall reduction in sheep numbers. In Scotland, between December 2001 and December 2002, the numbers of sheep fell by four per cent to 5.5 million. Despite this reduction in available hosts, the higher prevalence of fasciolosis in recent years in sheep and cattle has been largely associated with milder, wetter weather. Increased rainfall raises the water table, thereby permitting *L truncatula* to extend its habitat, while milder temperatures prolong the development period available. In Scotland, this has been reflected in the spread of the disease from poorly drained pastures in the west of Scotland to traditionally drier farms in the east of the country, which had never before experienced fluke disease, as illustrated in fig 3. Dumfriesshire, Ayrshire, Invernesshire and the far north of Scotland have been particularly badly affected, but significant numbers of outbreaks have also been seen in the Lothians, Borders and Perthshire.

Interestingly, outbreaks have continued into the spring and summer and are thought to be due to the mild wet conditions which favour overwintering of fluke eggs and metacercariae.

Diagnosis and diagnostic tests

CLINICAL SIGNS

Sheep

Clinical fluke disease (fasciolosis) in sheep is usually classified as acute, subacute or chronic, according to the number and stage of flukes present. However, any such classification is somewhat arbitrary, as there will be considerable overlap between these categories. It should always be remembered that an outbreak of fasciolosis will be a flock problem, even though only a few individuals may be showing typical clinical signs at any one time, and therapy must always be considered on this basis.

Acute fasciolosis

Outbreaks of acute fasciolosis are usually seen in late autumn and early winter, although in wet years this period may extend well into the spring and are associated with the presence of large numbers of immature flukes in the liver parenchyma. The simultaneous development of large numbers of immature flukes may be due to ingestion of large numbers of metacercariae over a short period from very heavily infected pasture, or prolonged migration of flukes in sheep previously exposed to the parasite. In both cases, acute haemorrhagic anaemia and hypoalbuminaemia will result, with sudden death occurring in animals where sufficient numbers of flukes are present. On examination of the remainder of the flock, animals may be weak, pale and, in some cases, exhibit abdominal pain with a palpably enlarged liver.

Subacute fasciolosis

Like the acute form of the disease, subacute fasciolosis occurs from late autumn to spring and also presents as an acute haemorrhagic anaemia with eosinophilia and hypoalbuminaemia. However, subacute fasciolosis is not so rapidly fatal and affected sheep may show clinical signs for one or two weeks prior to death. Large numbers of immature flukes will be present in the liver parenchyma, although not in quite the numbers seen in cases of acute fasciolosis. Parasites will, however, have developed further and a substantial proportion of the fluke population will be present as adults in the major bile ducts. This form of the disease may occur where sheep have ingested large numbers of metacercariae over a longer period of time, or the number ingested at any one time has not been sufficient to cause the acute form of the disease. Affected sheep lose condition rapidly, become markedly anaemic with obvious pallor and may have a palpably enlarged liver and resent abdominal palpation.

Submandibular oedema (bottle jaw) pictured overleaf may also be present in some cases.

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Figure 4 : *Subacute fasciolosis : Bottle jaw (Picture : Novartis Animal Health)*

Cattle and Sheep

Chronic fasciolosis

Chronic liver fluke disease, which is most frequently seen clinically in the winter and spring, is characterised by weight loss, anaemia, eosinophilia and hypoalbuminaemia and is due to the blood-sucking activities of adult flukes in the bile duct. In severe cases, submandibular oedema is prominent and terminal diarrhoea may occur. Concurrent infections with the abomasal nematode *Teladorsagia (Ostertagia)* may complicate the clinical picture. Liver fluke may also be responsible for subclinical disease, particularly in adult cattle, with only minor haematological and biochemical changes being seen. This will however result in lowered productivity which will be reflected in inadequate food conversion rates, poor carcass formation and reduced milk yields (solids not fat). Increasing evidence suggests that fasciolosis in adult cattle may predispose animals to *Salmonella* Dublin infection and, in high-yielding dairy cows, may precipitate metabolic disease around calving.

Age of flukes (weeks)	Mean Length (mm)	Range (mm)
4	2.38	1.0-3.5
6	4.39	1.5-6.0
8	5.18	1.5-11.5
9	6.54	2.0-13.0
10	7.62	2.0-13.0
12	6.77	2.0-16.0
14	15.43	2.5-25.0

Table 1: *Fluke Measurements (after JC Boray 1967)*

Diagnosis

Post mortem examination of fresh carcasses is the best method of diagnosis if liver fluke is suspected, as untreated animals provide the most accurate indication of the level of challenge. Measurement of flukes recovered will also give an indication of the age of flukes and the period of challenge (see table 1).

Post-mortem examination will also identify any lesions resulting from concurrent diseases such as black disease or parasitic gastroenteritis. Outbreaks of fasciolosis in sheep and cattle may be exacerbated by sudden deaths due to black disease (infectious necrotic hepatitis), which results from the activation and proliferation of the soil-borne toxigenic bacterium *Clostridium novyi*, hitherto dormant in the liver, in response to the anaerobic conditions produced by migrating flukes. Sudden or rapid death is due to a generalised toxaemia, which may occur despite very limited fluke damage to the liver. In the live animal, laboratory diagnosis can be based on a variety of tests on faeces and/or blood samples (see table 2 overleaf).

Fluke Egg Count (FEC): this is the standard method of diagnosis of the presence of the presence of adult flukes (chronic disease) and is not suitable for diagnosis of acute disease due to immature flukes. As fluke eggs are larger and heavier than roundworm eggs special techniques are used and a fluke egg count (fec) rather than a worm (roundworm) egg count (wec) should be requested from your diagnostic laboratory. Sufficient numbers of samples should be submitted to allow an estimate of the infection level in a group of animals, eg 10 fresh samples which can be pooled in the laboratory to reduce cost.

SACVS offers diagnostic packages for diagnosis of all common internal parasites.

Liver Enzymes: Elevation of liver enzyme levels (aspartate aminotransferase, AST and glutamate dehydrogenase, GLDH) can be useful for the diagnosis of acute fluke disease as early as two to three weeks post-infection, while raised L-gamma glutamyl transferase (GGT) levels can indicate chronic disease once adult flukes are present in the biliary tree.

Haematology:

Demonstration of peripheral eosinophilia can be particularly useful in adult cattle and has recently been used as an early indicator of fasciolosis in dairy herds where metabolic disease was initially suspected.

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Test	Type of sample	Reference range	Disease stage
Fluke egg count (FEC)	Faeces	N/A	Chronic
Aspartate aminotransferase (AST)	Clotted Blood	<60 iu/litre	All stages
Glutamate dehydrogenase (GLDH)	Clotted Blood	<13 iu/litre (cattle) <10 iu/litre (sheep)	All stages
L-gamma glutamyl transferase (GGT)	Clotted Blood	<22 iu/litre (cattle) <31 iu/litre (sheep)	Chronic
Differential leucocyte count (eosinophil)	Unclotted Blood	<10%	All stages
Detection of specific antibodies (ELISA)	Clotted Blood	N/A	All stages

Table 2: *Diagnostic tests for liver fluke disease*

All of these tests may also be used to investigate suspected anthelmintic resistance by submitting samples pre- and post-treatment (normally 3 weeks after treatment) .

Serology:
Various serological techniques on blood samples, including enzyme linked immunosorbent assay (ELISA), can be used to detect antibodies to *F hepatica* with a high level of specificity (over 90 per cent). The test currently used for diagnosis by the Veterinary Laboratories Agency (VLA) and SAC Veterinary Services, based on detection of antibodies to excretory/secretory (ES) antigens of *F hepatica* in serum, indicates only previous exposure to the parasite and does not provide information on current infection or the immune status of an animal.

There is no evidence that sheep ever become immune to fluke infection under field conditions and will remain persistently infected in the absence of treatment. Cattle by contrast develop a degree of resistance to the parasite partly due to the presence of more fibrous tissue in the bovine liver, which limits damage by immature flukes. The ELISA test described above is currently being validated by the VLA for the detection of antibodies to *F hepatica* in bovine milk for use as a screening test.

Treatment and Control
Control and, ideally, prevention of fasciolosis using control measures integrated with a forecasting system is preferable to treatment of affected animals, where animal welfare may be compromised and economic loss incurred. Control measures should be part of a flock and/or herd health plan within the Codes of Recommendation for the Welfare of Livestock and have two main objectives:

- To reduce the population of infected snails
- To eliminate flukes from animals

thus limiting the availability of *F hepatica* eggs and, therefore, miracidia to snail populations. Before any scheme of snail control is undertaken, an assessment of the control area for snail habitats should be made as this may be localised or extensive. The best long-term method for permanent eradication of extensive snail habitats is drainage, but this may prove prohibitively expensive. Where a snail habitat is localised, fencing off wet areas or avoiding grazing during periods of high risk should reduce infection.

FLUKICIDES
In recent years, the choice of licensed flukicides has been limited by a reduction in the number of products available, a selection of which appear in table 3. Most flukicides are effective against adult flukes, but activity is variable against the immature stages. It is therefore extremely important to check the individual datasheets for efficacy of products before treating animals, particularly in the autumn when immature flukes may predominate. Combined fluke and worm products may not be suitable if immature flukes are present, and there is increasing evidence of acute disease occurring from August until May of the following year. A specific system for fluke control tailored to individual farm needs is essential in addition to a strategic programme for the control of gastrointestinal helminths. This should be included in a health plan drawn up in consultation with the local veterinary surgeon. Advice for farmers on flukicide usage, particularly with regard to frequency, should take account of the published forecast for the year, previous farm history, results of abattoir returns if available and faecal monitoring, tempered with the knowledge that triclabendazole-resistant flukes have been recorded in the UK and Eire.

Over the past few years, triclabendazole-resistant

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Product (Manufacturer)	Species	Active compound	Efficacy
Fasinex (Novartis)	Cattle and sheep	Triclabendazole	All stages from two-day-old immature flukes to adults
Flukiver (Janssen)	Cattle and sheep	Closantel	Adult and immature flukes from three to four weeks, *Haemonchus contortus*
Trodax (Merial)	Cattle and sheep	Nitroxynil	Adult and immature flukes, *Haemonchus* spp. and gutworms
Valbazen (Pfizer)	Cattle and sheep	Albendazole	Adult flukes, gutworms, lungworms and tapeworms. Kills fluke and worm eggs
Combinex Cattle (Novartis) Combinex Sheep (Novartis)	Cattle and sheep	Triclabendazole and levamisole	Adult and immature flukes, gutworms and lungworms
Nilzan Gold (Schering-Plough)	Cattle and sheep	Levamisole and oxyclozanide	Adult flukes, gutworms and lungworms
Ivomec Super (Merial)	Cattle	Ivermectin and clorsulon	Adult flukes, gutworms, lungworms, mites and lice

Table 3: Flukicides for sheep and cattle

flukes have been recorded in sheep in Eire, Scotland, England and Wales. If symptoms persist following treatment, faeces samples should be checked for fluke eggs three weeks after treatment. If fluke eggs are still present, animals should be treated with an alternative flukicide.

Quarantine treatment for fluke

There is a need to avoid the introduction of resistant fluke on to an uninfected farm, but only where there are habitats on the holding that would support the intermediate host of the fluke, the snail *Lymnaea* truncatula . In such cases, animals (including cattle) brought onto farms where fluke transmission is possible, due to the presence of *Lymnaea truncatula*, should be treated with a product effective against immature flukes and held off snail contaminated pastures for 4 weeks (DEFRA Proceedings Working Party on Internal Parasite Control in Sheep, September 2003). Follow-up treatment may be required 6 - 8 weeks after the initial treatment. If in doubt seek veterinary advice.

Control

Recently published DEFRA guidelines on fluke control expressed concern about the widespread use of combination products for the control of liver fluke. The guidelines suggested that this often resulted in mis-timed fluke treatments and also leads to extensive inadvertent use of anthelmintic and unnecessary additional selection pressure on nematode populations likely to increase the risk of anthelmintic resistance. Consequently these products should be discouraged and replaced with use of flukicides as part of a fluke control strategy.

Monitoring is considered to be a key feature of control and flocks/herds should be checked for the presence of fluke before flukicides are used, unless already known to be infested by fluke and monitoring continued at regular intervals.

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Where fluke is present on a farm, a flukicide with immature activity should be used in October, and a further treatment given in January if faecal egg counts indicate that this is necessary. A flukicide with adult-only activity should be given to all animals at risk in May/June. The same flukicide should not be used year after year for autumn/winter treatments. Additional treatments will be necessary in wet years. As deer and rabbits act as fluke reservoirs, fluke eradication is not possible where the snail habitat exists.

Forecasting

The risk of severe outbreaks of fasciolosis increases following wet springs and summers. Forecasting systems, such as the Stormont 'wet day' forecast and the 'Mt' systems, based on rainfall and evaporation have been developed. In addition, geographic information systems (GIS) incorporating sophisticated computer models which simulate the life cycle of *F hepatica* and incorporate climatic, geographic and soil hydrology data are being introduced to predict the likely incidence and severity of fasciolosis. Accurate forecasts can normally be made by the end of the summer, but 'early warnings' may also be issued in the farming press (eg, if May and June have been exceptionally wet) to enable control measures to be instituted. SAC publishes monthly disease surveillance reports in the Veterinary Record incorporating information on fluke disease and available on-line at **http://www.sac.ac.uk/vet/External/MonthlyReport/Current.asp** and provides fluke data incorporated in the National Fluke Report produced by Novartis Animal Health available on-line at http://www.endoparasite.net/.

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