Liver Fluke

Liver fluke disease (fasciolosis) is caused by the trematode parasite *Fasciola hepatica*. Disease can result from the migration of large numbers of immature flukes through the liver, or from the presence of adult flukes in the bile ducts, or both. Liver fluke can infect all grazing animals (and man) but mainly affects sheep and cattle. It is most pathogenic in sheep.

Life-cycle

Compared to other helminths the life-cycle is complex, involving an intermediate host, the mud snail *Galba* (*Lymnaea) truncatula* and several free-living stages. The role of the snail, which prefers muddy, slightly acidic conditions, particularly areas associated with poor drainage, means that the incidence of liver fluke is far greater in the wetter areas of the country and in years when there is high summer rainfall. With the capacity of the snail to multiply rapidly (100,000 offspring in 3–4 months) along with the multiplication of the parasite within the snail, there is potential for very large numbers of parasites.

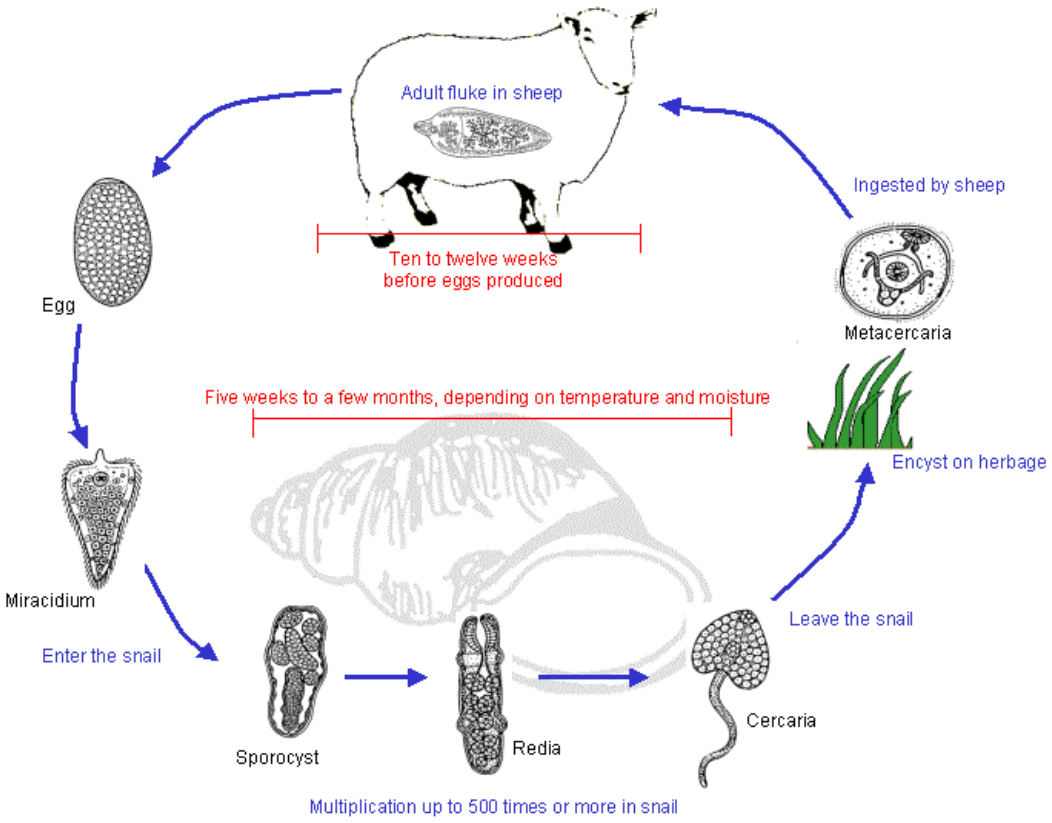

Fig. 7.1. ***Life-cycle of the liver fluke, Fasciola hepatica.***
(Drawings courtesy of Drs Oldham, Jacobs and Fox)

Adult fluke lay eggs that are passed out onto pasture in the faeces. At suitable temperatures, a miracidium develops within the egg, hatches and migrates in thin films of moisture, actively seeking

the snail host. Miracidia can only survive for a few hours outside the snail. Within the snail they undergo two further developmental stages, including multiplication, eventually becoming infective cercariae, which emerge from the snail when the temperature and moisture levels are suitable. The cercariae migrate onto wet herbage, encysting as metacercariae, the highly resilient infective stage of the liver fluke. Following ingestion, the young flukes migrate to the liver, through which they tunnel, causing considerable tissue damage. The infection is patent about 10–12 weeks after the metacercariae are ingested. The whole cycle takes 18-20 weeks.

Epidemiology

The hatching of fluke eggs and the multiplication of snails depend on adequate moisture and temperatures greater than 10ºC. Such conditions usually occur from May–October in the UK although patterns have been changing in recent years. The incidence of fasciolosis is highest in years when rainfall is above average during May–July. The epidemiology of liver fluke is often viewed as the result of two distinct cycles of snail infection and pasture contamination.

- *Summer infection of snails*

In wet summers, snail populations multiply rapidly and snails are invaded by hatching miracidia from May–July. If wet weather continues, the snails shed massive numbers of cercariae onto pasture during July–October. Conversely, if the climate in May–July is dry or cold, fewer snails appear, fewer fluke eggs hatch and levels of contamination in the autumn are much lower. Clinical fasciolosis resulting from summer infection of snails arises usually from ingestion of large numbers of metacercariae over a short period of time in July–October.

- *Winter infection of snails*

Less commonly, snails can become infected in late summer or early autumn and development within infected snails is delayed as the snails become dormant and hibernate. The cercariae are then not shed onto the pasture until the following spring. This can produce an initial and significant infection in herds or flocks in the spring.

Fasciolosis

Liver fluke disease in sheep occurs in three main clinical forms – acute, subacute and chronic fasciolosis. Which form occurs depends on the numbers of infective metaceriae ingested and the period of time over which they are ingested. Recent milder winters and wetter summers have seen changes patterns in parasite epidemiology and reported disease with earlier seasonal reports of acute disease. Table 7.1.outlines the clinical signs and treatment options for each form of the disease:

Table 7.1. *Diagnosis and treatment of fasciolosis in sheep*

Disease type	Peak incidence	Clinical signs	Fluke numbers	FEC (epg)	Treatment
Acute	July to December	**Sudden death** or dullness, anaemia, dyspnoea, ascites and abdominal pain.	1000+ mainly immature	0	Triclabendazole. Treat all sheep and move to a lower risk (drier) pasture if possible OR re-treat after 3 weeks. Further deaths may occur post-treatment from liver damage incurred.
Subacute	October to January	**Rapid weight loss, anaemia,** submandibular oedema and ascites in some cases.	500-1000 adults and immatures.	<100	Treat with a fasciolicide active against mature and immature fluke. If sheep cannot be moved to lower risk pasture, re-treat after 5-8 weeks.
Chronic	January to April	**Progressive weight loss, anaemia,** submandibular oedema, diarrhoea and ascites.	200+ adults	100+	All fasciolicides are active against the mature fluke involved in chronic disease. Treat and move to lower risk pasture.

Treatment and control

Control programmes must take into account the farm history, topography, geographical location and the prevailing weather. Most programmes rely heavily on flukicidal treatments. The choice of product and frequency of use will depend on the level of fluke challenge, the time of year, and the management and husbandry systems on the farm.

It is important to use the appropriate drug for each situation and to base treatments on fluke forecasts. Most flukicidal drugs on the market are effective in treating chronic fasciolosis, because they kill adult fluke, but few are effective in treating acute fluke infections in sheep caused by the immatures migrating through the liver (Table 7.2.). Triclabendazole (TCBZ) is generally the drug of choice but as resistance to flukicides can occur with repeated and frequent use, alternatives should be used wherever possible, particularly in late winter and spring, in order to reduce the potential for the development of TCBZ-resistance.

Fluke burdens can be monitored in sheep flocks by *post-mortem* examinations when the opportunity arises, or with FECs. Flocks should be monitored before a fasciolicide is used unless there is a history of fluke infection on the farm. Continued monitoring can help determine the need for repeated treatments. For treatment in late summer and autumn, a fasciolicide that is active against immature fluke is recommended. Treatment may need to be repeated in winter (January). If a spring treatment is required (April - June), then a flukicide with adult activity only can be used reducing the selection pressure associated with TCBZ.

The use of combination fluke and worm products should be discouraged as it can lead to off-target selection for resistance to broad-spectrum anthelmintics in nematodes, or fasciolicide resistance in *F hepatica*. However, there is evidence that closantel-BZ combinations have a synergistic activity that may enhance their activity against resistant *F hepatica* (and *H contortus*), and also help delay the emergence of resistance to either class of compound.

Where fluke infection is present, identification and exclusion of snail habitats from livestock offers some measure of control. Drainage eliminates the snail and offers an effective means of control, but the proliferation of environmental schemes to protect wetland areas has reduced the opportunities for this to be implemented. Simply keeping stock off the wettest fields in the autumn and the winter, when the incidence of disease is at its highest, can reduce the risk from fluke.

Table 7.2. ***Efficacy of flukicides available for use in sheep in the UK against susceptible fluke populations*** *(adapted from Fairweather and Boray, 1999).*

	Age of fluke (weeks)													
Flukicide	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
Albendazole										50 - 70%		80 - 99%		
Oxyclozanide														
Nitroxynil							50 - 90%			91 - 99%				
Closantel														
Triclabendazole (TCB)		90 - 99%					99 - 99.9%							

Resistance to fasciolicides

Resistance in the UK

TCBZ is the most widely used flukicide because of its activity against immature fluke. Unfortunately this has led to the development of resistance in several countries and reports of suspected resistance in the UK. Currently there are no validated field-based methods for the detection of fluke resistance and confirmation is extremely difficult. As a consequence, reported cases of TCB-resistance in the UK are very much anecdotal. An EU funded project DELIVER has evaluated an FECRT for fluke resistance investigations and several other in vitro and immunological methods have been investigated and reported but have yet to be validated for field use. Resistance, where it appears or is suspected, usually manifests firstly as a failure to kill the youngest immatures with subsequent re-appearance of fluke eggs in the faeces earlier than would be expected if the drug retained full

efficacy. As resistance develops eventually adult fluke are able to survive treatment as well. The possibility of other reasons for flukicide failure should always be considered, particularly if animals are in poor condition or may be suffering from liver damage.

Where resistance is suspected to a particular product, then an alternative flukicide listed in Table 7.2. should be considered, taking into account the variations in activity against immature fluke between products. However, it is also advisable to consider the other possible reasons for apparent failure because it is likely that although some cases are due to resistance, the situation is not as clear cut as resistance in roundworms. Firstly, there are no validated tests for resistance in liver fluke. A simple post treatment Faecal Egg count (FEC) is not conclusive and other methods are still under investigation. Secondly, there are a number of other reasons why treatment may not be fully effective and appear to fail. These include:

- Pastures with very heavy infestations can mean that farmers are caught out by the speed which animals become re-infected following treatment.
- Triclabendazole (TCBZ) is widely used because it kills early immature fluke and historically has been highly effective when used correctly. It does, however, have to be partly metabolised by the liver before it can work properly. If the liver is already damaged through a high fluke burden or other concurrent disease this has the potential to reduce efficacy.
- Inaccurate dosing through underdosing and/or badly calibrated and maintained equipment – the same old story, but so often the root cause of an apparent failure.
- Incorrect product choice – for example the use of an adulticide in the autumn leaving large numbers of immature flukes untouched to continue to cause disease.

Preventing the development of resistance

Rotational use of TCBZ, closantel or nitroxynil should be considered where flukicides are used strategically, although additional treatments may be required in years when TCB is not used. Opportunities to avoid the use of TCBZ should be exploited whenever alternate drugs will give satisfactory levels of control. For example the use of closantel or nitroxynil 3 weeks post-housing; treatment of chronic infections in the spring with an adulticide.

Quarantine

The need for quarantine treatments

Quarantine treatment strategies for liver fluke in introduced sheep, cattle or goats should be considered 'using a risk-based' and developed for farms considered "at risk" in conjunction with a veterinarian or advisor.

The three principal reasons for treatment are:

1. Sheep may be introduced onto a farm with no known snail habitat and, therefore, no history of fluke infection. The risk of introduced fluke establishing on the farm is very small (or zero, if there is no snail habitat) and treatment in this case is intended to remove any fluke in the sheep for the sake of their health. Treatment with a flukicide active against immatures is advised, with FEC monitoring in subsequent months to detect any small residual burden. The consequences of introducing small numbers of fluke, or resistant fluke, are not serious in the long-term.
2. The farm may have areas considered to be a suitable habitat for snails but no history of fluke infection. The risk of introduced fluke establishing on the farm is considered to be significant so treatment is aimed at removing all fluke, including any resistant fluke.
3. Liver fluke may be endemic on the farm, so introducing small numbers of fluke will not be serious, particularly if wildlife reservoirs exist. However, if the endemic fluke are fully flukicide - susceptible, the consequences of introducing resistant fluke are potentially serious.

Choosing a treatment strategy

The following factors should be considered when choosing a quarantine treatment strategy.

- Resistance to TCBZ is still relatively uncommon in the UK and, in most cases treatment with TCBZ will remove a very high proportion of susceptible flukes of all stages.
- Treatment of TCBZ alone will not remove TCBZ-resistant fluke.
- Treatment with closantel or nitroxynil is expected to prevent the output of fluke eggs for at least 8 weeks and probably more, provided the fluke are susceptible to the drug used. If the introduced sheep are infected with young immature fluke, treatment will have to be repeated after the immatures are old enough to be killed by these products (see Table 7.2.). In this context, it may be worth considering the use of two doses of closantel given 6 weeks apart (nitroxynil a minimum of 7 weeks apart for sheep
- Resistance to closantel and to nitroxynil has been reported in other countries.
- Treatment with more than one product with activity against immature flukes (closantel, nitroxynil, TCBZ) will reduce the risk of introducing fluke with resistance to any one product. It is not recommended, however, that two products are used at the same time, because of the potential risk to the health of the sheep.
- Sheep can pass fluke eggs for up to 3 weeks after adult fluke are killed. It is advised that sheep be kept on quarantine pastures or pastures with no fluke habitat for at least 4 weeks after treatment.
- FEC monitoring can be used to determine the need for treatments subsequent to the initial one.