Philip J Skuce PhD| Principal Scientist |Moredun Research Institute
Teagasc Hill Sheep Conference, Glendalough, 15th Feb 2024

Sustainable control of liver fluke in (hill) sheep

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Promoting livestock health and welfare through research and education

Knowledge Exchange

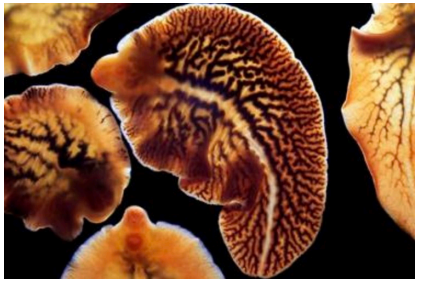
Diagnostics

Vaccines

Disease Control Strategies

The Liver Fluke

- Highly pathogenic flatworm parasite, *Fasciola hepatica*
- Complicated life-cycle involving tiny mud snail intermediate host, *Galba truncatula*
- Threat to sheep (and cattle) of all ages, little/no natural immunity
- Significant environmental component to disease risk - climatic conditions, grazing management, also wildlife hosts e.g. deer, rabbits, hares etc.



The ‘typical’ seasonal liver fluke life-cycle

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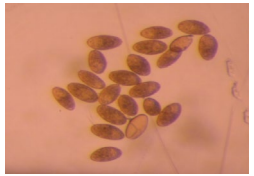

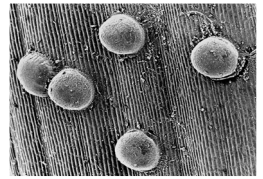

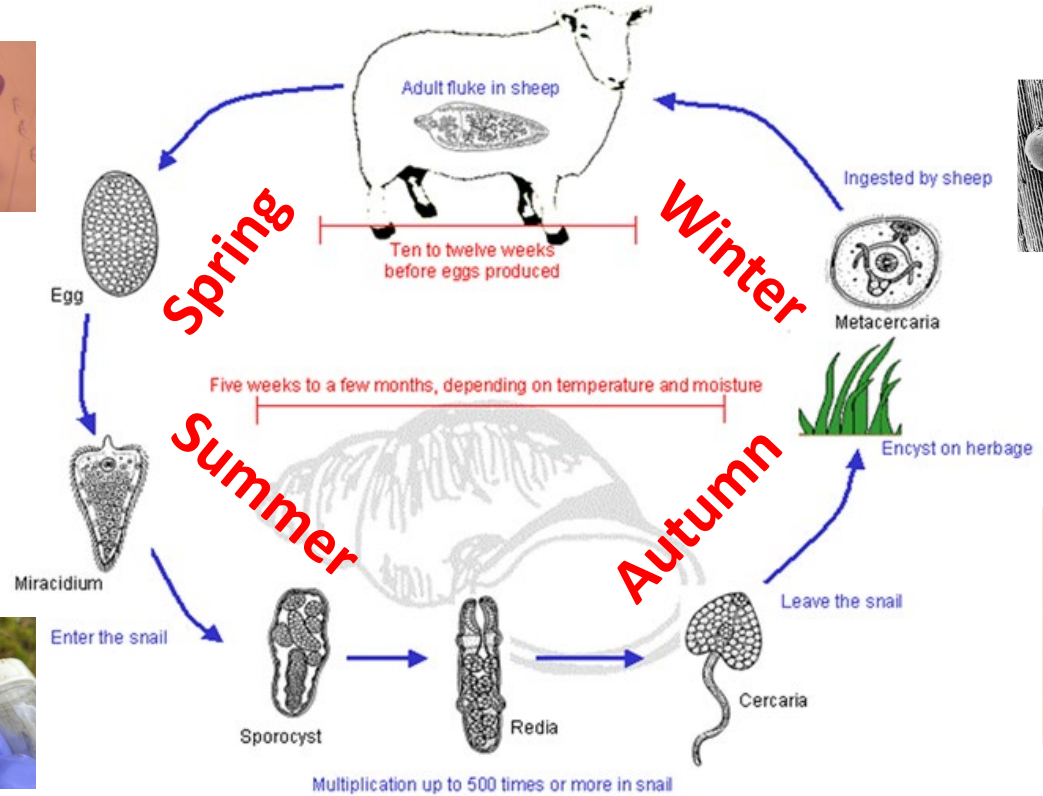

SCOPS
Sustainable Control of Parasites

Acute & chronic liver fluke in sheep

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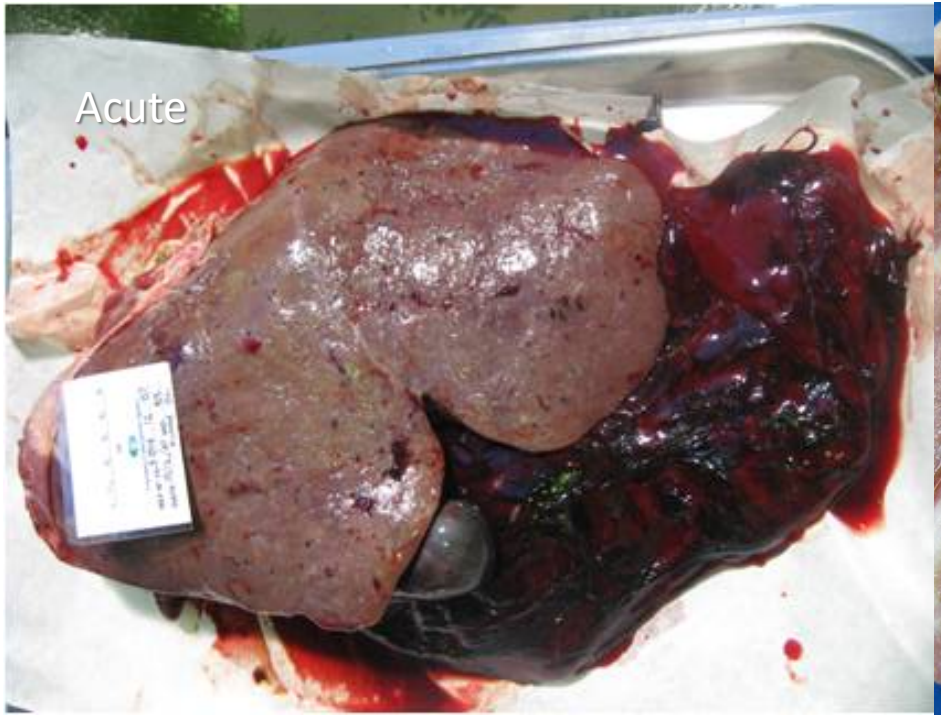

Perfect snail habitat

Think 'Goldilocks'! ☺

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- Wet (but not underwater)
- Bare mud (but not recently disturbed)
- Open (not shaded by hedges, trees or long vegetation)

Such areas include:

- Depressions caused by tractor tyre ruts, poaching, natural landscape features
- Cleared drainage ditches
- Banks on the sides of streams or ponds
- Soft ground around leaking water taps or pipes

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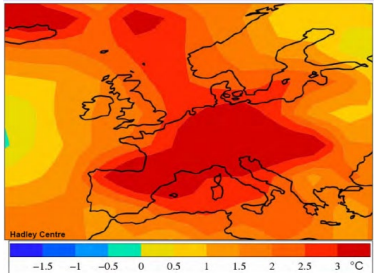
What's changed?

- **The climate/weather patterns** – warmer, wetter summers and milder winters, longer grazing = parasite seasons, more extreme events e.g. flooding
- **Drug resistance** – especially to triclabendazole (TCBZ), drug of choice for acute fluke, esp. in sheep
- **Animal movements** – to/from farms & markets, out-wintering etc., especially without effective quarantine treatment on arrival
- **Agri-environment schemes** – wetland/peatland restoration e.g. wader scrapes for wetland birds; saltmarsh etc. – require to be grazed!



Clinical signs – what to look for?

- Sudden death of previously healthy animals - worth investigating fallen stock!
- Severe abdominal pain, liver liable to rupture, animals recumbent & unwilling/unable to move
- ‘Bottle jaw’, anaemia e.g. pale gums & eyes
- General ill-thrift, poor performance, weight loss, poor body condition etc.

Fluke diagnostic options

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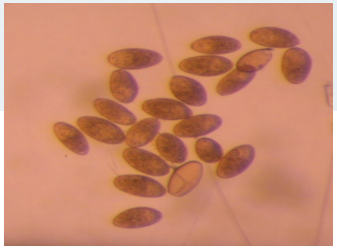
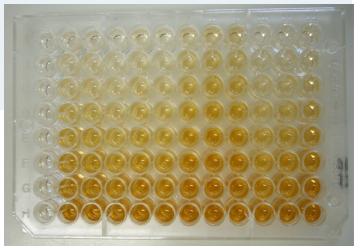
Invasive	Non-invasive
1. Post mortem/meat inspection – too late?	1. Clinical signs – too late?
2. Blood test (ELISA) for anti-fluke antibodies – earliest indication ~2 weeks post-infection	2. Faecal egg count (FEC), >10-12 weeks post-infection, adult fluke only
	3. Coproantigen test (cELISA), >6-8 weeks post-infection, late immature-adult fluke



Fluke diagnostic plan?

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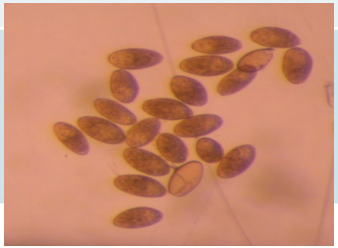
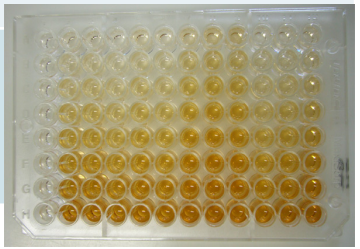
Blood test	Faecal test(s)
VERY useful indicator of early infection in young 1st season grazing animals, both sheep & cattle! Less useful in older animals as antibodies can persist, even after successful treatment	BOTH FEC & cELISA can be used to monitor infection AND assess treatment efficacy in sheep & cattle
Plan - use monthly on small group of sentinel animals (n>6) from mid-summer to indicate when (& where) they've encountered fluke, and inform treatment, timing and product choice	**Plan** - use composite FEC (n=10) monthly from late summer to monitor egg appearance, and inform treatment, timing and product choice **Plan** - use individual FEC or cELISA to test efficacy of treatment, d0 and d21 (FECRT/CRT), timing informed by composite FEC, above



Farm management options?

- Fencing
- Drainage
- Housing
- Treatment

Flukicides

- Frontline fluke control
- Not many products to choose from
- No new products in the pipeline

Efficacy of flukicides available for use in sheep in the UK against susceptible fluke populations

Active ingredient	Age of fluke in weeks (% kill rate)													Optimum time of year to use
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Albendazole										50-70%		80-99%			Spring / summer
Oxyclozanide										50-70%		80-99%			Spring / summer
Rafoxanide															
Closantel			23-73%		91%	91-95%				97-100%					Autumn
Triclabendazole (assuming a fully susceptible population)	90-99%	99-99.9%													Autumn

Thanks to Professor Diana Williams for this table.

Flukicides – important points to note

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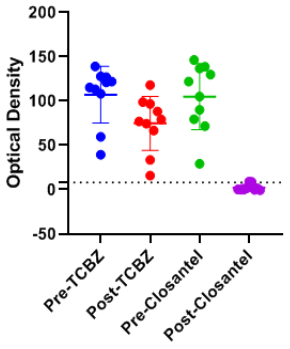
- Drugs that kill “worms” tend **not** to kill fluke e.g. the ‘mectins’. Also, most flukicides **don’t kill all stages** of fluke!
- Combination fluke & worm products? Also, fluke drugs **not persistent** – even in combination with a wormer which is!
- Constant **risk of reinfection** if grazing outside, no natural immunity and no such thing as a ‘preventative treatment’!
- Remember **5 R’s** - Need to use the **R**ight product at the **R**ight dose on the **R**ight animal at the **R**ight time and in the **R**ight way!
- Some of our frontline flukicides (& wormers) have potentially detrimental impact on important dung, soil & aquatic life - if you do need to treat, use ‘**as little as possible but as much as necessary**’ and dispose of unused chemical & containers carefully!

Case study – liver fluke in Argyll, 2018-

- ‘Fluke-central’ on West Coast of Scotland, first report of triclabendazole (TCBZ) resistance in UK, 1980s
- Current TCBZ-R status? Routine **composite FEC** monitoring on 10 x sheep farms to inform timing of treatment
- Summer 2018 v hot & dry – fluke ‘low & late’, eventually got to do FECRT & CRT ~Feb 2019 and confirmed TCBZ-R on all 10 farms!☹
- Most farmers got through 2018-19 without needing to treat, those that did **treated ~4 months too early & with a product that didn’t work!**



Rumen fluke?

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- Has certainly become more common in UK & ROI in past ~10 years, but how important is it?
- Important from a surveillance/diagnostic perspective, as eggs appear in FECs, **BUT**…
- Disease invariably caused by immature rumen fluke in intestine (= larval paramphistomosis)
- Little/no published evidence of production impacts e.g. carcase weight, conformation, fat classification, DLWG, diarrhoea index or welfare score (Atcheson et al., 2022)
- Farmers convinced animals improve in condition when treated with oxyclozanide – undiagnosed liver fluke?

Messages for farmers, vets, SQPs

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- Liver fluke is a far more pathogenic parasite; COWS and SCOPS message is **TEST BEFORE YOU TREAT**

- **Do not treat** for adult rumen fluke – increased selection pressure for resistance on parasite populations, importantly, liver fluke

SCOPS Sustainable Control of Parasites

COWS Control Of Worms Sustainably

LETTERS & NOTICES

In recent years there has been an increase in prevalence in the UK of the parasite *Calicophoron daubneyi*, a rumen fluke found in both sheep and cattle. Diagnostic laboratories are increasingly reporting the presence of rumen fluke eggs when screening faecal samples for liver fluke eggs, leading to a greater awareness of the presence of rumen fluke in sheep and cattle. COWS and SCOPS are concerned that the presence of rumen fluke eggs in faeces may result in the unnecessary treatment of animals with anthelmintics.

C daubneyi was first confirmed to be present in the UK in 2013,[1] and around the same time two confirmed reports of disease associated with paramphistomes, one in cattle and one in sheep, were published.[2,3] Since then, there has been an increase in the number of reports of the presence of rumen fluke,[4] but few reports of clinical disease. Hence, although infection is common, disease – which is associated with large numbers of immature parasites in the duodenum – appears to be rare.

There is no evidence in the literature that the presence of adult rumen fluke is associated with disease. A recent study in Northern Ireland showed no significant effect of infection in cattle on cold carcase weight, conformation or fat classification at slaughter, and no difference in daily liveweight gain, diarrhoea score or welfare score on farm.[5] There are no antemortem diagnostic methods for immature rumen fluke; detection of rumen fluke eggs only demonstrates the presence of the adult parasites in the rumen.

There is no licensed treatment for *C daubneyi* in the UK. Oxyclozanide has reported efficacy against the adult parasite and can be prescribed under the cascade by veterinary surgeons. A recent survey of over 450 farmers conducted by the University of Liverpool demonstrated confusion over rumen fluke, and found that over 50 per cent of respondents who were using anthelmintics to treat rumen fluke in both sheep and cattle were using products that were not suitable (eg, they did not contain oxyclozanide).[6]

Given the confusion surrounding the significance of rumen fluke in sheep and cattle and the fact that disease, particularly associated with the presence of the adult parasite in the rumen, is very rare, COWS and SCOPS are very keen to highlight that a positive rumen fluke faecal egg count (FEC) should not trigger anthelmintic treatment.

> **A positive rumen fluke faecal egg count should not trigger anthelmintic treatment**

The liver fluke *Fasciola hepatica* is a common and highly pathogenic parasite affecting sheep and cattle in this country. Resistance to triclabendazole is widespread in Great Britain,[7] hence maintaining the efficacy of other classes of anthelmintic is vital to controlling liver fluke.

COWS and SCOPS advocate diagnosis of infection and then targeting the stage of the parasite in the animal with the appropriate product. Oxyclozanide is a suitable product to use when animals are infected with adult liver fluke. We are keen that veterinarians and other prescribers discourage the use of anthelmintics unless there is clinical need, and do not advocate treatment for adult rumen fluke infection, as this will increase selection pressure for resistance on parasite populations, importantly, liver fluke.

Results from several research groups suggest that the epidemiology of *C daubneyi* is changing.[8] *C daubneyi* shares the same intermediate snail host as *F hepatica* and there is evidence that it is adapting to the UK *Galba truncatula* snail population. However, no data are available to suggest that the parasite is becoming more pathogenic. While it is important that we remain vigilant and aware of the presence of *C daubneyi* in UK sheep and cattle, COWS and SCOPS do not advocate use of an oxyclozanide treatment based solely on an incidental positive rumen fluke FEC.

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References
1 Gordon DK, Roberts LCP, Lean N, et al. Identification of the rumen fluke, *Calicophoron daubneyi*, in GB livestock: possible implications for liver fluke diagnosis. *Vet Parasitol* 2013;195:65–71
2 Mason C, Stevenson H, Cox A, et al. Disease associated with immature paramphistome infection in sheep. *Vet Rec* 2012;170:343–4
3 Millar M, Colloff A, Scholes S. Disease associated with immature paramphistome infection. *Vet Rec* 2012;171:509–10
4 Veterinary Investigation Diagnosis Analysis. Annual Report 2022. https://tahsoft.co/3YGJ84 (accessed 17 August 2023)
5 Richens I, Logan B, McCormick R, et al. The effect of naturally acquired rumen fluke infection on animal health and production in dairy and beef cattle in the UK. *Front Vet Sci* 2022; doi.org/10.3389/fvets.2022.968753
6 Hoyle RC, Hoser HR, Duncan JS, et al. A survey of sheep and/or cattle farmers in the UK shows confusion over the diagnosis and control of rumen fluke and liver fluke. *Vet Parasitol* 2022;312:109812
7 Ramadaheen J, Graham-Brown J, Stephens N, et al. Lack of efficacy of triclabendazole against *Fasciola hepatica* is present on sheep farms in three regions of England, and Wales. *Vet Rec* 2019;184:502
8 Rondelaud D, Vignoles P, Dreyfuss G. Changes in the populations of two Lymnaeidae and their infection by *Fasciola hepatica* and/or *Calicophoron daubneyi* over the past 30 years in central France. *Animals* 2022;12:3566

PROFESSION

Limitations of the RCVS statutory membership exam

FURTHER to the recent letter from Asif Rao (*VR*, 22/29 July 2023, vol 193, p 82), I would like to address the limitations faced by expat vets when attempting the RCVS statutory

Letters are not peer-reviewed, unless stated

Research update – diagnostic testing

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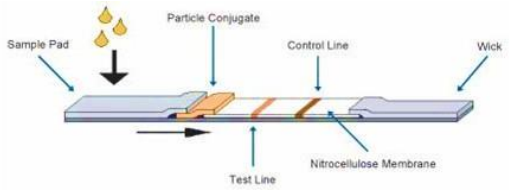
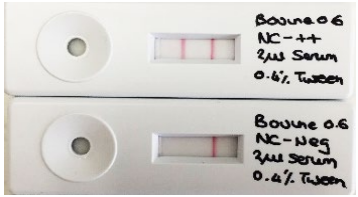
- Faecal egg counts (FEC) still main fluke diagnostic method used
- Bottleneck in speed of testing and return of test results, typically several days! ☹
- Developments in ~automated commercial testing options, use of AI & Machine Learning etc., most notably FECPAKG2 fluke module & MicronAgritech device

Research update: University of Liverpool liver fluke lateral flow test

- Antibody detection test
- Detects exposure to liver fluke
- Can be used on both sheep and cattle
- Drop of blood





Contact: Prof Diana Williams, University of Liverpool (williadj@liverpool.ac.uk) and/or PDRA, Dr Tessa Walsh (T.Walsh2@liverpool.ac.uk)

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UKRI Biotechnology and Biological Sciences Research Council

GLOBAL ACCESS ga DIAGNOSTICS

Research update: a vaccine for liver fluke?

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- Highly desirable, big international research effort = ‘Holy Grail’ of fluke research
- Challenging for a number of reasons:
  - Complex organisms, big genomes etc.
  - Lack of natural protection in sheep or cattle
  - Snail intermediate host to amplify life-cycle
  - Wildlife reservoir hosts to spread infection
- Gut antigen approach to vaccination *cf* Barbervax® - *Haemonchus* & liver fluke both blood-feeders?
- Employed same chemistry, 3 x vaccine trials to date, results not convincing, shelved for now ☹

Best practice advice

SCOPS

www.sco

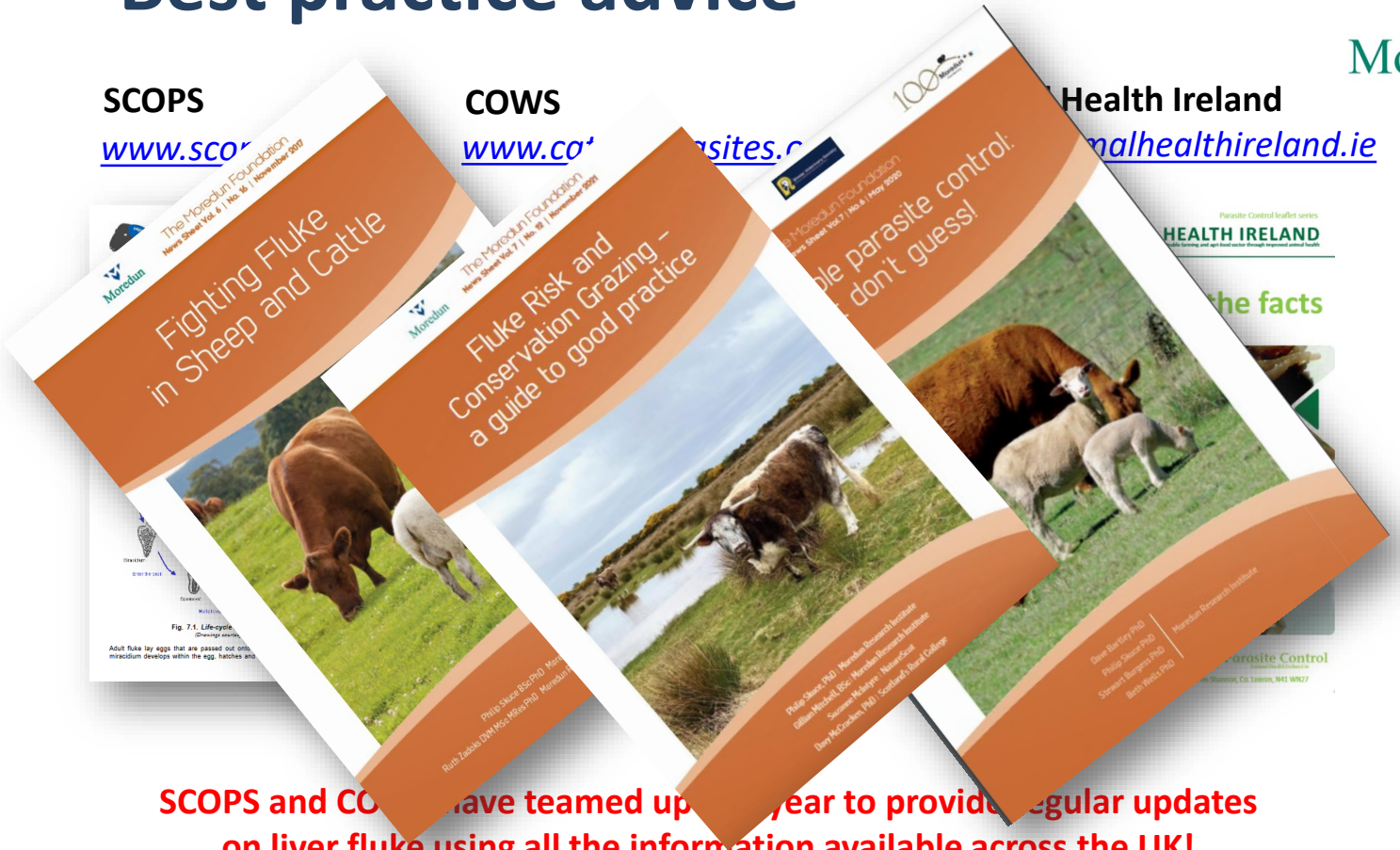
COWS

www.co

sites.c

Health Ireland

malhealthireland.ie



SCOPS and CO have teamed up year to provide egular updates on liver fluke using all the information available across the UK!

Other useful resources

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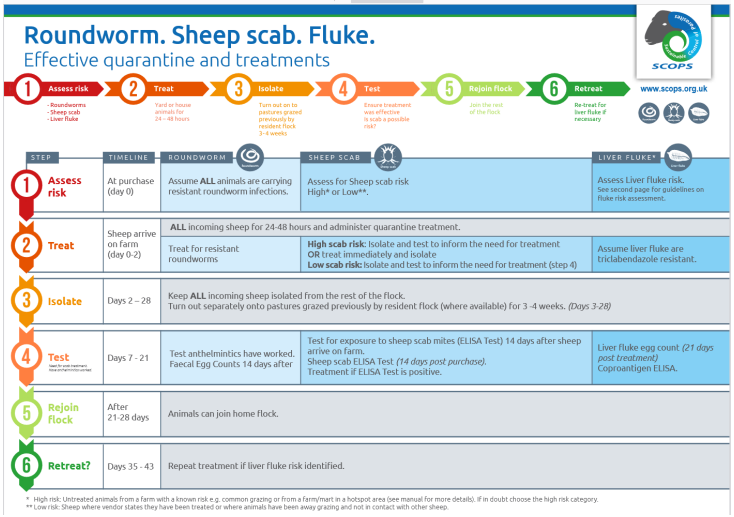
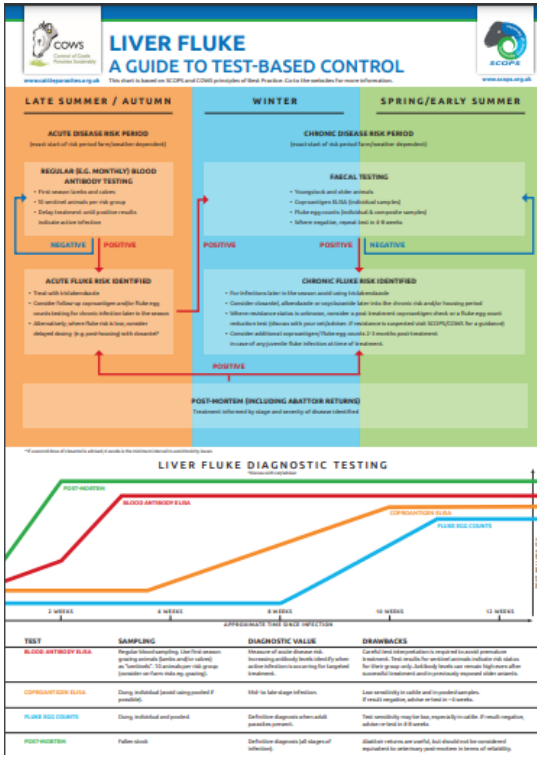
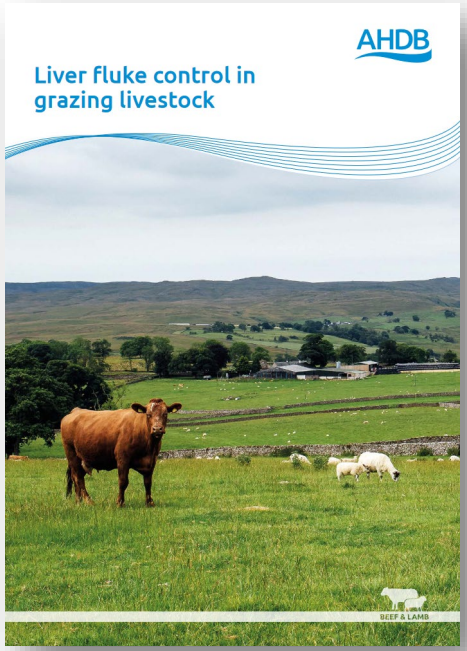


https://www.scops.org.uk





https://ahdb.org.uk

Take home messages…

- ✓ Have a working knowledge of the fluke life-cycle & be able to risk assess a field/farm for fluke
- ✓ Understand what diagnostic tests are available and what they tell you about fluke infection
- ✓ Know the liver fluke status of your animals & farm – test, don't guess!
- ✓ Know which products work on your farm and which don't – test, don't guess!