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LIVER FLUKE TRANSLATING RESEARCH INTO PRACTICE













Control Of Worms Sustainably COWS

Mary Vickers

Who, why, what?



Aim



COWS aims to provide the best available, evidence-based information to the cattle industry in relation to the sustainable control of parasites in cattle

www.cattleparasites.org.uk

Twitter: @COWSworms















Animal & Plant Health Agency

























COWS also has input from farmers and independent consultants

Why?



- Anthelmintic resistance less common than in sheep
- Suspect resistance reported mainly with pouron products (macrocyclic lactones) and triclabendazole (flukicide).
- Some treatment failures reported; usually after pour-ons
- SCOPS leading the way





Current resistance/ poor efficacy status



Parasite: parasiticide	Solution
<i>Cooperia</i> spp to macrocyclic lactones (Intestinal worms)	In FGS calves, treat with LEV or BZD or administer concurrently with ML
<i>F. hepatica</i> to triclabendazole (TCBZ) (Liver fluke)	Use an alternative flukicide
<i>P. ovis</i> to macrocyclic lactones (Psoroptic mange)	Isolate infested animals and repeat treatment until cured

AR risk factors



- AR is inevitable
- High frequency, short interval treatments
- Under dosing





Worms: the commonest cause of ill-thrift









Matrix for risk assessment

Risk factor	High	Medium	Low
Age (grazing seasons, GS)	<1 year (1st GS)	1-2 yrs (2nd GS)	>2 years (adult)*
Weight gain (<2 yrs old) 2 months after turnout	<0.7 kg/day	0.7-0.8 kg/day	>0.8 kg/day
Faecal worm egg count (FGS) 2 months after TO (epg)	>200	50-200	<50
Field type	Permanent pasture	Silage/hay aftermath	Newly sown fields
Grazing history	Grazed by cattle <1 year old within last year	Grazed by cattle 1-2 years old within last year	Grazed by adult cows, sheep** or other species within last year



Sustainably

COWS – current scope



- Gut worms (Parasitic gastroenteritis)
- Lungworms (Parasitic bronchitis)
- Liver fluke (Fasciolosis) + Rumen fluke
- External parasites (Lice & Mange mites)
- Farm level approach to Parasite control
- Specific subjects
 - Administration of anthelmintics
 - Anthelmintic resistance
 - Quarantine treatments



How to blend science with reality?

Planning treatments

- Must be evidence-based
- Must be practical for farmer
- Must consider farm system
- Should have some flexibility
- Ensure accurate dosing
- Measure the success







The 5 R's for the effective use of wormers

Use the RIGHT product for the type of worm

Aritherminities belong to different classes and are active against different worms, and in some cases specific developmental stages of worms.

Products should be chosen to specifically larget the worm, or stage of development that is most Ukely to occur or already identified as present on-farm.

Other considerations, such as withdrawal periods, and any known antihelmintic resistance asses, should also be taken into account.

Consult with your vet, SQP, farm advicer or veterinary pharmacist for detailed advice on choosing the right product for specific on-farm problems.

Only use products legally authoritied for use against a particular host species or type of stock in the UK.

✓ Treat cattle at the RIGHT time

There is no one-size fits all solution to perasite control. Treatment depends on assessing variess factors, including gasture risk, animal type and time of the year.

For youngsteck, monitoring growth is a good indicator of when to treat for worms. If daily live weight gain (DLWG) fails below target, generally 0.7 to 0.8kg/day after wearing, anthelatimic treatment should be considered.

The risk of disease in cattle is later in the sasser, post mid-summer, when worms have accumulated on the posture. However, wormers can be used in the first free months of the grazing season to reduce gasture contamination with search eggs. A group egg-count sit to eight seaks post turnout and weight/condition monitoring can give a good indication of whether sarily season treatment is indication of whether arity season treatment is indication.

Dose cattle at the RIGHT rate

In most situations, anthelminities are administered at a specific dose rate [mi] according to the animals' live weight [kg]

Therefore it's important te:

- Real the product label or summary of product characteristics (SPC)
- Ensure desing equipment is well maintained, calibrated and clean
- Weigh animals, or use a weigh band to calculate the connect docage for each animal.

Administer wormer in the RIGHT way

Antheimintics can be administered to cattle in different ways. These include; cubcutaneoux injections; ear injections; intra-ruminal baluses; pour-on products; and orai drenches.

Always read the graduct label to ensure the selected graduct is administered in the correct way. Antibelminics should not be home mixed with any ether products.

Don't home mix

anthelmintics

✓ Treat the RIGHT animal

There is little to be gained from any arithelmintle treatment before weaning. However, as gracing intake increases, youngstock will potentially be exposed to high levels of worm infectations.

Effective freatments in youngstack, when they are most susceptible to worm intections, will reduce egg contamination anto pasture and further reduce levels of infection in the emitrorment.

Older cattle generally have a good level of immunity to gut and lung worms and therefore, depending on the farm situation, treatment may not be necessary. However, animals of all ages must be included in liver fluxe cattrol plans. Dose according to accurate live weight



The 5 R's for the effective use of wormers



The right product for the right type of worm

The right animal

The right time

The right dose rate

Administered in the right way



Incorrect parasiticide administration

- Under-dosing
 - Poor efficacy when treating clinical cases
 - Reduced persistency & duration of protection
 - Increased risk of resistance
- Over-dosing
 - Risk of toxicity
 - Withdrawal periods for meat and milk are determined using the recommended dosage; higher dosages mean that withdrawal periods should be increased



Knowledge transfer



- Training of vets, SQPs, and farmers
- Via stakeholder comms routes
- COWS branded resources & events





s can be carried out at a beel level to check for exposure, or at an individual level if there is concern about clinical sig

Liver fluke

Faecal sample analysis can help detect if liver fluke is present in cattle The liver fluke life cycle



Reduce the exposure to high risk fluke areas

JUT

Communications



GRICULTURE & HORTICULTUR

- AHDA conference
- Farmer facing shows
- Press articles
- Film clips
- Website content
- Webinars
- Leaflets
- Social media
- Working through partner comms routes as well





Thank you

www.cattleparasites.org.uk

Twitter: @COWSworms



Introduction to liver fluke and improved diagnosis

Philip Skuce, Stuart Dawes, Gillian Mitchell, Grace Cuthill & Ruth Zadoks Moredun Research Institute, Edinburgh philip.skuce@moredun.ac.uk

> BBSRC-IPA Stakeholder meeting, AgriSearchNI, Hillsborough, 12th Oct 2016

V Moredun

Liver fluke

- Highly pathogenic flatworm parasite
- Complicated life-cycle involving intermediate mud snail host
- Threat to sheep <u>and</u> cattle of all ages
- Risk significantly influenced by weather esp. mild winters & wet summers!...





AGRICULTURE & HORTICULTURE DEVELOPMENT BOARD



Cattle - typically, **chronic fluke**! Bovine liver responds dramatically to liver fluke infection = 'pipestem fibrosis'



Cost of liver fluke?

Direct production losses:

– e.g. 10% reduction in adult liveweight gain, 30% reduction in lambs/calves; poor scanning rates, feed conversion ratios etc.

- Estimated cost to the producer:
 - EBLEX, 2011 £25-£30 per head (sheep)
 - Swiss study, 2005 300€ per head (beef & dairy)
 - Harbro Ltd., 2013 ~450,000 cattle, 'fluky' animals 2.5kg lighter @ £60, also 27 days older!
 - EBLEX figures, 2013, even higher = 10kg lighter, lower BCS @ £90!
- Liver condemnations at slaughter:

Can be 100s of Kg/day - UK liver condemnation rates ~10% in sheep & 25% in cattle (EBLEX, 2013)









What's changed?

- Climate change warmer, wetter summers and milder winters, longer grazing = parasite seasons, more extreme events e.g. flooding
- **Drug resistance** specifically to triclabendazole (TCBZ), drug of choice for acute fluke
- Animal movements to/from farms & markets, out-wintering etc., especially without effective quarantine treatment on arrival
- Agri-environment schemes wetland restoration e.g. wader scrapes for wetland birds; protected habitat for natterjack toads etc. — require to be grazed!













Liver fluke forecast

• Liver fluke risk essentially "predictable", and is based on "Ollerenshaw index" (1950s):

$$Mt = n \left(\frac{R}{25.4} - \frac{P}{25.4} + 5 \right)$$

Mt = Fasciolosis risk value, n = Number of rain days per month, R = Rainfall (mm/month) P = Potential evapotranspiration (mm/month).

- Still forms basis of mainland UK NADIS parasite forecast (<u>http://www.nadis.org.uk</u>)
- Based on regional weather patterns this year, liver fluke risk for 2016:

'For Scotland, northwest England and north Wales, a **high risk** is predicted '



Dr C.B. Ollerenshaw, CVL Weybridge (retired)



Liver fluke diagnostic options

- Invasive tests
- –post mortem/meat inspection
- blood sample for liver enzymes
- blood sample for antifluke antibodies

- Non-invasive tests
- -clinical signs
- -bulk tank milk ELISA
- -faecal egg count (FEC)
- -coproantigen test
 (cELISA)



Liver fluke control 4-point plan



1. Pasture protection - don't let the Spring snails get infected! 2. Reduce snail population - drainage, topping rushes, improving poached areas etc. Summer 3. Avoid high cyst challenge - graze animals away from known/suspected high Autumn risk areas 4. Strategic treatment of 'at risk' Winter **animals** - treat right animals at right time with appropriate product



Liver fluke control – flukicides

But, remember...

- 1. Drugs that kill "worms" tend **NOT** to kill fluke!...
- 2. Most flukicides **DON'T** kill all stages of fluke!



Summary of different flukicidal products licensed for use in cattle

Active ingredient	Administration route	Stage of fluke killed
Trickshonderedo	Oral	2 weeks onwards
Iriciapenaazoie	Pour-on	6-8 weeks onwards
Closantel	S/c injection or pour-on	7 weeks onwards
Nitroxynil	S/c injection	8 weeks onwards
Clorsulon	S/c injection	Adults only
Oxyclozanide	Oral	Adults only
Albendazole	Oral	Adults only



onto herma with no evidence of resistance.

When developing a parasite centrol plan, make same you speak to your vet, SGP, form advisor or



and two free-living stages of the fluke.

Liver flake refection is seakonal, with a peak of efective cysts/tapically seen on pasture in late spectrum and welp automer, leading to the risk of diseases in cattle over the winter. This peakonal pattern is due to the trop-living stages of liver ability to survive for up to a year or more when canditures are right.

The Cycle

1. Adult Rate incensis the bott that arepassed nat in the slung of intected cattle T. At satable temperatures, alone 10°C,

Roke eggs will develop and hatch release minapidia, the famili steges that look like excress/opts tedpelies, which swim to the commonly observed in except classed, signs can be soon before eggs can be detected in during





Active i 1 inishe

Mitralign

Dogto boigt

"Summary at different flukicidal active ingredients licensed for use in cattle

Whether subclimital or clinical fluto inhection

Administration route	Stage of Roke Killed
.0ral	Z-weeks intwarts
Pour-on	6-1 weeks snoweds
s/c injection or pair-on	7 weeks proverts
We injusting	If weeks shwards
alcinistion	Adults only
Onal.	Ada its only
Oral	Adults only
	Adveloping the notion Data Post-on No injustion or pain-on who injustion and injustion Oral Oral

Tank samples and individual blood samples can be sent for analysis, which helps standy 2 cattle have been exposed to over flate our the past months

Setting to know how to control and manage liver fluxs

Liver Take control glans should take into account hand flake history, paol braitment, the presence of high risk areas for shoul habitaty. and three of year.

An officiate carried plan will include the use of flationites to present disease and reduce picture conternation, as well as gracing strategies to avaid heavily conternitated particle.

Years good and allult cattle should be treated after housing, and animals kept outside may require additional insumers depending an risk

II. Antitiony detection IEEEAI texts - bulk milk-







Its seeds, both will have a sightfrown inspace on productivity, and increase an animal's susceptibility to other intections.

Take home messages...

- ✓ Fluke is a year-round issue...
- Make best use of all available information farm history, farm location, abattoir returns, diagnostic samples, on-farm risk factors, climatic conditions = <u>informed decision-making</u>!
- Consider management options and, if you need to treat, use right drug at right time on right animals at right dose
- Work with your vet and AH advisor to devise sustainable fluke control strategies tailored to your individual farm

WP1: Aims

- Development and validation of herd-level diagnostic tests to identify cattle farms with fluke infection
- 2. To discriminate between liver fluke and rumen fluke (paramphistome) infection









WP1 Update

 Selection of 5 study farms (in discussion with CEH) - based on proximity, logistics, type of operation, fluke history etc.

- 3 rounds of sampling completed over grazing season 2014, >600 faecal samples analysed
- Weather exceptionally dry and warm 2014-2015, not ideal for fluke or snails!









WP1 Update

- Taking faecal samples from ~40 animals/visit to compare...
- ✓'Grab' vs 'floor'
- ✓ FEC vs cELISA
- 10g vs 40g sample
- cELISA +/- Australian modifications
 - overnight soak to improve SN
 - reducing kit cut-off by 1/3

Inclusion of genuine fluke-free controls – practical? BBSRC











cELISA consistently less sensitive than FEC in cattle, as in sheep (worked better in deer!)




Pooled faecal sample testing

Comp.	cELISA	EPG
1	1.329873	0.2
2	7.946805	0.4
3	4.768083	0.3
4	10.41194	0.45
5	1.978592	0.2
6	1.589361	0.2
7	7.233214	0.2
8	1.492053	0.1
9	1.364764	0.1
10	7.071960	0.2

- Composites made using^{worms} 40 samples from a herd
- 10 g from individual samples selected at random to make up a composite of 100g, 10g tested
- Composites: cELISA less sensitive than FEC

3 +ves in 10 reliably detected; 1 +ve in 10 not reliably detected by FEC, none by cELISA





Herd-level testing?

- Still need cheap, quick test that can be easily carried out in (veterinary) practice – based on composite FEC, not cELISA*
- Detailed mathematical modelling approach used to explore number of samples required, impact of resampling same animals etc.
- Pooled FEC, based on 10 x 10g samples, still method of choice for herd-level testing







*BioX launched 'new & improved' cELISA, March 2016 - need to re-evaluate?

of

(Proposed) Test for Adult Cov

- Sample only cattle not wormed within the last 13 weeks
- Collect 10 individual randomly-picked fresh >10g samples
- To increase likelihood of testing positive when fluke is present, test at housing, during winter/spring
- If test is *negative*, herd needs to be re-sampled at least once
- Two consecutive negative tests would give 95% confidence that fluke is truly absent

BBSRC don't know how FEC relates to fluke dam

DNA-based testing?

- 1. Evaluating LAMP rapid visual readout with potential advantages over PCR
- 2. Have developed liver fluke and rumen fluke LAMP assays
- 3. LAMP for liver fluke
 specific in faeces, specific in snails
 sensitivity similar to FEC
- 4. LAMP for rumen fluke
 - specific in faeces, non-specific in snails
 - sensitivity higher than FEC?

More work to do on faeces, but useful for screening environmental samples









DEVELOPMENT BOARD

Summary

- cELISA more rapid & convenient test for processing multiple samples BUT...
- cELISA consistently <u>less sensitive</u> than FEC
 - even with modified cut-offs
 - individual and composite samples
- Pooled FEC, based on 10 x 10g samples, still method of choice for herd-level testing
- Have produced DNA-based methods to discriminate between liver fluke and rumen fluke in faecal and environmental samples



















Thanks to Moredun team, BBSRC-IPA collaborators & funders!









Translating research into practice

How much is liver fluke costing you?

Sue C. Tongue

Alyson Barratt, Jude I. Eze, Carla Correia-Gomes, Madeleine K. Henry, Cath E. Milne, Alistair W. Stott and others



Liver fluke has an adverse impact on health, welfare and productivity





CHANGED PRIORITIES AHEAD









welcome to **qboxanalysis**

- Scottish abattoir data
- Average adjusted carcase weight reduced by 0.63kg (0.33 - 0.93kg) - Sanchez-Vazquez & Lewis, 2013
- Average adjusted carcase weight reduced by similar amounts analysis of updated data set

- Dairy data (University of Liverpool & Tesco)
- Reduced milk yield Howell et al., 2015
- Possibly other factors





Improving the Control of Liver Fluke Infection in Cattle in the U.K.





BEEF & LAMB











Worms







The United Kingdom of Great Britain and Northern OWS Ireland. Control O Worms



Four countries



Dec 2015 9.75 M cattle

> 1.75 M – Dairy breeding herd

1.60 M – Beef breeding herd



The British cattle industry is extremely varied.

Sustainably



The British cattle industry is extremely varied.





DI

This leads to a number of challenges....

Aim: relative costs of control

measures?

Who benefits? Who pays?

Control Of Worms

n?.2

Translating the diversity of practice into a research question and an appropriate framework



A suite of herd-level bio-economic models

• The dairy cow



- Stochastic
 - @Risk

 Partial budget models

- The beef suckler cow

 The growing animal



Fluke v.



Worms Sustainably

Inputs





Parameters:

- Physical
 - e.g. herd size, production system etc
- Performance
 - e.g. calving interval, milk yield, daily live weight gain (DLWG) etc
- Fluke prevalence
- Economic
 - e.g. fluke related losses, milk price, value of cull cows, heifer and fattening animal etc

Average loss per infected animal in the herd (£/year) ALPIAH





OUTPUTS Comparative Losses



The average (median) loss per infected animals (£/year) in a dairy herd **varies** depending on the average milk yield per herd (I/cow/year).







The average loss per infected animal (£/year) is **lower** for autumn/winter calving suckler herds than for spring/summer calving herds.







ALPIAH

The average loss per infected animal (£) fear is **higher** for spring/summer born bee replacement heifers than others.



The average loss per infected animal (£/year) is **lower** for spring/summer born beef finishers than others (18 month system).





The average loss per infected animal (£/year) is **lower** for spring/summer born beef finishers than others (24 month system).





Comparative average losses – growing animal model options





Sensitivity analysis





Beef finishing systems (all)



Herd fluke prevalence within finishing system Herd fluke prevalence at entry to finishing system Expected daily lwg (no fluke)





Spring/Summer calving suckler herd

Fluke prevalence in cows Fluke prevalence in calves Reduced calf growth due to own infection



Autumn/Winter calving suckler herd

Reduced calf growth due to reduced milk Additional costs for fluke affected cows Expected daily lwg calf (no fluke)



Dairy herd





Reduced milk yield Affected cows - additional costs Average milk price per litre



Aim: relative costs of control measures? Who benefits? Who pays?

National Economic Welfare Models

Herd-level & PBM

National economic welfare methodology



- Introduction of liver fluke
 - Fall in supply
- No shift in demand





The national models



• The dairy cow



• The growing animal (x2)









Animal level prevalence in national dairy herd of approximately

10% 20% 30%




£ per household per yearcows















Not infested - NI







£ per cow per year









£ per cow per year









£ per cow per year

















The national models



• The growing animal (x2)





Proposed Control Measures

Aim: relative costs of control measures? Who benefits? Who pays?

National Economic Welfare Models

Herd-level & PBM







Not infested - NI

Infested - I

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Translating research into practice

How much is liver fluke costing you?





ALPIAH

Comparative average losses – growing animal model options







Known non-infested

Known infested







Improving the Control of Liver Fluke Infection in Cattle in the U.K.

















BEEF & LAMB







Any questions?





Leading the way in Agriculture and Rural Research, Education and Consulting

Translating research interventions practice

All about "the snail"

Nicola Beesley University of Liverpool





Why is "the snail" important?



Who is "the snail"?



- Galba truncatula
- Warm and wet conditions
- Resistant to drought and frost
- Hermaphrodites
- They are tiny!





Where is "the snail"?











When does "the snail" get infected?



- Summer infection
 - Snails infected between May and June
 - Metacercariae produced from August to October
- Winter infection
 - Snails infected in late autumn
 - Metacercariae produced the following year

HIGH RISK PERIOD = AUTUMN





How does "the snail" influence the cover liver fluke life cycle?



How might "the snail" contribute cows to liver fluke diversity?



Snails might be infected by more than one miracidia

- Experimental infections
- Snails can become infected with more than one genetically distinct isolate





What are we doing to understand "the snail" better?

- Field study on 40 farms in Shropshire
 - Some fluke positive, some fluke negative
 - Identifying and categorising snail habitats
 - Collecting snails to identify infection
 - Identify risk factors and the benefits of changing practice to combat these risk factors
- Where are the infective stages on pasture





What can you do to combat "the snail"?

- Fence off "suitable habitats"
- Avoid wet pastures during fluke season (September / October)
- Plough, reseed or crop rotation of heavily grazed areas
- Drain wet areas (dependent on your agrienvironmental status)
- Fix leaks promptly to avoid temporary habitats establishing



Acknowledgments













Impact of liver fluke on cattle health

Translating Research into Practice Belfast, 12th October 2016

John Graham-Brown

The A

Fasciola hepatica

Introduction

- The parasite
- The disease
 - Stages
 - Numbers
- The effects
 - Direct
 - Indirect
- The solution?
 - Vaccination

The parasite

- Infects several mammalian species
 - Cattle
 - Sheep
 - Humans
- Infection through consumption of contaminated plant material
 - Grass or similar pasture based forage
- Juvenile worms migrate through the intestines and liver
- Adult worms live in the bile ducts of the liver
 - 2.5cm
 - Feed on blood





- 1. Ingestion of metacercariae from pasture
- 2. Juvenile fluke penetrate small intestinal wall to enter the abdomen
- 3. Juveniles migrate to the liver

1

4. Penetration of liver capsule and migration through tissue:-

Acute fasciolosis (4-6 weeks)

5. Migrating fluke gain enter bile ducts and become sexually mature:-

Chronic fasciolosis (12+ weeks)

- 6. Eggs are produced and passed back to the digestive tract
- 7. Eggs passed in faeces

The disease: Stages

- Acute (juvenile) infection
 - 4-6 weeks post infection
 - More common in sheep
 - Juvenile flukes penetrate liver capsule and migrate through parenchyma
 - Cause damage and haemorrhage
 - Diagnosis based on antibody ELISA
- Chronic (adult) infection
 - 12+ weeks post infection
 - Adult fluke reside within bile ducts
 - Feed on blood
 - Diagnosis on ELISA and faecal egg counts













"Pipestem liver"

The disease: Numbers

- 1 adult fluke:
 - Drinks ½ ml blood per. day
 - Produce 10,000s eggs per. day
- 1 egg:
 - Infects 1 snail
- 1 infected snail:
 - Produces 1000s of metacercariae
- 1 cow/sheep:
 - Can be infected by 100s 1000s fluke



Bos taurus

The effects: Direct

- In cattle often "sub-clinical"
 Often undiagnosed/treated
- Liver condemnation
 - ~ ~500,000 in UK (2010)
- Weight-loss/Poor growth
- "Bottle jaw"
 - Blood loss
 - Accumulating infection
- Reduced milk yield
 - Estimated 8-15% overall reduction
 - Reduction in butterfat
- Impaired fertility
 - Delayed bulling in infected heifers
- Untreated can remain infected for years
 - Ongoing losses
 - No immunity


The effects: Indirect (1)

- F. hepatica causes "immune-modulation"
- Extends parasite longevity within host
- Action through production of modulatory antigens
 - "Excretory-Secretory" products (cathepsin-proteases)
 - Tegumental proteins
- Alter the immune response and reduce protective effects
 - Impaired cell mediated responses
 - Increased regulatory responses
 - Non-protective immunity



• Evidence of a generalised immune-modulation

Bovine Immunology



The effects: Indirect (2)

- Evidence of a generalised immune-modulation
- Altered immune responses to other diseases
 - Salmonella dublin
 - Mycobacterium bovis: Infection and diagnosis



The solution?

- Improved control
 - Less reliance on Fluke drenches: drug resistance
- Better management techniques
 - Increased availability and uptake of diagnostics
 - Pasture management
 - Parasite forecasting
- Vaccination?
 - Trials are ongoing
 - Reduce fluke burden and egg production





Our work is funded by:

paravac



References:

Fasciola hepatica is associated with the failure to detect bovine tuberculosis in dairy cattle. <u>[Claridge, P Diggle, C M McCann, G Mulcahy, R Flynn, J McNair</u>, S Strain, M Welsh, M Baylis & D J L Williams. Nature Communications 3, Article number: 853 (2012). www.nature.com

Induction of protective immunity in cattle against infection with Fasciola hepatica by vaccination with cathepsin L proteinases and with hemoglobin. J.P. Dalton, S. McGonigle, T P Rolph, and S J Andrews. Infect Immun 64(12): 5066-5074 (1996).

Websites: www.cattleparasites.org.uk www.liv.ac.uk/liver-fluke

