Worm control in livestock: bringing science to the field.

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Abstract

Parasitic roundworm infections are ubiquitous in grazing livestock. Chemical control through the frequent 'blanket' administration of anthelmintics (wormers) has been, and remains, the cornerstone in controlling these infections, but this practice is unsustainable. Alternative strategies are available but, even with the plethora of best practice advice available, have yet to be integrated into routine farming practice. This is probably due to a range of factors including contradictory advice from different sources, changes to advice following increased scientific understanding and top-down knowledge exchange patterns. In this article, we discuss the worm control options available, the translation of new best practice advice from science bench to field and ideas for future work and directions.

Worm infection limits productivity in grazing livestock

Parasitic roundworms (gastrointestinal nematodes) are ubiquitous on pastures grazed by livestock. Although infections are generally sub-clinical, they result in considerable losses in livestock productivity [1 http://www.discontools.eu/Diseases]. Estimates of losses of up to 10% of sale value [2] and of around £80 million and €334 million per annum, respectively, for the UK and EU sheep markets alone [3].

Chemical control, through frequent and often indiscriminate use of **anthelmintics** (wormers, see Glossary), was widely recommended as a strategy to optimise production, but resistance to these drugs has increasingly been recognised, making the long-term viability of this approach untenable. The increasing prevalence and wide-spread dissemination of worms resistant to most of the available anthelmintic classes has forced the industry as a whole to develop a deeper understanding of nematode epidemiology and the selection pressures applied to the nematode community by anthelmintics. Most, but not all, of the principles that are detrimental to sustainable worm control are well established within the scientific community. However, many of these messages have failed to be routinely implemented by the farming community. Therefore, there are two main challenges for the provision of sustainable nematode control: a holistic understanding of the impacts of various control options and effective dissemination to, and uptake in, the farming community. In this opinion article, we summarise the opportunities and challenges that are present in the translation of new ideas and uptake of best practice advice in gastrointestinal nematode control options in livestock. We discuss several areas of worm control, highlighting the evidence present (or if appropriate, knowledge gaps), the current methods for dissemination of advice, and provide our ideas for the future.

A range of different options are available to tackle worm infection

Traditionally, the control of parasitic nematodes on farms included an element of 'evasion', e.g. infection intensity was minimised through carefully planned grazing strategies (Table 1). For example, in spring, over-wintered larvae of the pathogenic species *Ostertagia ostertagi* die off rapidly and, therefore, a delay in turnout of calves until early summer, on pasture already mowed that year, is highly effective [4]. So-called 'leader-follower' systems were also commonplace on UK farms. These grazing strategies employ differences in the levels of host resistance, or immunity, of ruminant age groups and host species to limit infective pressure in young, immunologically naïve, animals. Perhaps the most commonly used method was alternating cattle and sheep to graze plots, with cattle 'hoovering up' the worm species pathogenic to sheep and *vice versa*. Alternatively, calves and lambs were allowed to graze pasture first before the older, immune, animals then grazed the remainder. On pastures thought to be heavily contaminated, the older animals grazed the plots first thus removing large parts of the infective burden. A third important 'evasive' strategy is rotational grazing; instead of offering a large plot of land to animals for prolonged periods of time, it is divided into several sub-plots with animals returning to them only when the larvae have died off. For example, rotating calves monthly over 4 plots, especially if the plots are mown after they are grazed, is likely to control worm burdens, while facilitating the build-up of immunity [5].

Several concurrent trends in UK ruminant farming have made the evasive control practices less popular with farmers. Ruminant farms have intensified significantly over the past decades and, therefore, there has been pressure to both maximise pasture utilisation and optimise labour costs per animal unit. These modern farms normally only farm one ruminant species. The ascendance of *Mycobacterium avium paratuberculosus* (Johne's disease), transmitted from cattle to sheep and from older cattle to young stock, has further limited the 'leader-follower' options. During the seventies, new, broad-spectrum, anthelmintics came onto the market and these instilled a feeling that more animals could safely be kept on smaller plots, without moving them to 'clean' pasture, as long as they were wormed regularly. The advice on worm control therefore made a step change from avoidance of burdens to acceptance that infective pressure at pasture may be high but that it can be controlled before becoming overly pathogenic.

There have been at least three distinct anthelmintic-based control strategies to date. Initially, it became commonplace to treat at least all young stock at set intervals, with the length of the interval between treatments (normally 4-6 weeks) determined by the residual effect of the drug used. Frequent treatment administrations have been shown to select heavily for **anthelmintic resistance** [6]. When this started to emerge, a call for drugs of different classes to be rotated slowed the build-up of resistance somewhat but could not stop the emergence of multiple-drug resistance on farms, directly threatening the livelihoods of farmers [7]. A second strategy therefore focuses on lowering drug application frequency by targeting treatments to periods of high worm abundance levels (**targeted treatment, TT**). Crucially, TT is applied at group level, e.g., a whole flock of lambs will be treated at the same time. Given the over-dispersed distribution of parasites in animal populations, a key challenge to TT has been obtaining, and interpreting, a meaningful monitoring parameter reflecting the current worm burden [8]. If, the burden of the treatment group is over-estimated, then the method will result in a higher-than-necessary dosing frequency, whilst it is designed to do the opposite. However, if the burden is under-estimated, then disease and associated production losses may be witnessed when the test indicates a low burden. Moreover, even though doses are given less frequently, all animals are dosed at the same time and this still gives rise to bottlenecks in parasite populations which select for anthelmintic resistance. A third method, **targeted selective treatment** (**TST)** [9] specifically aims to lower the proportion of the parasite population exposed to anthelmintic drugs at any given time, and to lower the frequency of resistant alleles in the population by diluting these alleles with the offspring of non-resistant worms (e.g., ensuring that a proportion of worms remains *in* ***refugia***). This is achieved by assessing individual animal-based patho-physiological parameters, such as weight gain, and identifying the animals which may benefit from treatment, while leaving animals which achieve certain parameter thresholds untreated. It has been shown repeatedly that this can be done without any overall negative effects on productivity [6, 10]. TST also brings significant savings on anthelmintic drug costs [11]. With farmers moving away from grazing management-based control strategies and TST currently the key interpretable anthelmintic-based strategy explicitly focussing on *sustainable* worm control, it is therefore pertinent to understand why TST has not been implemented on most farms as yet.

Moving towards sustainable control

The change from suppressive worming programmes to refugia-based sustainable control programmes has been advocated since 1992, with the Sustainable Control of Parasites in Sheep (SCOPS, www.scops.org) industry group, established in 2004 [12, 13], attempting to increase their uptake. The main challenge has been that suppressive worming regimes are prescriptive, easy to follow and, for many years, have yielded good productivity. Refugia-based approaches, on the other hand, may not be as straight forward to implement. Initial concerns about reductions in productivity attached to these approaches were shown to be unfounded [6, 14, 15].

For example, dosing groups of animals and moving them to **'clean' pastures** at the same time is valid from a productivity point of view and appeals to common sense as it lowers the parasite challenge to lambs. However, moving lambs on to clean pasture where there is little refugia to "dilute out" the resistance worms can be highly selective for resistance and is therefore no longer recommended [13, 16].

Reversion to susceptibility in field studies, where anthelmintic to which resistance is present is avoided for a period of time, then reintroduced, show that the reversion to susceptibility is short lived [17, 18]]. It has been hypothesised that, although there is assumed to be a lack of fitness associated with resistant individuals, as their number increases, the genes of susceptible and resistant worms co-adapt meaning that differences in fitness are no longer obvious [17].

The dosing of whole-groups, whether lambs or ewes, is still common place, even though some workers [6] showed that the productivity of lambs did not decrease if targeted treatments were used. If whole group treatments are carried out, are there times when this could be acceptable? In cases where there is a high risk of disease, for example due to infection with Nematodirus species, where clinical disease can occur quickly, or fluke, then whole group treatment would be recommended. Also, if high levels of refugia are present on pasture, then the impact of whole group treatment on the development of resistance would be less than if refugia was low.

Sometimes, drugs with anthelmintic properties will have to be applied to the whole flock/herd, for the control of other parasites. For example, macrocyclic lactones are commonly used for scab control [19]. About 15% of the wormers currently used in the UK also have endectocidal activity and there is much discussion about the effects of their use for scab on the development of anthelmintic resistance. Crilly et al.[19] showed on farms that used macrocyclic lactones for scab control that the ewes expelled eggs earlier than would be expected but resistance was not definitively diagnosed. Therefore, more information is required on the effect of off-target administrations, such as psoroptic mange (scab) treatments on the development of resistance in nematodes, as the selection pressure will increase as the level of sheep scab infection continues to rise in the UK.

The first, commercially available gastrointestinal nematode vaccine was recently licensed for use in sheep in Australia and South Africa [20]. Research is on-going for other species, but are currently in the early stages of testing [21-23]. However, this approach holds promise as an additional tool in the armoury for sustainable nematode control.

Translation of new ideas and knowledge to veterinarians, farmers and farming advisors

For mindsets on worm control to be successfully changed, the new control measures have to be underpinned by sound science and the message from the scientific community to farming industries has to be a united one; both have proven to be stumbling blocks in the past. For example, the way in which different anthelmintic classes should be best employed has been the subject of sustained and continued debate. Annual rotation of drugs has been advocated by many as a tactic to slow down the development of resistance. The theory behind this is that resistant worms pay an ecological fitness cost and so are 'weaker' than the susceptible ones, and fewer will survive when not exposed to wormer, lowering the number of worms carrying resistant alleles to a certain anthelmintic in the population. However, little data are available to support this theory. Within-season rotation is another option and one study suggested that the effects on slowing the development of resistance were minimal [24]. Modelling studies have hypothesised within-season rotation may be beneficial, but the full impact in the field has not yet been assessed [25, 26].

Historically, information transfer has occurred in a top-down approach, in a unidirectional fashion, rather than as an exchange of views by all interested parties. The latter is considered essential to facilitate effective exchange of information.

Information regarding the control of parasites of sheep is readily available from a wide range of actors (other farmers, veterinarians, agricultural merchants, farm advisors, pharmaceutical industry, levy boards, researchers and farming press to name a few), in an array of formats (journals, internet, social media, books, leaflets, scientific and popular press articles, newsletters and websites). As an example, the phrase “*control of parasites of sheep*” has 0.5 million hits on Google™, 250,000 hits on Google scholar™). A number of extension programmes, for example, SCOPS in the UK and PARABoss (www.wormboss.com.au) in Australia, are also available. The advent of the digital age has opened up the opportunities to use a wide range of new platforms including the use of video tuition, animations (moredun.org.uk/worm-animation), infographics, electronic-learning tools and decision support systems, but one area of concern is that the connectivity for many rural areas is still poor (www.ofcom.org.uk/research-and-data/infrastructure-research/connected-nations-2016), albeit getting better, and many farmer are frustrated by slow download-speed, potentially leading to poor uptake through these mediums.

Although information is generally readily available, previous surveys conducted into farmer behaviour have shown a variable uptake of some advice and recommendations provided to farmers regarding the treatment and control of gastro-intestinal nematodes (Bartley, D.J. PhD thesis, Edinburgh University, 2008) [27]. showing that, as scientists, we do need to improve connectivity to the end users and simplify the messages that we are conveying.

So, what do we need to do to become more effective at communicating advice? The answer is likely to be multifaceted and include factors listed in Figure 1 (Key Figure). Firstly, we need to identify how farmer behaviour is best influenced; for example, what format would be preferred for the exchange of information? Then, the important factors are unifying the messages to minimise contradiction and/or ambiguity; tailoring advice to specific audiences and situations; ensuring guidance is compatible with farming practices and based on sound data; trying a range of formats be they theory based or practical, online or hard copy, peer to peer or academic and providing the appropriate infrastructure for effective knowledge exchange. Workshops, on farm events, or farmer discussion groups can provide valuable opportunities for producers, researchers and farm veterinarians to get together and discuss issues and help put across practical applications to encourage farmers to practice sustainable worm control. One thing is for certain: improved communication among all parties is essential to ensure the long term sustainability, productivity and profitability of farming.

Looking to the future

Alternative ways of controlling worms of livestock do exist; so, how can the industry and research move forward? What should be the steps to ensure that uptake is occurring in the farming community?

Uptake of innovation is dependent on many factors, but two are paramount: the technology itself and the respondent (farmer/practitioner). Both need to be recognised if innovation is to be adopted. Milne and Paton [29] reviewed barriers to innovations in livestock systems and the importance of knowledge exchange. They identified three main areas important to innovation: attributes of the innovation, its dissemination and adopter characteristics. The lead barriers to adoption were insufficient information; unrealistic/inaccurate information; and high implementation and/or operating costs. They argued that "*innovations must 'fit' with existing systems*" and that "*realistic assessments of the risks associated with an innovation and how they compare with alternative options are also crucial*". Accordingly, any positive or beneficial aspects of sustainable worm control options must be demonstrated to practitioners, for uptake to take place. TST can be advantageous for practitioners as the TST approach on a hill farm showed a reduction of wormer use (~40-50%), without a reduction in production (lamb weights at sales), thus bringing potential financial advantages to the farmer [30].

So, how could the implementation of these methods be facilitated? Pecuniary incentives could certainly help uptake, but often, farmers' reasons are more than just financial. In studies of TST and the use of electronic identification (EID) of animals, it was found that the main barriers for further implementation and use were the (perceived) cost of the technology, the lack of specific training on how to use the equipment, and the diversity of systems and type of technology available on the market [31]. These factors have been confirmed as equally important for farms in other European countries [32]. There is a clear need for improved tools to help deliver pen-side worm control treatment options in a user-friendly format, with appropriate supporting information (impact of decisions; e.g., economically) (Box 1).

In addition, further research is required to fully understand the impacts of socio-economic and psychology factors on farmers' behaviour and their decision making processes. For instance, Charlier et al. [33]propose looking at economic and social context to understand factors that drive animal health ("ECONOHEALTH"). Likewise, Charlier et al. [34] state the importance of better economic impact assessment combined with non-economic factors for more effective health control strategies in cattle. Moreover, Van de Velde et al. [35] further argue that it is not just farmers' behaviour that it important on adoption intentions, but the influence of the significant others (e.g. family, veterinarian, etc.)[36].

Additionally, how can we promote the adoption of new strategies/technologies, as well as ensuring on-farm applicability? There is certainly a role to play for advisory services and technical consultancy, to help promote these alternative ways in a format readily understandable and useful for farmers. There is a clear need for information and training materials to be adapted to the relevant educational levels of the farmers targeted [32, 37, 38].

However, measuring success and uptake of any new method remains difficult. Production parameters within the sheep industry vary greatly, due to the diversity of sheep systems and practitioners' views. It is thus challenging to benchmark results, making the assessment of success or failure of new techniques on farms difficult. Modelling or participatory exercises (e.g. future planning scenarios and techniques), such as those used by Boden et al. [39], looking at the future of the sheep industry, and resilience to disease are certainly valuable. These techniques provide a means to explore "what if" scenarios, and allow forecasting the effects of introducing new methods on farms, as well as taking into account practioners' views and attitudes.

Concluding remarks.

Infection with parasitic roundworms is ubiquitous in grazing livestock. Although frequent use of anthelmintics was, and in some cases, still is the cornerstone of control of these infections, this approach is not sustainable in the long-term due to the development of anthelmintic resistance. Other, alternative approaches are available but, in general, they have not been adopted into routine farm management.

A plethora of information is available, but this is sometimes contradictory, which can lead to confusion. Co-ordination of information from all sources should be possible, but may be difficult to achieve. Several questions still need to be answered before optimised worm control can be a reality for most farmers (see Outstanding questions box). There is a need for new and improved tools to help farmers and veterinarians to make optimised worm control treatment decisions. This can be achieved by the development of pen-side or automated decision support systems, using the cloud for ease of access and data storage; however, improvements to internet accessibility will be required to make this reality. Before these systems can be developed, more information is required on the best methods for knowledge exchange between interested parties, so that whatever method is identified as most useful can be applied to the decision support systems developed.

Box 1 New tools will improve use of best practices among farmers.

A variety of new tools are required to improve the use or dissemination of best practice advice among livestock farmers. These can be in several different areas, for example:

Automated performance monitoring and/or treatment decisions with user-friendly decision support systems. These could be in the form of apps or pen-side 'one-stop shops' (i.e. multi-purpose, multi-disease treatment indicators).

Individualised on-farm risk factor analysis and disease tracking, i.e. which diseases occurred on which fields and which control measures have been historically applied. This could be combined with epidemiological knowledge to optimise future control options

Economics of various treatment options. Farmers, veterinarianss and their advisors need to see and understand the costs and benefits of various treatment options, including comparisons between traditional and sustainable control strategies. These need to include not only the economics but also effects on parasite populations or animal performance. Modelling of these and the associated economics would provide farmers, veterinarians and their advisors with concrete information on which to base their decisions.

As the number of technology driven decision support or recording systems increase, so will the demand for secure data storage, which can be reliably accessed from remote places where internet connections may be slower than average.

Table 1. Key control options for the management of worm infections in grazing livestock.

Option	Strategy	Selection for anthelmintic resistance	Factors preventing uptake
Infection evasion	Late turnout	-	Diminished pasture utilisation, Laborious (care for housed animals) Cost Space
	Leader-follower system	-/+ *	Johne's disease transmission, Move towards mono-species farms
	Rotational grazing	-	Investment needed (fencing), space, Planning for multiple groups / flocks Move towards mono-species farms Johne's disease transmission,
Chemical removal of worm burdens	Dosing all animals at set intervals	+++	None
	Targeted treatment of all animals (TT)	-/+	Interpretation of monitoring data Requires in-depth knowledge of parasite situation on farm Identification of animals to treat
	Targeted selective treatment of individual animals (TST)	-/+	Unclear parameters for identification of animals to treat Investment in monitoring tools

			(electronic weigh scales, etc.)

*if worm control is assisted by the application of wormers in one host species, there is potential for resistant worms to be passed on to the other host species. Key: - = does not select for AR, +/- = minimal contribution to the development of AR, +++ = selects heavily for AR.

Glossary

Anthelmintic: Chemicals which can be used to control worm infections. Five different classes are currently available in the UK for use in sheep.

Anthelmintic resistance: the heritable reduction in the sensitivity of roundworms to anthelmintics when animals have been administered the correct dose of the drug, in the correct manner, using drugs that are within date and have been stored correctly.

Clean pastures: pastures that have no, or very low levels of worms present. This can occur if grass is newly seeded, if crops have been harvested e.g. hay, or if there has been drought conditions.

Refugia: parasite subpopulations from either the stages within the host or free-living stages on pasture that are not exposed to anthelmintic treatment, and that have the ability to complete their life cycle and pass on susceptible alleles to the next parasitic generation [39, reviewed by [10]. This is generally achieved by ensuring that a proportion of the parasite population remains unexposed to drug, through either TT or TST (see below).

Targeted treatment (TT): Treatment of a whole group of animals at a time selected to either minimise the impact on the selection for anthelmintic resistance, or to maximise animal productivity.

Targeted selective treatment (TST): The treatment of only some individuals within a group at one time, instead of the more common 'whole-flock' treatment, where all animals in the group are treated simultaneously (for review see [10])

Figure 1, Key Figure. Factors influencing effective knowledge exchange and uptake/implementation of advice with particular reference to sustainable worm control. Effective communication of information to producers is complex and likely to be influenced by a number of internal and external factors. The multifactorial nature to individual perceptions to advice and the uniqueness of drivers and barriers to effective knowledge exchange means that we need to develop strategies to disseminate information effectively. A quote often attributed to Albert Einstein states that "information is not knowledge. The only source of knowledge is experience" Veterinarians are often cited as trusted brokers for advice but it is essential that advice that they receive and ultimately give out is current, implementable and consistent from different data providers and is borne out of experience in different situations.

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