Controlling Liver Fluke on Welsh Farms







Hybu Cig Cymru / Meat Promotion Wales Tŷ Rheidol, Parc Merlin, Aberystwyth SY23 3FF Tel: 01970 625050 Fax: 01970 615148 Email: info@hccmpw.org.uk

www.hccmpw.org.uk

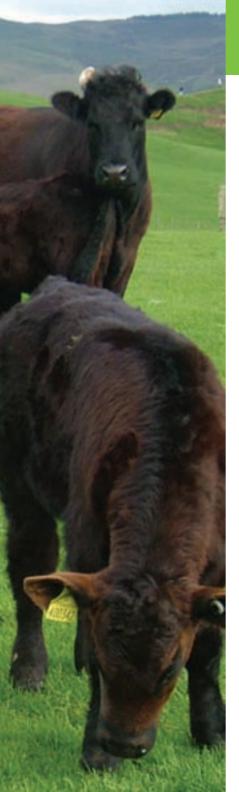
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In recent years Wales has seen an increase both in the number of farms affected with liver fluke (Fasciola hepatica) and the severity of infections on farms traditionally affected by the parasite. This trend has also been accompanied by an increasing number of farms reporting reduced effectiveness of flukicides containing triclabendazole (TCBZ). Flukicides are the most commonly used and often the only realistic option for liver fluke control. Therefore, the failure of TCBZ which has the greatest spectrum of activity against liver fluke in both sheep and cattle, is a major blow to any meat producer.

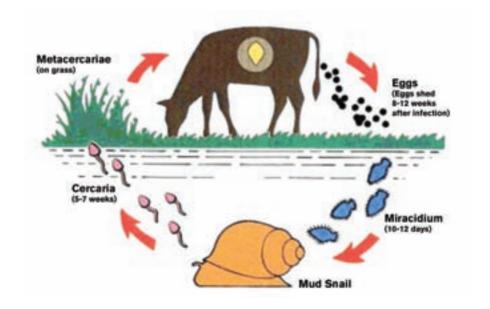
This booklet provides information and guidelines for producers in Wales on how to protect their livestock from liver fluke and prolong the life of the treatments available (flukicides). However, these are guidelines and as such for effective control producers should always consult with a veterinarian or livestock advisor to devise a more specific health plan for their livestock. This booklet is the culmination of 4 years of research into TCB7 resistant liver fluke carried out at the Institute for Biological, Environment and Rural Sciences (IBERS) at Aberystwyth University, in collaboration with the Animal Health Veterinary Laboratories Agency (AHVLA) laboratories in Aberystwyth and Carmarthen, and the Welsh Regional Veterinary Centre (WRVC), Gelli Aur.

Lifecycle

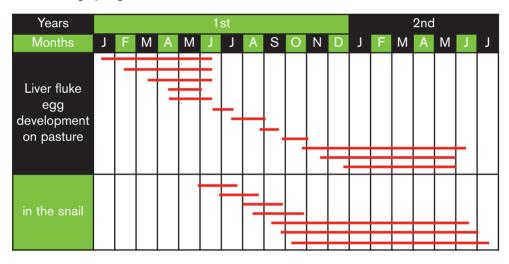
Liver fluke infects both an intermediate host and a vertebrate host during its lifecycle (see diagram below). In the U.K. the most common vertebrate hosts are sheep and cattle but only the mud snail. Galba truncatula (also named Lymnaea truncatula) is the intermediate host. To complete its lifecycle the parasite must infect both these hosts.

If sheep and cattle graze wet and/or muddy areas of fields which are suitable habitats for snails they are at risk of ingesting the infective stage of the parasite - the metacercariae, which can be found attached to grass and other herbage in these areas. The metacercariae are very small (around 160µm in diameter) when ingested and are encased by a shell of hard protective protein. They pass through the digestive tract of the host (sheep or cow) to the small intestine where they hatch from their protective shell and burrow through the wall of the intestine and into the body cavity of the host. Once in the cavity they migrate to the liver reaching the liver 4-7 days after being eaten by the host.

The liver fluke will then migrate through liver tissue, entering the bile ducts after 4-6 weeks. Once in the bile ducts liver fluke will mature into adults. Here they can produce up to 25,000 eggs per day which are shed in the host's faeces.



To complete the life cycle the eggs from adults in the bile ducts of a sheep or cow are deposited on to the ground in the host's faeces but only fully develop once they are separated from the faeces. Under perfect conditions eggs can develop and hatch in 9 days but often take longer. Studies done in the field have shown eggs that are placed on pasture between October and April will develop and hatch in the following May/June (see figure below). Eggs placed on the pasture by the host before mid-August, are likely to develop and hatch before the winter. If this happens and the larvae called a miracidia at this stage, manages to find and infect a suitable snail host in autumn, then the parasite will have a chance to also overwinter by this method, as long as its snail host also survives the winter. However, the survival of liver fluke by both of these methods is down to both the severity of the winter and the conditions the following spring.



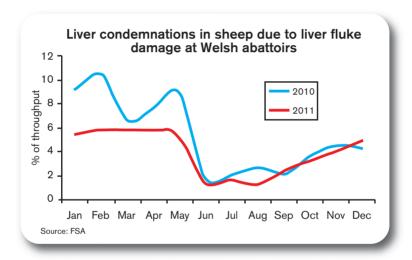
Ollerenshaw (1967): The red lines show the length of time taken for eggs to develop and hatch on pasture and length of time taken by the parasite in infected snails to develop according to the time of year.

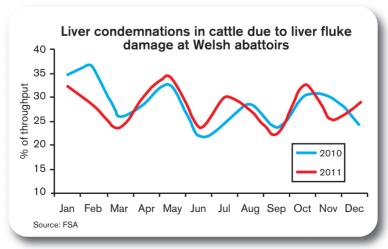
It is the adult liver fluke in the vertebrate host that naturally survives the winter best and this is the reason why treatment of animals in the autumn/winter is crucial as it stops the depositing of eggs on the pasture in the spring and early summer that will have a greater chance of developing and completing their life cycle to re-infect livestock in the autumn.

Liver fluke on Welsh beef and sheep farms

Although farmers are not penalised for condemned livers, a damaged liver will affect production with infected animals losing up to 1.2kg/week. In Wales the succession of wet summers and mild winters that occurred between 2006 and 2009 saw a major increase in the number of cases of acute liver fluke due to the successful overwintering of eggs and the ideal conditions for the intermediate snail host.

The graphs below illustrate the liver condemnations from stock slaughtered in Welsh abattoirs during 2010 and 2011.

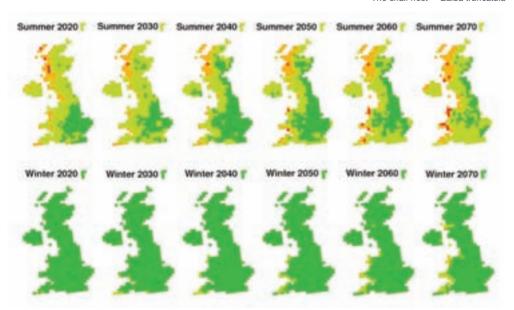




However, with very cold conditions during the winters of 2009/2010 and 2010/2011, the number of eggs successfully overwintering on pastures was significantly reduced and the dry spell in the spring of 2011 also appears to have affected the number of snails present for the surviving eggs to infect. This has led to reduced cases of acute infections during the winter of 2011/2012. However, with long term climate trends predicted for Wales of milder winters and wetter summers due to climate change, periods of intense infection similar to 2006-2009 are predicted to occur more frequently in the future.



The snail host - Galba truncatula



(Fox et al, 2011) Projected change in fasciolosis risk. Summer and winter F. hepatica risk across the UK at a resolution of 25 km squares, 2020-2070. Risk categories are based on those used by Ollerenshaw & Rowlands (1959): Little or no disease (dark green), occasional losses (light green), disease prevalent (orange), serious epidemic (red).

Diagnosis

The number of liver fluke inside a host can vary between infected animals and the symptoms caused will vary due to this. Therefore initial diagnosis should be made by a veterinarian. However, the following is clarification of the clinical (visible) symptoms caused by the 3 main classes of infection levels in an animal: (Number of metacercariae is based on sheep: cattle will normally not be affected by acute type, accept in years of high incidence.)

- Acute Type Fasciolosis: 1000 or more metacercariae
 - sudden death following clinical signs
 - abdominal haemorrhaging (bleeding)
 - jaundice (yellowing of eyes and mucous membranes)
 - pale mucous membranes



Ewe with bottleiaw

- Subacute Fasciolosis: 800-1000 metacercariae
 - weight loss is the dominant feature
 - lethargic
 - anaemic
 - may die
- Chronic Fasciolosis: 200-800 metacercariae
 - weight loss
 - development of bottle jaw
 - ventral oedema (swollen belly)
 - emaciation (extreme weight loss)

Many of these symptoms are also signs of other diseases in sheep or cattle and therefore, if any of these symptoms are observed in your animals then only by further examination, such as post mortem in the case of acute and through faecal egg counts in the cases of subacute and chronic, can a robust diagnosis be made. However, before undertaking such tests farmers should contact a veterinarian for advice on how to proceed.

Guidelines for producers

There is no quick and easy method of control for liver fluke but through careful, targeted management strategies and using many of the tools available a farm can certainly reduce the financial costs from liver fluke. The following guidelines are the main tools available to a farmer for liver fluke control. Discuss your situation with your veterinarian or sheep advisor and develop a health plan to ensure the best results for your farm.

Liver condemnations

Liver condemnations can be used as an indicator of infection occurring on a farm and through careful examination can give clues as to where and when certain groups of animals from a farm are developing liver fluke infections. However, a liver condemned for liver fluke does not always mean alot of liver fluke, it could be just one adult was seen in one or two of the ducts but the livers looked otherwise in good health or the liver may have been so full the bile duct was swollen and the outside of the liver was disfigured by the scars. If you are unsure then ask the slaughterhouse if they are able to say more about your batch of animals.



Fluke in bile duct of an infected liver

Faecal Egg Counts (FECs)

Faecal egg counts have been very useful for many years in identifying liver fluke infections on farms. There are many limitations to the use of liver fluke egg counts but when used correctly and in conjunction with other information from the same group of animals they can help to produce a very accurate overall picture of liver fluke populations on a farm.

> A recent project at IBERS, which carried out monthly FECs on sheep and cattle farms in Wales, found that monthly faecal egg counting gave useful data on the incidence of liver fluke on the farms, and in one case increased egg counts were seen between June and July in a group of animals normally treated in November. Such monthly testing of faeces may not be a financially justified method of monitoring on farms but the project at IBERS has indicated the need for farms to ensure treatments for liver fluke are given at an optimum time for their farm. Therefore, to check that applications are given at the best possible time in the year it is recommended that farmers take a composite (combined sample) faecal sample from at least 10 animals of the same group 2 months before and another from the same 10 animals 1 month before the month where they would normally be treated.

For example if a farmer usually treats a group of ewes in January then they should take a composite sample

Fluke Egg Source: NADIS

for faecal egg counting from 10 ewes in November and mark the animals they collected from. Then collect and send for counting another composite sample from the same 10 animals a month later in December. If a significant rise in egg counts is seen between the two months or the egg count is high in both months

then this may indicate changes are required to the farm's treatment strategy to achieve optimal cover. However, any such results must be discussed with a suitably qualified person or veterinarian.

Drainage and fencing

Drainage and fencing can be highly effective and although costly in the short term could result in savings in the long term. But with a high number of farms entered into environment schemes there may also be contractual issues prohibiting such work in certain areas.

However, if drainage and fencing are seen as financially possible the best method to proceed is through targeting one field at a time providing fields with lower risk of liver fluke infection for vulnerable groups of animals to graze during periods of high infection risk in the late summer and autumn months.

Unlike nematodes, liver fluke can only be found in areas where the intermediate snail is present. This is why fencing off areas and drainage will always be an important method of control. However, sometimes changes to a farm's grazing system can also help by avoiding high risk areas at high risk times of the year. The majority of infection occurs from July to December and therefore reducing the time spent grazing high risk areas during those months could reduce the level of infections.

A combination of monitoring through faecal egg counting and liver condemnation reports can help plan effective control of liver fluke. The use of NADIS (National Animal Disease Information Service) forecasts can be helpful to plan ahead for potentially very high risk periods. These forecasts can be accessed via the HCC website at www.hccmpw.org.uk



Flukicide treatment

Flukicide treatment is the most common method of control but will not stop reinfection and although some flukicides can kill 99% of most stages of liver fluke in an animal, the fact they do not kill 100% of all stages means the development of resistant liver fluke against all flukicides is possible. For this reason it is important to use flukicides as directed by the data sheet which comes with every container of flukicide, and follow the 3 steps to ensure all flukicides will remain as effective as possible for as long as possible on your farm:

- 1. Weighing: Make sure your scales are accurate and weigh the largest animals at least to ensure you use a dose that is either correct or slightly over for all the animals in the group.
- 2. Calibrate and maintain the drench or pour-on gun: Always check the gun delivers the correct amount using a measuring cylinder. Alternatively remove the plunger from a syringe and cover the end for the needle with your finger to

improvise a measuring cylinder. Always wash the gun after use in soapy water and replace worn parts before storing away for the next time. Also ensure the tube between the gun and bottle has not perished or kinked before use and clean before re-storing for the next time.

3. Dose correctly: Ensure the animal is restrained correctly using a suitable handling system that allows you to safely administer the dose to the animal correctly. For oral doses the gun nozzle needs to go over the tongue but avoid lifting the head to ensure the dose goes into the rumen and not into the true stomach (abomasum) which will reduce the drug activation. For pour-ons on cattle ensure

an even application along the area indicated on the products data sheet. Some pour-ons are waterproof but if not ensure the animals are dry and are not exposed to rain for at least 2 hours. For cattle, separation of the animals may be necessary to avoid licking, leading to some animals ingesting the dose from another animal's back. Never use combined flukicide and nematocide (wormer) as this approach can lead to unnecessary use of some wormers which will encourage the development of resistance to the wormer in the product being used. Further information on the responsible use of wormers can be found at www.scops.org.uk

Although there may appear to be many different flukicides available to treat liver fluke there are only three specific flukicides* available in the UK that will effectively kill adults and to a varying degree juvenile liver fluke. The most effective of these is triclabendazole (TCBZ) which is a benzimidazole but has no effect on nematodes. TCBZ can effectively kill all stages of liver fluke older than 1 week. There have been reports of resistance to TCBZ in Wales and if this happens on a farm the next most effective flukicides are closantel or nitroxynil. However, these two drugs will not effectively kill liver fluke less than 6 weeks old in the animal.

* Albendazole and oxyclozanide are available but have no effect on liver fluke less than 10 weeks old in sheep or cattle, and may impact on nematode control so may be best avoided

Weeks after infection of Sheep	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Triclabendazole (TCBZ)		90-9	99%		99-100%									
Closantel					50-90% 91-99%					%				
Nitroxynil						50-90% 91-9			1-99	%				

(Fairweather and Boray, 1999) Table of the spectrum of effectiveness of the three main flukicides available to sheep and beef farmers in the UK the percentages represent the percentage of liver fluke expected to be killed during the different weeks after infection in sheep. The drugs have a very similar spectrum of activity in cattle.

The best long term strategy for flukicide is to use flukicides in rotation; ensuring parasites do not come in contact with just one flukicide. A commonly suggested rotation is using closantel or nitroxynil in the spring and TCBZ in the autumn/winter. However, it is important to tailor treatment plans to your circumstances to ensure maximum cover and longevity of all flukicides and therefore advice should be sought from a suitably qualified person or your veterinarian.

Quarantine

Quarantine of animals brought onto the holding is necessary to stop the introduction of liver fluke with flukicide resistance.

Currently in the UK, resistance has only been reported for triclabendazole, and therefore, closantel or nitroxynil containing products are the best options for protection against confirmed flukicide resistant liver fluke.

However, to ensure no contamination of pastures with eggs from resistant liver fluke the animals should be kept off pasture for 5 weeks to ensure all liver fluke inside the animals are mature enough to be susceptible to either closantel or nitroxynil. The animal must then remain off pasture for a further 4 weeks to ensure all eggs have passed out through the faeces after treatment, giving a total of 9 weeks off pasture.

If such a long period of segregation is not possible then the animals should be kept off pasture for as long as possible (ideally at least until they have been treated) and then turned out on to the driest piece of land available to minimise the number of eggs being deposited near to or in a snail habitat. With effective quarantine methods resistance development can be delayed by reducing the risk of introducing drug resistant liver fluke to your farm.



Drug resistance the what, how and where

Using flukicides is the main method of liver fluke control in sheep and cattle. Flukicides offer a safe and relatively simple method of control for sheep and cattle owners. However, resistance to flukicides will develop quicker without careful and responsible application of flukicide drugs.

Resistance to a flukicide is when a liver fluke comes in contact with the active form of the drug at the correct and normally lethal concentration inside the host but survives and successfully reproduces. Once this occurs selection for the offspring from the resistant liver fluke will allow the development of a resistant population in a flock or herd.

However, flukicide resistance must not be confused with flukicide failure which is when a liver fluke does not come in contact with the correct lethal concentration. Flukicide failure can lead to resistance if it is not dealt with.

Failure of a flukicide to kill liver fluke in a sheep or cow can occur because of any combination of the following:

- Incorrect storage of the flukicide or use of flukicides past their shelf life
- Inaccurate application
- Damage to organs of treated animal: For example a damaged liver from migrating liver fluke could change the rate at which the drug is metabolised into the active form of the drug (Although this requires more research to show how much liver damage affects drug metabolism)
- Diet of the treated animal: Studies have shown different types of diets can affect the blood concentrations of the active form of a drug
- Number of liver fluke in the treated animal: There currently is no test to identify
 how many liver fluke are in an animal before treatment. Therefore some liver fluke
 in an overcrowded bile duct may not come in contact with enough of the active
 form of the drug

To help the livestock industry identify if a flukicide provides effective cover in flocks or herds, the World Association for the Advancement of Veterinary Parasitology (WAAVP) produced the following guide:

Percentage of Parasites Killed by Flukicide (Efficacy)	Effectiveness of Protection to Flock or Herd
99.9-98%	Highly effective cover
98-90%	Effective cover
80-89%	Moderate cover
Less than 80%	Insufficient cover

If you suspect that the flukicide you have used has not worked you must contact a veterinarian to determine if this is due to resistant liver fluke or flukicide failure. Although resistance tests have been shown to work in the IBERS laboratories. resistance tests have yet to become commercially available.

Therefore determining if resistance or failure has occurred can only be done through a faecal egg count reduction test combined with a series of blood tests, to show the drug has been metabolised correctly. For the majority of cases these two tests will show if it is resistance or failure. However, currently the only conclusive answer can be achieved by collecting several of the liver fluke at slaughter and placing them directly in specific concentrations of the active form of the drug in a laboratory to see if they die. Such tests can in theory already be done but are costly due to the specialised materials required and are therefore unlikely to be done. But when faced with losing the capability of using one of the three most effective flukicides available, there have been some farms which have seen the merit of confirming resistance definitively.

Source: NADIS

New diagnostic tests

The current tests for liver fluke are limited in their capabilities due to the lack of ability to test for juvenile liver fluke or even give an accurate indication to the number of adults present. However, progress has been made in recent years and recently a test has now become available to laboratories that can detect both juvenile and adult stages of liver fluke found in the bile ducts of the infected animal. This test picks up proteins released by both juveniles and adults that pass through the intestinal gut tract and out through the faeces. The test has been found to be more sensitive than faecal egg counts and it is hoped that this test will soon replace faecal egg counting in laboratories.

However, this new test still requires a laboratory and so research is currently being directed at new quicker methods capable of being done beside the animal, or that can produce a result within an hour or two with a simple dipstick. The technology for such tests has already been developed for testing the blood from humans to detect heart damage and a research group has just announced they have developed such a test for the tropical liver fluke. So it may not be long before farmers are able to test quickly and accurately for liver fluke without sending samples away to be tested.

Vaccines

A potentially better method for control would be the development of a vaccine against liver fluke. Unfortunately such vaccines are unlikely to become available to farmers for their sheep or cattle for many more years. Therefore, also with the lack of new flukicides on the horizon, it is important for farmers to ensure the existing flukicides are effective against liver fluke for as long as possible.

Tests for resistance

With the lack of vaccines and the ever increasing levels of resistance being reported by veterinarians and farmers, there is a growing need for a test to confirm resistance quickly and by non-invasive means. The precursor to such a test has been developed in the laboratories in IBERS and is now being validated for development into tests for farmers and veterinarians to use in the field.

Key points

Remember the Five Fluke Facts:

- 1. Liver fluke must infect a snail to live! Unlike nematodes liver fluke must find the snail after hatching so sheep or cattle on well-drained dry soil are less likely to pick up liver fluke or infect that pasture with liver fluke.
- 2. Liver fluke come in waves! This year might be a low incidence year and the next, and even the one after. But if you have seen bad cases of liver fluke in your animals in the past, then always watch for livers being condemned and make sure your treatments are well timed for maximum disruption to the liver fluke life cycle.
- 3. Always treat correctly! Take your time and treat as accurately as possible. You might very well want to get onto another job, but a little more time when treating today can mean fewer losses to liver fluke in the future. Always quarantine and treat against fluke especially TCBZ resistant ones.
- 4. Think long term on control of liver fluke! Look to longer term controls of liver fluke such as drainage, fencing or grazing rotations to reduce the number of liver fluke infecting your flock or herd. Work out a whole farm parasite control plan that includes liver fluke as part of your animal health plan to ensure your flock or herd are protected and keep updating the plan each year as best as you can.
- 5. Parasites appear on farms but do not go away! Quarantine controls are a must. According to on-going trials once you have introduced TCBZ resistant liver fluke you have got it for a very long time or possibly forever.

