

LIVER FLUKE EXPLAINED

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Fluke Life Cycle

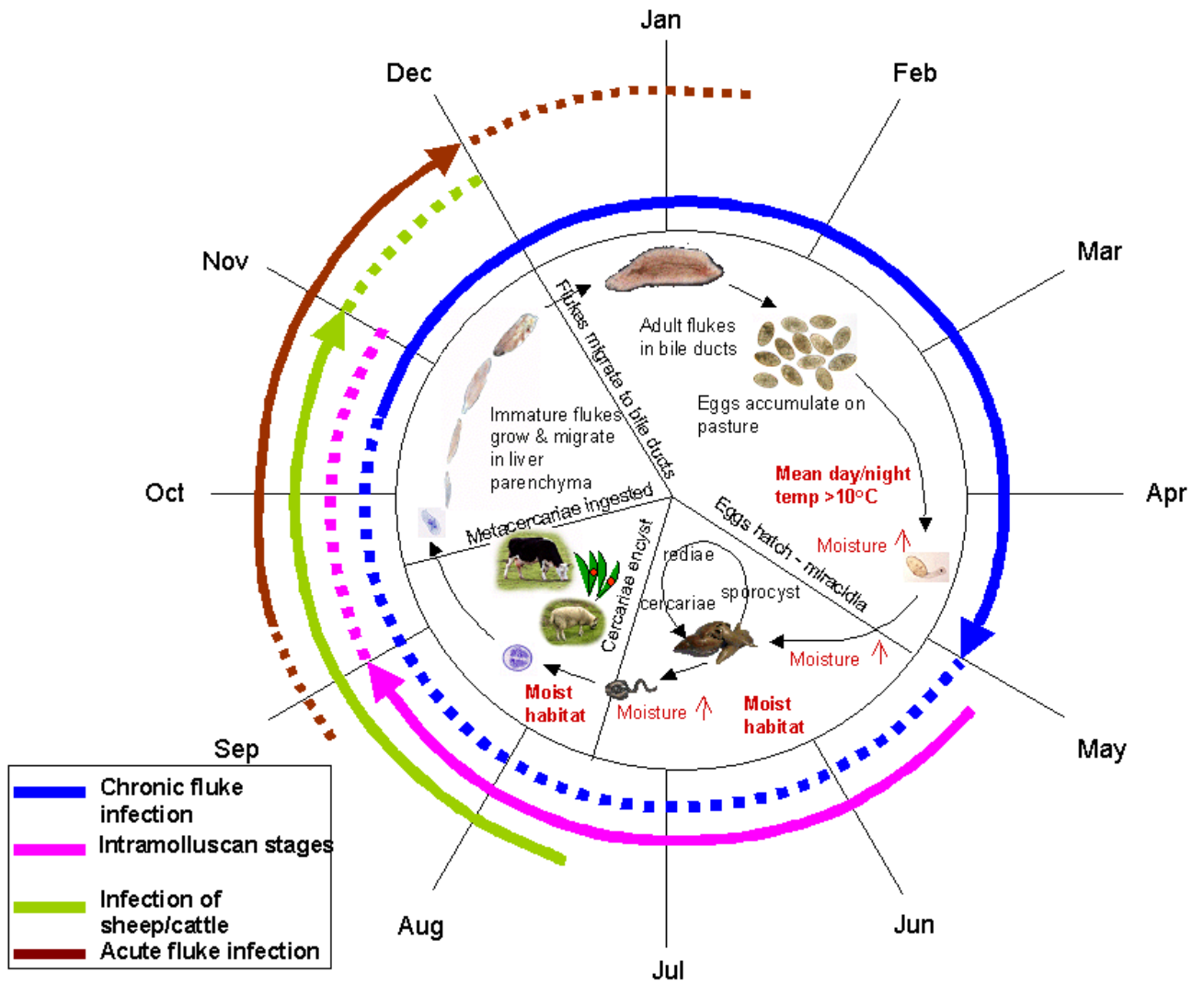
Completion of the life cycle of the liver fluke *Fasciola hepatica*, is closely dependant on climatic conditions. Factors such as the survival and development rate of the fluke eggs, availability and distribution of the snail intermediate host *Lymnaea truncatula*, rate of development of infection within the snails and survival on pasture of the metacercaria larvae are closely linked to the temperature and humidity of the environment. The timing and intensity of the metacercarial peak on pasture in late summer and autumn in any year are also closely related to the climatic conditions prevailing in the preceding six to nine months.

The minimum temperature for development of *F. hepatica* eggs is about 10°C (Figure 1). The rate of development ranges from 80 days at this temperature to 10 days at 25°C. Thus, eggs shed onto pasture in winter and spring usually begin to develop in early April, accelerating as the mean day/night temperature rises, with large numbers of miracidium larvae hatching in late May. Snails also emerge from hibernation and begin breeding when the temperature exceeds 10°C, so the availability of the new generation of juvenile snails in late spring approximately coincides with hatching of the miracidia. Fluke egg development, survival of miracidia and successful location of snails by

the free-swimming larvae are very dependant on the presence of adequate moisture, as indeed is the emergence, feeding, breeding and distribution of the amphibious snail hosts.

At 15°C, larval development of *F. hepatica* within the snail is completed in 80 days, decreasing to 30 days at 25°C. Assuming that adequate moisture is available, cercaria larvae may therefore be expected to emerge from the snails to encyst on vegetation from mid-July onwards. The shedding of cercariae by snails is triggered by the temporary drop in temperature that follows a shower of rain. The peak of metacercarial availability on pasture in Northern Ireland usually occurs around mid-August, and sheep and cattle grazing in heavily infested areas may ingest very large doses of metacercariae within a short period at this time of year.

Figure 1. Life cycle of *Fasciola hepatica*



Following ingestion by sheep, the juvenile flukes hatch from the metacercarial cysts in the intestine, migrate through the gut wall, locate the liver within a few days, and begin to burrow through the hepatic parenchyma towards the bile ducts. As they feed on the host's tissues and blood they grow and develop rapidly, causing increasing damage and haemorrhage as they increase in size and voracity. In sheep, the appearance of clinical signs such as ill-thrift, diarrhoea, anaemia, pallor of mucous membranes, weakness and icterus depends on the number of migrating flukes and their size. Typically, in heavy infections of 1000 or more metacercariae, the signs of acute fascioliasis begin to appear after 5 weeks. Morbidity and death due to fluke infection are therefore seen from about late September until 5 or 6 weeks after the first frosts, often in late October, that help reduce the metacercarial burden on the pasture and send the snails into hibernation.

Epidemiology

Most cases of acute fascioliasis result from ingestion of metacercariae in late summer from eggs hatching in the same year. These eggs were shed during the winter and spring by adult worms inhabiting the bile ducts of chronically-infected untreated sheep and cattle that survived infection in the previous year. However, some metacercariae do survive on pasture over winter, particularly if the conditions are mild. In addition, immature fluke infections in snails cease development when the intermediate host enters hibernation deep in the mud at the onset of winter. These resume

development when the snails reactivate in April, and may give rise to a crop of metacercariae on the late spring/early summer pasture. So sheep and cattle may begin to acquire low levels of fluke infection from the beginning of the grazing season due to these overwintering larvae. While such infections rarely cause significant clinical signs, the damage to the liver may have implications for the metabolism of anthelmintic drugs later in the season.

Control

In the face of losses due to acute fluke infection, it may be necessary to dose the survivors at 4 to 6 week intervals until December using a flukicidal drug that is active against the most immature stages. In moderate risk fluke areas, sheep should be dosed at 10-week intervals from September to late January. As a preventative measure in high-risk fluke areas, it is advisable to dose all sheep at 10-week intervals from April to November, with an additional treatment in January to remove chronic infections.

Animals that ingest lower numbers of metacercariae usually survive the acute phase of infection, during which immature flukes migrate through the liver parenchyma. Once the flukes become established in the major bile ducts, they mature and begin producing eggs 8-10 weeks after the initial infection. The eggs pass into the intestine with the bile. Provided that there is not a subsequent invasion of young flukes, the liver parenchymal tissue regenerates and recovers function, albeit with substantial fibrous scarring. It is these animals, harbouring chronic

infections of mature fluke, that provide the source of fluke eggs for contamination of the pasture during the winter and spring months, and therefore represent the main contributors to disease in the next year. In any management programme for control of fascioliasis, it is essential to eliminate mature flukes from over-wintered stock by dosing several times during the winter months or before lambing, using a flukicide that is active against the adult worms.

Cattle, unlike sheep, develop a degree of natural resistance to second and subsequent infections by incoming juvenile flukes. Worm survival is poorer in cattle as compared to sheep, and the rate of maturation is slower. As a result of these differences, cattle rarely suffer from acute fascioliasis. However, chronic infections are common in over-wintered stock, necessitating one or more treatments during the housing period with flukicide active against the adult worms, in order to reduce the risk of pasture contamination after turn-out.

Flukicidal Anthelmintics

Clearly, when initiating a regime of anthelmintic dosing to control liver fluke infection in sheep and cattle, it is important to consider the stage of the fluke life-cycle to be targeted, and to select an anthelmintic product with the appropriate spectrum of activity. In Table 2, anthelmintic compounds licensed for control of fascioliasis in the UK (autumn 2003) are listed with corresponding product names and an indication of their efficacy against flukes of different ages. For the prevention or control of acute

infections in sheep in the late summer and autumn months, it is necessary to use a product active against the earliest possible stages. Treatment of chronic (adult) fluke infection in sheep and cattle during the winter and early spring, to reduce pasture contamination by eggs, can be carried out using less expensive products that are active only against the adult worms in the bile ducts.

The efficacy of triclabendazole against fluke of all ages down to 2 days old in sheep, has ensured its widespread use since its release in the early 1980s. However, fluke resistance to this drug is now well established in sheep overseas, particularly in Australia, and instances of apparent resistance have been recorded in the north west of Ireland. Resistance has also been found in fluke infecting cattle. It is unclear whether the survival of flukes in triclabendazole-treated animals here is due to development of true drug-resistance, or whether it reflects an inability of the host's liver, already severely damaged by migrating parasites, to metabolise the drug effectively to the active form. When triclabendazole resistance is suspected, it is advisable to change to other anthelmintic products capable of killing juvenile flukes, such as those containing closantel. The latter compounds are administered in the active form and do not require metabolism in the liver. As with all anthelmintic products, the manufacturer's recommended dosing levels and intervals should be strictly adhered to, as under-dosing can encourage the emergence of resistant strains of fluke, whilst over-dosing can result in toxicity if liver function is

already compromised by fluke damage.

Farmers are recommended to obtain the advice of a veterinary surgeon when developing fluke control programmes.

Other Control Measures

Apart from the use of anthelmintic drugs to eliminate flukes from sheep and cattle, the likelihood of infection on individual farms may be reduced by measures targeted at the molluscan intermediate host. Drainage of potential snail habitats is consistent with environmentally-sensitive programmes of land improvement, and can have long-term benefits for parasite control. Molluscicides may be effective in limited, well-defined areas where there is a temporary drainage problem, but the compounds available are non-selective and may cause significant environmental damage. Their efficacy is reduced in extensive and well-established snail habitats where the population can be augmented by immigration from surrounding areas of untreated land.

Table 2. Anthelmintics active against *Fasciola hepatica* and licensed in UK (autumn 2003). (Note that some products contain compounds active against other parasites)

Active Compound (Examples of trade names)	% Active Compound	Route of Administration	Species	Efficacy (fluke age)	Metabolism in liver necessary?	Withdrawal Period (meat)/withholding time (milk)
Closantel (<i>Flukiver, Mebadown Super, Supaverm</i>)	5%	Oral	Sheep	3-4 weeks to adult (delays egg production by up to 13 weeks)	No	Meat: 42 days
Nitroxylnil (<i>Trodax</i>)	34%	Subcutaneous	Sheep and cattle	6 weeks to adult	No	Meat: 60 days Unsuitable for lactating dairy cattle
Triclabendazole (<i>Fasinex, Combinex</i>)	5%	Oral	Sheep	2 days to adult in sheep	Yes	Meat: 28-56 days depending on product
(<i>Fasinex, Combinex</i>)	10% or 12%	Oral	Cattle	2 weeks to adult in cattle		Meat: 28-56 days depending on product Unsuitable for lactating dairy cattle
Clorsulon (<i>Ivomec Super</i>)	10%	Subcutaneous	Cattle	Adult	No	Meat: 35 days Unsuitable for lactating dairy cattle
Albendazole (<i>Albenil Low Dose, Albenil SC, Albex SC, Albex, Endospec SC, Ovispec S&C, Tramazole</i>)	2.5% or 10%	Oral	Sheep and cattle	Adults and eggs	Yes	Meat (sheep): 4 days Meat (cattle): 14 days Milk: 60 hours
(<i>Valbazen SC/ Valbazen Total Spectrum Wormer</i>)	2.5% or 10%	Oral	Sheep	Adults and eggs	Yes	Meat: 8 days

Table 2. (continued)

Active Compound (Examples of trade names)	% Active Compound	Route of Administration	Species	Efficacy (fluke age)	Metabolism in liver necessary?	Withdrawal Period (meat)/withholding time (milk)
Ricobendazole (<i>Allverm, Rycoben SC</i>)	2.5% or 4%	Oral	Sheep	Adults and eggs	No	Meat: 3 days
(<i>Rycoben</i>)	7.5%		Cattle			Meat: 14 days; Milk: 72 hours
Netobimin (<i>Hapadex</i>)	5%	Oral	Sheep	Adults	Yes	Meat: 5 days
(<i>Hapadex</i>)	15%		Cattle			Meat: 10 days; Milk: 48 hours
Oxyclozanide (<i>Levafas Diamond, Levafas Fluke and Worm, Nilzan Drench Super, Nilzan Gold, Systemex Plus Fluke SC, Zani</i>)	3% or 6%	Oral	Sheep and cattle	Adults	No	Meat: 28 days Unsuitable for lactating dairy cattle