# Delaying anthelmintic resistant parasite development on sheep farms

**In an effort to combat the development of anthelmintic resistance on sheep farms in Ireland, four key actions have been identified by industry experts from Teagasc, the Department of Agriculture, Food and the Marine, UCD and veterinary representatives. The four key actions that have been selected are cost-effective and easy for farmers to implement. With the support of the veterinary profession, the overall aim will be to slow the development of anthelmintic resistance and increase the lifespan of the currently available anthelmintic treatments. In this article, Maura Langan MVB, Vet Advisor, Norbrook, explores the four key actions**

Grazing sheep are naturally exposed to gastrointestinal nematodes (GIN). A large number of different GIN species can infect sheep, but they are generally broken into two groups which can be distinguished on the basis of egg morphology: i) Nematodirus or ii) Strongyle worm species.

Nematodirus has a different life cycle to most other GIN; Nematodirus eggs require a prolonged period of cold weather followed by a period of warmer weather (>10°C) to hatch. Therefore, eggs passed out by lambs in spring/summer hatch in a synchronised manner the following spring and thus infect the following year's lamb crop. Lambs rapidly develop strong immunity to Nematodirus and usually have protective immunity by approximately 12 weeks of age.

Strongyle worms (eg., *Trichostrongylus* spp., *Teladorsagia circumcincta*) generally all have a similar life cycle with both free-living and parasitic stages and can complete their lifecycle in as little as five weeks when conditions are favourable. Eggs laid by adult female worms in the gastrointestinal tract are passed out with the dung. The eggs hatch to L1 larvae which feed on microbes in the dung. The L1 stages develop to L2 stages (which continue to feed in the dung) and subsequently to L3 (infective stage). The L3 migrate out of the dung onto the grass where they can survive for many months until ingested by grazing sheep. Once ingested, they travel to their preferred site of infection in the gut (abomasum or small intestine) where they further develop into mature adults with female worms laying eggs. Worm larvae, therefore, accumulate on pasture over the grazing season and consequently, are generally a greater problem in the second half of the grazing season.

Sheep develop immunity to GIN over time and generally have good immunity by one year of age. GIN can cause disease, including scour and ill-thrift in naïve lambs and are commonly associated with appetite suppression and sub-clinical disease resulting in reduced growth rates.

## ANTHELMINTIC RESISTANCE

Control of GIN has, to date, generally relied on the administration of anthelmintics from one of the anthelmintics classes: namely, the benzimidazoles 1-BZ, levamisole 2-LV, macrocyclic lactones 3-ML, amino-acetonitrile derivatives 4-AD or spiroindoles 5-SI. However, such an approach is unsustainable, it is both threatened by, and promotes, the development of anthelmintic resistance.

Anthelmintic resistance is defined as the ability of a parasite to survive an anthelmintic treatment that ordinarily should kill them. Anthelmintic resistance is a heritable trait; resistant GIN pass on genes conferring resistance to their offspring and so, once resistance arises, it is very difficult to reverse.

Anthelmintic resistance to each of the three commonly-used anthelmintic classes (1-BZ, 2-LV and 3-ML) has been demonstrated to be widespread on sheep farms in Ireland (Keegan et al., 2017) and farms with multi-drug resistant GIN have also been reported (Keegan et al., 2015). Anthelmintics from different classes have different modes of action. However, actives within the same class share the same mode of action, so when resistance develops to one product or active, others in the same class may also be affected. For these reasons, it is

important that sustainable worming strategies are adopted in order to increase the lifespan of existing treatments.

## AVOIDING RESISTANCE

There are a number of factors known to accelerate the development of anthelmintic resistance. These include, but are not limited to, high anthelmintic treatment frequency, treatment of adult animals, under-dosing and reducing the in-refugia population.

Refugia is defined as the proportion of GIN in the population not exposed to anthelmintic treatment. In order to reduce the selective pressure for the development of anthelmintic resistance, it is desirable to reduce anthelmintic use where possible and to ensure a population of worms remain unexposed to the drug, such as the free-living GIN on pasture or GIN in sheep that have been untreated.

Treatment of adult animals, namely ewes around lambing, to suppress the peri-parturient rise in GIN faecal egg count with the aim of reducing subsequent pasture contamination is a common practice on Irish farms. However, this practice also represents a risk to the development of anthelmintic resistance (Patten et al 2011) for the following reasons.

Firstly, the use of a treatment at the start of the grazing season that is not completely efficacious will seed the pasture with resistant GIN, which will then be propagated during the remainder of the season. Secondly, few farmers are capitalising on any reduced pasture contamination by subsequently reducing the number of anthelmintic treatments administered to their lambs.

Given the current level of resistance on Irish sheep farms, it is important that sustainable strategies to manage GIN and to delay further development of anthelmintic resistance are implemented as a matter of urgency.

In an effort to combat the development of anthelmintic resistance on sheep farms in Ireland, a campaign centred on four key actions has been initiated that will help maintain a susceptible worm population and prolong the efficacy of commonly-used anthelminthic products.

## THE FOUR KEY ACTIONS

**Action 1. Do not treat adult ewes for GIN unless there is a demonstrated need.**

Adult ewes should have good immunity to GIN and, therefore, should not require treatment. Lactating yearling ewes or thin/compromised mature ewes may warrant treatment, but in such cases the treatment should be targeted to the individual animal and not the whole flock. The presence of Haemonchus contortus may also necessitate the treatment of mature ewes, although this parasite is rare in Ireland. If the mature ewe flock requires routine treatment for GIN, this may imply an underlying nutritional or health issue that necessitates veterinary investigation.

Given that many farmers are unaware of the anthelmintic resistance status of their farm and the limited use of faecal egg count monitoring to inform treatment decisions on Irish sheep farms, leaving ewes untreated at lambing is a practical and effective way of reducing the selection pressures for resistance. Untreated ewes are also a good source of refugia and thus help maintain a susceptible GIN population within a farm.

Another issue is the inadvertent selection for resistance in GIN by the use of injectable group 3-ML products for external parasite control, or the use of a combination wormer/flukicide when targeting fluke. In these instances, plunge dipping or a flukicide-only product may be a more appropriate treatment choice.

**Action 2. Use only products from group 1-BZ (white drenches) to treat Nematodirus in lambs.**

The unique lifecycle of Nematodirus battus means anthelmintic resistance is much slower to arise in this GIN than in other strongyle species. No definitive resistance has been confirmed in Ireland in Nematodirus to any of the three commonly used anthelmintic classes.

In light of the fact that there is a high level of resistance among strongyle species to Group 1-BZ products in Ireland and that group 1-BZ products can effectively treat Nematodirus in lambs, it is therefore prudent to solely use 1-BZs for treatment of Nematodirus. Parasitologists at the Department of Agriculture, Food and the Marine, in collaboration with Met Éireann, predict when peak hatching of Nematodirus eggs will occur and subsequently produce a Nematodirus forecast that advises lamb producers when to treat at-risk lambs for this parasite.

This approach ensures that the other product groups, namely 2-LV and 3-ML, that are more widely effective against strongyle species, are reserved for later in the season.

**Action 3. Quarantine drench – prevent 'buying in' resistance.**

As the resistance status of farms from which farmers are buying in stock is likely to be unknown, a strict biosecurity protocol should be in place on each and every sheep farm in order to prevent importing resistant GIN onto a farm. For this reason, all purchased sheep should receive a quarantine treatment on arrival onto the farm.

The quarantine treatment protocol should include using one of the new, prescription-only, anthelmintic groups ie., 4-AD or 5-SI, and in combination with another product. Such a treatment regime is represented by either option one or two below.

1. Group 4-AD + either Group 2-LV or Group 3-ML
2. Group 5-SI + Group 2-LV

In addition, the purchased sheep should be housed for 48 hours following the quarantine treatment to ensure any eggs already in the gastrointestinal tract have been eliminated. Finally, the purchased sheep should then be turned out onto dirty pasture, ie., ground grazed frequently by sheep.

**Action 4. Use faecal egg counting to determine anthelmintic efficacy on the farm and to inform treatment decisions.**

Once anthelmintic resistance arises, it accelerates rapidly through a worm population if further selection pressure for resistance is applied by continued use of the same anthelmintic class. Therefore, establishing anthelmintic efficacy on farm will help to inform treatment decisions and ensure an anthelmintic known to be effective is always used. Either a drench test (composite faecal sample), or a faecal egg count reduction test (individual animal samples) can be used to establish efficacy of the products currently being used on farm. Quite simply put, the best anthelmintic is one that works!

In terms of informing treatment decision-making, faecal egg counting should also be used in lambs from weaning onwards to establish the need for anthelmintic treatment and how to best time such treatments. Such an approach will help to reduce the overall usage of anthelmintics – which ultimately contributes to the development of resistance – while remaining cognisant of the problems arising from gastrointestinal parasitism in sheep production systems.

These four key actions are now being promoted to farmers with the overall aim of driving simple and effective change at farm level and ultimately preserving the usefulness of the currently available anthelmintic treatments.

*Support for this initiative is provided by Norbrook, Zoetis, Chanelle and Elanco. Further information is available at https://www.teagasc.ie/animals/sheep/flock-health/anthelmintic-resistance/*

## REFERENCES


- Keegan JD, Keane OM, Good B, De Waal T, Denny M, Hanrahan JP, Fitzgerald W, Sheehan M. A nationwide survey of anthelmintic treatment failure on sheep farms in Ireland. Ir Vet J. 2017 Feb 9;70:7.
- Keegan JD, Keane OM, Farrell L, Byrne W, De Waal T, Good B. Characterisation of ivermectin and multi-drug resistance in two field isolates of Teladorsagia circumcincta from Irish sheep flocks. Vet Parasitol Reg Stud Reports. 2015 Dec;1-2:3-9.
- Patten T, Good B, Hanrahan JP, Mulcahy G, De Waal T. Gastrointestinal nematode control practices on lowland sheep farms in Ireland with reference to selection for anthelmintic resistance. Irish Veterinary Journal 2011, 64:4