Managing Multiple Resistance

Increasingly, we are recognizing that 'multiple' anthelmintic resistance on a farm does not necessarily mean the end of the sheep enterprise. However, swift and positive management actions are needed where resistance to two or three of the current broad-spectrum groups is confirmed. SCOPS has a support tool for producers and advisers at https://www.surveymonkey.co.uk/r/MAR_DS. Key areas to consider for multiple anthelmintic resistance are:

Which worm genera are resistant to which anthelmintic groups?

Under typical UK field conditions, there tends to be a seasonal succession of genera with *Nematodirus* dominating in early spring, followed by *Teladorsagia* in early summer, and *Haemonchus* and *Trichostrongylus* in late summer and autumn. Based on recent field data it is probable that resistance will vary between genera and hence also the time of year, so this will have a significant influence on effective strategies available.

Knowledge of which worm genera are resistant to which anthelmintic groups, and at what time of year these genera require control, can provide farmers with alternative control options. For example, a farm with 1-BZ resistance that was diagnosed later in the season (and not likely to be Nematodirus) may still use a white drench in early spring for *Nematodirus* control, or a farm with multiple-resistance may use narrow-spectrum products containing closantel to target *Haemonchus* at certain times of the year.

Avoidance strategies (chapter 2. SCOPS Principles, section 2.4 Reduce Dependencies, Pasture based assessments pasture based assessments)

Changes to the production system (e.g. lambing date, introduction of creep feeding, rotational grazing or lower stocking densities) may be necessary as a means of avoiding high levels of challenge and/or pasture contamination. By planning in advance, pasture can be managed to avoid infection and reduce the need for anthelmintic treatments (e.g. making use of new leys, crop/livestock rotations, rotational grazing, mixed grazing, and pasture contamination/risk mapping).

Genetic improvement (chapter 2. SCOPS Principles, section 2.4 Reduce Dependencies, Pasture based assessments pasture based assessments)

Introduction of new genetics, to increase the sheep's ability to resist worms, and selecting for nematode-resistance or nematode-resilience in replacement sheep could form part of a longer-term strategy to reduce infection levels on farm and reduce the need for anthelmintics. For example, selecting for individuals that shed fewer nematode eggs (of all species) can help reduce overall pasture contamination. Selecting for resilience may also become more important, but its role in controlling *Haemonchus contortus* is still unclear.

Adjust targets

Expectations may have to be actively managed – i.e. it may be necessary for the farmer to realise that even if it is possible to control the parasites sufficiently to maintain good welfare standards, productivity may still be reduced. In some situations, the most appropriate strategy to cope with multiple resistance is working towards finishing lambs earlier (at a lighter weight), or selling them as stores, to remove them before the buildup of pasture contamination. Adviser involvement is essential in the evaluation of the economics of continuing the sheep enterprise, given the limitations multiple resistance will impose.

Make use of new actives (Chapter 4. Anthelmintics, section 4.1 Broad Spectrum, Using Groups 4-AD and 5-SI)

The use of both the 4-AD product and the 3-ML/5-SI dual-active products is essential, but it is imperative that they are integrated into the farm heath plan/strategy rather than simply used as substitutes for the original three groups. If there is good knowledge of the AR status, worm genera involved and regular monitoring, the high level of efficacy of these new compounds can be used to prolong the life of the existing products where the frequency of resistant worms is not too high.

Use of the existing actives sequentially

The principle of using two actives together (such as is recommended for quarantine, chapter 2. SCOPS Principles, section 2.3 Quarantine)v is a recognised technique for increasing efficacy compared to that

of either active used alone. If this technique is to be used for nematode control, other than in the quarantine situation, it must be under the strict guidance of an experienced veterinary surgeon. Each of the actives must be given at their full dose and they must be administered to the sheep separately (i.e. sequentially and via different equipment), **never mixed**. The administration of more than one active is a last resort strategy that must only be used on farms where there is full adherence to SCOPS principles, with responsible monitoring and management of anthelmintics and full knowledge of the farm AR status.

What is the rationale behind the use of two different actives?

Because each class of anthelmintic has a discrete mode of action it is expected that the mechanisms for resistance will also be separate. If this is true, then the likelihood of a single individual worm carrying the appropriate genetic mechanisms for resistance to two compounds is lower than having the mechanisms to both. Therefore, if two distinct mode of action anthelmintics are administered, it would be expected that if one is less effective, the second will add to the kill rate.

Interactions (efficacy) between two compounds can be additive:

The following example illustrates the situation for a sheep which has 1000 worms and when Anthelmintic A is 80% effective and Anthelmintic B is 90% effective:

- Anthelmintic A = 80% effective leaves 200 alive worms of the original 1000
- Anthelmintic B = 90% effective kills 180 of the surviving 200 worms, to leave a total of 20 worms
- Therefore A + B = 98% efficacy (20 worms from 1000 worms)
- The additive effect is 98% efficacy