

Anthelmintic Resistance – A Potential Crisis for Sheep Producers?

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Parasitic gastroenteritis, caused by roundworms (nematodes), is well recognised as a major production-limiting disease, particularly in lambs. Effective parasite control has become heavily dependent on anthelmintics. The development of anthelmintic resistance by roundworms poses a potential crisis for sheep producers and measures to avert and delay this are essential. This report summarises the main results from studies at Teagasc, Athenry, examining the anthelmintic resistance status of Irish lowland commercial flocks and recommendations to combat the challenges facing producers in controlling parasites are outlined.

Gastrointestinal Parasites

The main roundworms that affect lambs are *Nematodirus battus* in the spring, while later on in the season, a number of other roundworms feature, among which *Teladorsagia* (formerly known as *Ostertagia*) and *Trichostrongylus* species (black scour worm) are the most important. In general, the lifecycle of all these gastrointestinal parasites (with the exception of *Nematodirus battus*) is similar. Adult worms in the sheep's gastrointestinal (GI) tract mate and the females lay eggs, which pass out in the sheep's faeces. The egg develops in the faeces and hatches to release a feeding larva (L1 stage). This L1 subsequently undergoes further development to the L2 stage and then to the non-feeding infective stage (L3), which subsequently migrates on herbage awaiting ingestion by a suitable host. Once ingested, the L3s will complete their development to adults (at their preferred sites along the GI tract) within 15 to 21 days, for most common roundworm species. The life cycle of *Nematodirus battus* is slightly different in that development to L3 occurs entirely within the egg and hatching occurs in response to a cold stimulus the following spring. Thus *N. battus* is a parasite that can largely be avoided if grazing lambs on the same pasture each year is avoided.

Anthelmintics

While there are many anthelmintic products on the market that are highly effective against a broad spectrum of roundworm species, they can be grouped based on their mode of action into four classes of compound:

1 (BZ): -Benzimidazoles and probenzimidazoles (e.g..albendazole, fenbendazole, oxfendazole, mebendazole). –oral formulation

2 (LM): -Levamisole - oral formulation

3 (ML) -Macrocyclic lactones (including abamectin, doramectin, ivermectin, and moxidectin) -oral / injectable formulations

4 (AD) -Amino acetonitril derivatives (monepantel) – oral formulation

Anthelmintic Resistance

There is no doubt that the advent of broad-spectrum drugs has played a crucial role in diminishing the effects of parasitism in grazing sheep, and has supported an increase in productivity. However, parasites are developing resistance to these anthelmintics, which is allowing worms to survive exposure to the standard therapeutic dose of the anthelmintic, survive and produce offspring. So over time, with increased anthelmintic use the development of anthelmintic resistance is inevitable as resistant worms become more prevalent in Irish sheep flocks. Clinical evidence (persistent diarrhoea, lack of thrive) for failed treatment then becomes apparent. Resistance can occur within anthelmintic classes and to more than one class of anthelmintic.



It is important to check that your wormer type is working on your farm – use dung testing.

Methods to Detect Anthelmintic Resistance

The most widespread methods used to detect anthelmintic resistance are the drench test, faecal egg count reduction test, egg hatch assay and larval development test. The drench test involves determining the faecal egg count at a suitable interval (time depends on the class of anthelmintic) post anthelmintic treatment. The faecal egg count reduction test involves calculating the mean reduction in faecal egg count at a defined interval post treatment (which is dependent on the anthelmintic being tested) for a sub-group of the flock (minimum of 12 to 15 sheep faecal sampled pre and post treatment). While these are suitable for testing all anthelmintic groups, it is only reliable if more than 25% of the worms are resistant. The egg hatch and larval development assays involves examining the development of eggs and larvae, respectively (from eggs obtained from a pooled fresh faecal samples from a sub-group of the flock) in various concentrations of the

anthelmintic. The larval development test can be used to detect resistance to both benzimidazole and levamisole. This test is available at some veterinary practices and the Regional Veterinary laboratories.

Evidence for Anthelmintic Resistance

The evidence for nematode resistance to benzimidazoles worldwide is compelling. Results from studies in Irish flocks reveal an alarming incidence of anthelmintic resistance to two of the anthelmintic classes currently available on the market (Good *et al.*, 2003; Good *et al.*, 2006; Patten *et al.*, 2007, Good *et al.*, 2011). Using the faecal egg count reduction test on 16 farms involved in collaborative projects with Teagasc, resistance to benzimidazole was evident in 94% and to levamisole in 38% of flocks. Similar results were also observed in a nationwide survey of 64 representative Irish farms using the larval development test. Anthelmintic resistance was observed in *Teladorsagia*, *Trichostrongylus* and *Cooperia* species. As yet, there is no evidence for anthelmintic resistance in *Nematodirus battus*. The evidence above clearly shows that Irish flock owners need to realise that the development of anthelmintic resistance is in progress on many of their farms.



A strict approach to worm control in lambs is required to protect the efficacy of anthelmintics

Measures to Delay Anthelmintic Resistance

The development of anthelmintic resistance poses a potential crisis for sheep producers and measures to avert / delay this are now essential. Last year (after a gap of 25 years) the launch by Novartis of a new class of anthelmintic (AD, monepantel) to the market was a welcome development. This presents both an opportunity and challenge to become more effective at delaying the development of resistance. Measures by sheep producers to delay anthelmintic resistance and prolong the lifespan of anthelmintics are now essential. The essential actions required to slow the progression of anthelmintic resistance are:

- the effective (proper) administration of anthelmintics
- only use anthelmintics when necessary
- use the most appropriate anthelmintic

- reduce dependence on anthelmintics
- avoid the introduction of resistance onto a farm by treating purchased stock on arrival (either macrocyclic lactone / monepantel) followed by a quarantine period
- maintain anthelmintic susceptible population of worms
- test for anthelmintic resistance (regularly)

Essentially, if the underlying principles of delaying resistance namely (a) best anthelmintic practice and (b) strategies that reduce the selection pressure for resistance are adhered to, the emergence of anthelmintic resistance will be minimised.

The Future for Anthelmintics

Fundamental to sustainable parasite control is a reduction in the reliance on anthelmintics with more effort directed in managing parasites than just the ‘treat and forget’ approach of the past. The future for anthelmintics in the control of gastrointestinal infections lies in our increased understanding of how anthelmintic resistance develops and research in to the development of more sensitive methods for detecting resistance in order to monitor and provide the capacity to develop case specific action programmes that prolong the lifespan of anthelmintics. Meanwhile the adoption of best anthelmintic practices to preserve the effectiveness of anthelmintics in controlling the impact of parasites on animal performance is crucial.