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Lungworm in Cattle: Treatment and Control

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Abstract

Treatment options for clinical parasitic bronchitis (PB) are largely based on anthelmintics, with supportive therapy including non-steroidal anti-inflammatories (NSAIDs) and antibiotics, when indicated. Macrocyclic lactones (MLs), benzimidazoles and levamisole are all effective against adult and larval lungworms, so the choice of product depends on other criteria, including duration of action and ease of administration, which can be important in dyspnoeic animals. Control of PB in youngstock can be accomplished through the use of anthelmintics in early-season strategies designed to limit pasture *D. viviparus* larval populations, but are not easy to implement in herds other than on autumn-calving dairy farms. Likewise, though vaccination provides predictable control of PB in youngstock, it is best suited to calves from autumn calving herds, however, it can also be used pre-turnout as a 'booster' in previously exposed, older cattle. Grazing management has a limited role to play in the control of PB both because of unreliability and because some of the recommendations run counter to recommended grassland management practices. Veterinary clinicians need to familiarise themselves with all possible options and outcomes for the control of PB and tailor their recommendations to the individual farm and farmer.

Key words: *Dictyocaulus viviparus*, grazing management, vaccination, anthelmintic treatment

Introduction

Parasitic bronchitis (PB) or verminous pneumonia in cattle results from infection with the lungworm *Dictyocaulus viviparus*. The outcomes of infection range from mortality through clinical and subclinical disease and production losses to carrier animals, which are important epidemiologically, but in which adverse effects are minimal. The need for prompt, effective treatment of clinical cases and long term control of infection are self-evident. The various options available to large animal clinicians in the treatment and control of PB are examined critically in this paper, which follows on from a companion article in this journal on the epidemiology, pathology and immunobiology of lungworm in cattle. As with its predecessor, this article aims to complement and extend the review article previously published in *Livestock* (Tilling, 2014).

Treatment of Clinical Cases

All of the principle groups of anthelmintics licensed in cattle are effective against adult and larval *D. viviparus*; hence there is a wide choice of actives and formulations that can be used to treat clinical cases of lungworm. The optimal treatment approach to severe clinical cases of husk needs to be based on criteria other than just efficacy however because some patients will be in a critical state in which even handling could precipitate a potentially fatal deterioration in their condition. In such cases, there is a strong argument to use injectable or topical products as opposed to oral drenches.

The relative importance of speed and mode of action in treatment responses in PB is unknown, though this does not stop quite widespread opinions being held on the merits or otherwise of various products (Tilling, 2014). Table 1 shows the comparative speed and mode of action of

fenbendazole and levamisole (Oakley, 1980). Also included in the table is an estimate for macrocyclic lactones (MLs), but their speed of action against *D. viviparus* has not been specifically measured. Evidence from clinical (Taylor et al., 1990) and parasitological (Eysker et al., 1996) studies indicate that MLs act at a rate similar the benzimidazoles.

Although both benzimidazoles and levamisole seem to be equally effective in treating clinical cases (Downey, 1980), there are reports, based on studies conducted in the 70s and 80s (Table 2), of different mortality rates in calves following treatment (Jarrett et al., 1980; McEwan et al., 1979). Some of the histopathology described in these cases is identical to what has been observed in fatal cases of PB in animals that had not been treated (Jarrett et al., 1954, 1957b). No specific studies on MLs have been conducted, though there is a description of similar histopathology in two calves that failed to respond to treatment with an ML (SAC, 2014), however it has also been reported that the incidence of such lesions has become less common since the introduction of the MLs (Taylor et al., 1997). The overall conclusion from this limited evidence base is that histopathological changes are present in the lungs of animals that die of PB, whether treated with anthelmintics or not, though there is some evidence for higher mortality following fenbendazole treatment.

The possibility that the clinical signs of husk can be exacerbated by anthelmintic treatment has been documented in observations on animals treated with diethylcarbazine (Jarrett et al., 1962), fenbendazole or levamisole and the propensity of either one of the last two drugs to elicit such responses has been the subject of some debate (Jarrett et al., 1980; McEwan et al., 1979; Oakley, 1980, 1981; Urquhart, 1981). One of the arguments put forward is that, because the action of levamisole is to paralyse worms, they are removed rapidly from the lungs without degenerating *in situ*, thereby reducing any associated inflammatory changes in the airways that may result from the release of bioactive compounds from degenerating worms (Oakley, 1981). In treatment of severe clinical cases of PB, there is no objective evidence for any differences in sequelae between levamisole and MLs, both of which act by paralysing susceptible parasites, and the rationale (speed and mode of action) proposed by some who speculate on such differences (Tilling, 2014) does not stand up to scientific scrutiny (Pouplard et al., 1986; Taylor et al., 1990). Cattle with heavy lungworm burdens and severe clinical signs must be treated with an anthelmintic or they may die of overwhelming infection, but farmers should be warned that in a few cases, exacerbation of clinical signs may follow treatment (irrespective of which product is used) and such cases need supportive treatment. Given the importance of host responses in the pathophysiology of husk, it would be prudent to include treatment with anti-inflammatory drugs in severe or non-responding cases. Equally, in adult cattle, which may be showing clinical signs related to the re-infection syndrome, the use of non-steroidal anti-inflammatory drugs (NSAIDs) to counter the immunopathology, would seem to be indicated.

A further consideration in therapy is the persistent activity of anthelmintics, which is an important criterion if treated animals are to be kept in the field where they acquired infection and/or when low risk pastures or premises are not available. All the MLs possess persistent activity against *D. viviparus*, but neither fenbendazole drench, nor levamisole do; essentially they are effective for ~24 hours against worms that are present at the time of treatment, but offer no protection against subsequent (pasture) challenge. The value of persistency in the protection of cattle following treatment was demonstrated in a study in which clinical cure rates were good and equivalent one week after treatment, when lungworm numbers in the lungs were reduced by 100% and 93% for

ivermectin (injection or topical) and levamisole respectively (Figure 1). However, when treated animals were challenged 14 days after treatment, the ivermectin-treated animals remained free of parasites, whereas calves treated with levamisole showed clinical signs and developed patent lungworm infections (Taylor et al., 1990) due to limited immunity and a lack of anthelmintic activity.

Control of PB in young stock

Pasture management

Delayed turnout

There is some evidence from Denmark and the United Kingdom (UK) that over-winter larval survival on pasture declines markedly in late April and May and that late turnout of calves can result in avoidance of lungworm challenge and, through lack of auto-infection, low pasture *D. viviparus* larval populations over the remainder of the grazing season (Jacobs and Fox, 1985; Jorgensen, 1980). Whilst adoption of this practice is likely to be limited on grassland farms, where optimal grazing of high quality spring grass is widely recommended (Frame and Laidlaw, 2011), from a parasitological point of view, control of both lungworm and parasitic gastroenteritis in young calves can be achieved using late turnout (Nansen et al., 1987).

Rotational grazing

Though there are reports of successful control of husk using weekly paddock rotations (Eysker et al., 1992), this is likely to be impractical on many commercial farms and furthermore in these studies, pasture rotation was found to be ineffective in the simultaneous control of PGE.

Dose-and-Move

Several studies have shown that 'dose-and-move' can be effective in the control of lungworm (Eysker et al., 1996; Eysker et al., 1997), though adequate control of husk was not achieved on several farms in a larger scale study (Eysker et al., 1997). Mitigation of potential increased risks of selection for anthelmintic resistance through this practice have been addressed elsewhere (Forbes, 2017), though this aspect is of more relevance to PGE than PB.

Vaccination

A vaccination approach to the control of PB, researched in Glasgow in the 1950s (Jarrett et al., 1957a), was based on irradiated infective *D. viviparus* larvae. Following further development by Allen & Hanburys Ltd, Ware, Herts, a commercial vaccine was launched in February 1959 under the trade name 'Dictol' (Poynter et al., 1960). The vaccine is currently available under the trade name Bovilis® Huskvac (MSD Animal Health); it is categorised as a POM-V product. Each 25 ml dose of vaccine comprises 1000-2000 irradiated, viable infective larvae (L3) of *D. viviparus*. The recommended schedule is to vaccinate calves ≥8 weeks of age with two doses, administered four weeks apart; animals should not be turned out onto pasture until 2 weeks after the second vaccination. If indicated, cattle can be given a single dose of vaccine as a 'booster' before turnout in subsequent years (NOAH, 2015). The shelf-life is 90 days and vaccine is typically supplied early in the year in order that eligible calves can complete the course of vaccination before turnout.

For optimal protection, it is recommended that vaccinated animals are exposed to low-grade exposure of *D. viviparus* in order that the Phase 1 immune response is maintained. Whilst this advice is useful, it is in fact very difficult to manage at farm level because of the inherent variability in lungworm epidemiology and the possible confounding effects of concurrent measures to control PGE, for example anthelmintic use and pasture management. Nonetheless, under commercial farming conditions, good control of PB would be expected over the grazing season following vaccination pre-turnout, though some vaccinated animals will develop patent infections and immune protection may be overwhelmed by high challenge (Downey, 1965). It should also be remembered that vaccinated animals can become carriers and initiate outbreaks of PB in naïve calves (Cornwell and Berry, 1960), thus mixing vaccinated and unvaccinated calves is not recommended, nor should the vaccine be used in herds where *D. viviparus* is not present.

Given the guidance for use of the vaccine, it is evident that there are some practical and logistical limitations on its use. It fits optimally into an autumn calving dairy herd, where calves should be of the right age to complete the vaccination course prior to turnout, however, these conditions are not met in spring-calving herds and, although vaccination at pasture, vaccination of animals less than 8-weeks of age and shortened intervals between doses have all been trialled (Benitez Usher et al., 1976; Downey, 1968, 1984), these practices are not always successful and are not data-sheet recommendations. Equally, with the exception of dedicated spring-calving herds, most dairy farms in the UK calve cows all year-round (Gates, 2013), hence at any one time, only a proportion of the annual calf crop is eligible to participate in the vaccination protocol. Finally, there is a cost element, which needs to be factored in to discussions of nematode control, particularly in FGS calves. Currently the ratio between the ex-distributor (www.farmacy.co.uk) cost of a course of lungworm vaccination (2 doses) and the cost of two (250 kg) doses with a generic ML pour-on is around 20:1, so a value judgement is needed to determine the optimal course, taking into consideration the likely need for concurrent PGE control.

Anthelmintics

Strategic

The control of PB through the strategic use of anthelmintics has been well documented (David, 1999); the majority of these strategies are based on anthelmintic administration to FGS weaned calves at or within three weeks of turnout, with coverage extending until at least mid-July. Adoption of these practices was facilitated by the introduction of the ML anthelmintics, which have persistent activity against *D. viviparus* (Armour et al., 1987) and which provided better control of PB than short acting products (Jacobs et al., 1985). Long-lasting anthelmintic boluses and injections also greatly simplify the implementation of strategic programmes as only single treatments are required to provide the required coverage (Jacobs et al., 1986).

The principles behind this approach are essentially those used in the control of PGE, which is to treat animals in a schedule that minimises/limits the contamination of pasture with worm eggs or larvae, thus treatment intervals are a function of the pre-patent period and the duration of persistent efficacy (if any) against the target parasites. The first treatment must be given within 3 weeks (the pre-patent period) after turnout to eliminate the first generation of gravid female worms; however, for convenience many farmers elect to administer treatments at turnout. Topical MLs, all of which have persistent activity claims of 4-6 weeks against *D. viviparus*, can be used in regimes using two or

three treatments at 5-8 week intervals. Equivalent (or greater) coverage can be achieved using moxidectin 10% long-acting injection (120 days persistency against *D. viviparus*) or benzimidazole intra-ruminal boluses (105-147 days). As strategic treatments are designed to minimise contamination of the pasture in which the cattle are kept, treated cattle should be kept in the same field throughout the grazing season. If cattle are moved to different pastures on which untreated cattle have grazed, they may be at risk of PB again, particularly if anthelmintic activity has ceased by then.

Anthelmintic treatment of cattle at housing can also be considered as strategic, as it can remove not only adult and larval worms, but also inhibited *Dictyocaulus viviparus* larvae, which are important in carrier animals and the perpetuation of infection from one grazing season to another. In regions where over-winter survival of *Dictyocaulus viviparus* on pasture is minimal, elimination of lungworm from farms for several years can be achieved through anthelmintic treatment of cattle during the winter housing period (Ploeger and Holzhauer, 2012).

Targeted selective treatment (TST)

In the control of PGE, the concept of treating only individuals that would benefit most from anthelmintic treatment is becoming established as an approach that can mitigate the potential risk not only of anthelmintic resistance (Kenyon et al., 2013), but also environmental impact (Cooke et al., 2017), by enhancing the size of the refugia. Amongst domestic ruminants, most work on TST has been conducted in youngstock and the most promising marker is not in fact a parasitological measure, but daily live weight gain (Busin et al., 2014; Jackson et al., 2017), which has been shown to be a good surrogate for adverse effects of PGE in both lambs and young cattle. In terms of animal performance and resistance management, modelling studies have also shown that live weight gain is a superior marker as a determinant for TST in young cattle (Berk et al., 2016) and lambs (Laurenson et al., 2016) compared to parasitological measurements.

There has been much less work on the use of TST in controlling PB. In one study designed to evaluate TST in the control of both PGE and PB, faecal samples were collected at 3-weekly intervals and examined for lungworm larvae using the Baermann technique; calves were treated if positive (O'Shaughnessy et al., 2015). Despite this sampling and treatment schedule, hoose was inadequately controlled and ~20% of the animals had to be removed from the study on welfare grounds, mostly because of dictyocaulosis. The authors proposed that vaccination should be used to control lungworm, where it is endemic, before attempting to employ TST for the control of PGE, to avoid the disruptive effects of hoose.

Another approach, which was adopted on a Swedish organic farm, was to treat individual animals on the basis of seropositivity to *D. viviparus* (Hoglund, 2006). Sampling was carried out at monthly intervals in the wake of outbreaks of disease and twice a year otherwise over a period of three years. Generally control of lungworm infection was good under this regime, however clinical PB did occur in August and September of the second year, but affected animals responded well to treatment with ivermectin injection. Given the sampling frequency and the cost of collecting and processing the samples, it seems unlikely that this approach would be readily adopted by commercial farmers currently.

Reflections on current options for the control of parasitic bronchitis

It is useful to remember that the 'classical' measures to control PB: vaccination and/or strategic anthelmintics were researched and developed in FGS, weaned calves from autumn/winter-calving dairy herds. As strictly seasonal autumn-calving dairy herds now comprise a small percentage of the national herd (Gates, 2013), a rethink of how control of PB (and PGE) is best managed in youngstock under other systems is long overdue.

Spring calving herds

FGS calves from spring-calving herds, whether dairy or beef, are not good candidates for either vaccination or strategic anthelmintic programmes: different approaches are needed.

Spring-born beef suckler (cow-calf) systems

Pre-weaning, it is unusual for suckler calves to suffer clinical parasitism, though small production losses can occur (Forbes et al., 2002). Lungworm is most likely to occur between weaning and housing if calves are grazed on infected pastures. Given that their immune status is largely unknown at this time, it is safest to assume that they are naïve and therefore susceptible to PB, so unless the risk status of the pastures they will graze can be confidently predicted, it may be prudent to treat all calves with an injectable or topical anthelmintic with persistent activity to provide coverage up to housing. If housing occurs within the period of persistency, then a housing dose (for PB & PGE) may be unnecessary.

Before the start of the second grazing season, vaccination can be considered, particularly for replacement heifers that are destined to stay within a herd where dictyocaulosis is endemic. For steers that are to be marketed before two years of age, strategic anthelmintic regimes can make sense, though the schedules can be relaxed slightly (Taylor et al., 1995), on the assumption that some exposure and naturally acquired immunity to PB (and PGE) has occurred during the FGS. As a general rule, it is recommended to keep vaccinated and unvaccinated stock apart (Cornwell and Berry, 1960), so this needs to be considered if different regimens are used in steers and heifers.

Routine anthelmintic treatments for PB should not be required for adult cattle, other than at housing, and vaccination would only be indicated in herds with high levels of PB. Otherwise, control of dictyocaulosis is based on **vigilance and prompt treatment** (Michel, 1969) whenever infection or clinical signs are detected. Indeed, on farms or in groups of cattle where no vaccination or preventative anthelmintic treatments are undertaken, then vigilance and treatment remains the best option, irrespective of the system.

Spring-calving dairy herds

On grass-dependent, spring-calving dairy farms, calves are frequently put out to grass from an early age, sometimes before weaning off milk-replacement. For convenience, paddocks close to the steading and calving area are used for the calves and this is therefore quite likely to be in the same location each year, with a potential risk of infection carrying over. However, because such paddocks may only be grazed by calves for a few months in spring each year, there is the opportunity to manage them for the remainder of the grazing season in a way that limits infectivity, such as shutting them up for silage. Grazing with adult cows is also an option, but the risk of contamination of calf paddocks with infective larvae of *D. viviparus* (and *Ostertagia ostertagi*) is quite high. Moving

FGS calves onto recently cut silage fields can provide relatively clean grazing and anthelmintic treatment at this time may be justified to help control PB (Eysker et al., 1996; Forbes, 2017).

As for SGS beef calves, the options for PB control in yearlings/heifers include vaccination and strategic anthelmintics with the option of vigilance and treatment if no preventative actions are taken. Booster vaccination before turnout should be considered for milking cows in herds that have experienced several episodes of PB and/or the re-infection syndrome in adult animals. In such herds, housing treatments for lungworm could also be included to eliminate infection in carrier animals. Irrespective of preventative measures, during the grazing season, vigilance and treatment is the order of the day. If disease levels are unacceptable, then a review of grazing practices may be required as high frequency rotations with high stocking rates may result in levels of challenge that can overwhelm vaccination and/or medication.

All-year-round (AYR) calving dairy herds

There are self-evident logistical problems in managing parasites in AYR herds as at any one time there will be calves ranging between a few days old and 12 months of age on the farm. Probably the most pragmatic approach is to divide calves into a limited number of cohorts and manage them as separate units. For example, all calves born in autumn and winter could comprise a cohort and these would be appropriate candidates for vaccination and/or strategic anthelmintic medication. Calves born in the spring and summer may be managed as one or two cohorts, depending on how they will be managed post-weaning, in particular whether they will graze and where. From July onwards, high levels of larval challenge can be expected on fields where untreated cattle have grazed from turnout. Unless there is adequate anthelmintic protection in place, it would be best if young calves were not mixed with cattle that have grazed since turnout, nor should they have access to fields on which older cattle have previously grazed.

Management of bulling heifers and young cattle from 12 to 24 months of age up to first calving will again depend on their month of birth and how much exposure to parasites they have experienced in their first 12 months of life. Control of PB (and PGE) in second year animals can be loosely based on the approach used in calves, though it may be possible to run them in larger cohorts and vaccination of all older animals before turnout becomes a viable option. In the milking herd, preventative measures include a booster vaccination before turnout, if the impact of dictyocaulosis warrants it, and anthelmintic treatment at housing to remove lungworm burdens from all cattle, including potential carriers. During the grazing season, under most circumstances, vigilance and treat is the mantra.

Closing remarks

Husk is a fascinating, but at the same time, frustrating disease: fascinating because of the many intriguing aspects of the biology of the parasite; frustrating because of its idiosyncrasies, which can make diagnosis challenging, treatment responses unpredictable and control difficult. Although good control of PB in youngstock is achievable, there remain many unanswered questions regarding dictyocaulosis in the dairy herd. For example in herds where the same groups of cattle can experience several clinical episodes during a single grazing season, despite the fact that they would

be expected to have acquired a protective immune response following initial exposure. Depending on herd demographics, it is quite possible that there may be animals within the same group experiencing a primary lungworm infection and others that are suffering from the re-infection syndrome. Booster vaccination could provide a means to equalise the immune status of a herd before turnout, but cost, convenience and culture can be significant barriers. Because of the potential fatal outcomes to infection in milking cows and the financial penalties that can arise through loss of milk yield and treatment costs (Holzhauer et al., 2011), many farmers are understandably averse to risk taking and may elect to treat entire groups or herds with anthelmintic – on several occasions. This practice may in itself lead to some level of enzootic instability, as primary infections that are treated at an early stage may not induce a full protective immune response (Hoglund et al., 2003). Whilst this scenario is highly speculative (McLeonard and Van Dyk, 2017), it does highlight the conundrum facing dairy farmers and their veterinary surgeons, who face a proverbial ‘Catch 22’ dilemma in deciding what are optimal practices for vaccination, anthelmintic use and grazing management to control lungworm on a farm-by-farm basis.

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Key points

- Anthelmintic treatment of clinical cases of lungworm needs to be assessed carefully, particularly if animals are in respiratory distress
- Apparent treatment failures may be due to irreversible lung pathology
- Control of parasitic bronchitis through vaccination and/or strategic use of anthelmintics is logistically difficult in calves other than those derived from autumn calving herds.
- In the absence of preventative measures, the management of lungworm depends on constant vigilance and prompt treatment when indicated
- Grazing management is of limited value in the control of parasitic bronchitis and some of the recommendations contradict those for optimal grassland and grazing management

Tables

Active	Formulation	Duration of activity	Speed of action	Mode of action
Moxidectin	Injection & topical	6 weeks	24 hours (estimated)	Paralysis (glutamate)
Doramectin	Injection & topical	6 weeks		
Eprinomectin	Injection & Topical	4 weeks		
Ivermectin	Injection & topical	4 weeks		
Albendazole	Oral	1 day	36 hours*	Destruction (β -tubulin)
Fenbendazole	Oral	1 day		
Levamisole	Oral, injection	1 day	3 hours (inj)*	Paralysis (acetylcholine)

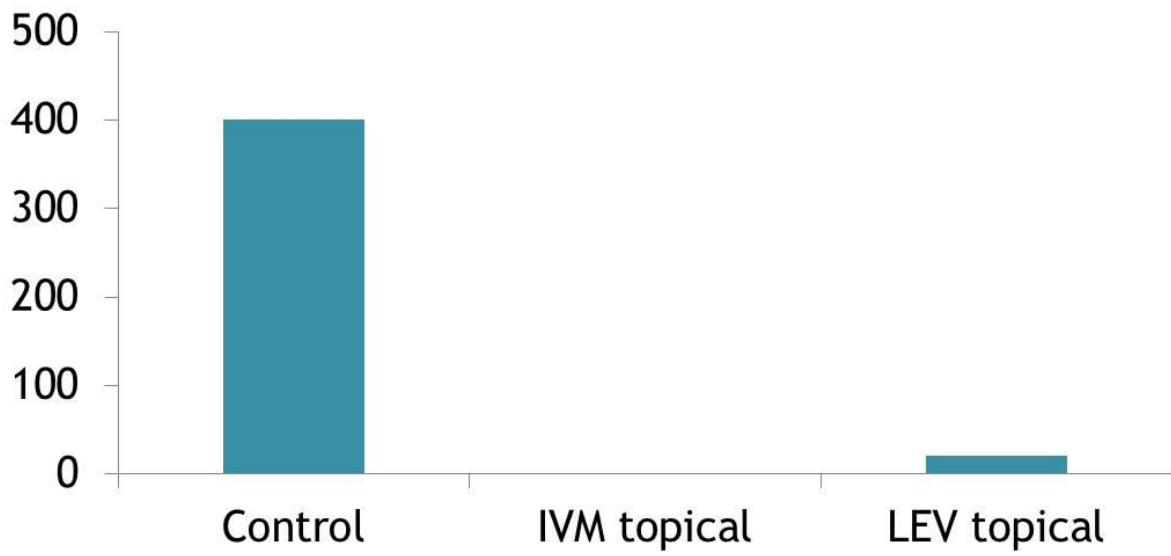
1. Summary information on anthelmintics than can be used to treat clinical cases of parasitic bronchitis (NOAH, 2015; Oakley, 1980).

Observation	Control	Fenbendazole	Levamisole
Five efficacy trials; 30-40 L3 <i>Dictyocaulus viviparus</i> *			
Efficacy	-	+	+
Mortality	52	38	0
Pathology study; 40 L3 <i>Dictyocaulus viviparus</i> *			
Green bronchial exudate	+++	+	
Consolidation; giant cells	+++	+	
Alveolar epithelialisation	+++	+	+

2. Potential outcomes and lung pathology in treated and untreated cases of dictyocaulosis (Jarrett et al., 1954; McEwan et al., 1979).

Figures

Worm counts 7 days post treatment



1. Comparative efficacy of topical formulations of ivermectin and levamisole against induced lungworm infections (Taylor et al., 1990).