Popular Article

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Detection of Anthelmintic Resistance in Livestock

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Resistance to anthelmintics has been most frequently recorded in sheep and horses, and has generally involved the benzimidazoles group of compounds. In sheep it has been most frequently reported from areas where *Haemonchus* spp. abound and the annual cycles of infection and anthelmintics treatment are numerous. This resistance or tolerance as it is frequently called, may be incomplete and can then be overcome by using higher dosage rates. Cross-resistance within chemical groupings has been reported and less frequently multiple resistance involving different chemical groups. Most reports of resistance refer to gut nematode species in sheep.

Several factors may predispose the development of drug resistance, such as regularly using anthelmintics below their recommended dose, continued reliance upon a single type of anthelmintics or excessive and indiscriminate treatment of animal. Increasing the dose of a 'resistant' compound will temporarily affect a cure until worms become resistant to that dose too.

In the absence of completely novel anthelmintics entities, the best control measures are to minimize the frequency of dosing to alternate treatment between different classes of anthelmintics or take advantage of the prophylaxis offered by slow-release rumen devices and especially to make full use of clean pastures.

Testing of Anthelmintic Drugs

Initial screening of compounds for anthelmintics activity is usually carried out in laboratory species, principally rats and mice for reasons of cost and convenience and also because usually only very small quantities of such compounds are synthesized. *Nippostrongylus* spp. infection in the rat, *Nematospiroides dubius* and *Syphacia obvelata* in the mouse and *Ascaridia* spp. in chickens are common screens for efficacy against gastrointestinal

parasites. In vitro screening tests have been developed. Early attempts used free-living stages of trichostrongylids and more usefully, in vitro culture systems of parasitic stages of trichostrongylids, have been utilized systems using entirely free-living nematodes have also been described. Many compounds showing activity against free living nematodes however have little effect on parasitic species and such a screen at extremely high concentrations only detects some active compounds. One further problem with in vitro screens is that prod drugs, which are themselves inactive but which are metabolized to active metabolites in the host, may possibly be missed. Unless the metabolic pathway is similar in rodents and in the target species, prod rugs may also be missed in the rodent screens. Drugs warranting further investigation after preliminary screening are then evaluated in the target species using a number of tests.

1. **Critical Tests**

Critical testing involving collection and counting of all worms passed in the faeces of infected animals for a period of days after treatment with the anthelmintics. The animal is then either slaughtered and all remaining worms counted or less commonly, may be treated with an anthelmintics drug of proven efficacy and further worm expulsion noted.

Efficacy in terms of percentage of total worms expelled can then be calculated. It is advisable to collect faeces from untreated control animals at the same time, as worm expulsion can occur for reasons other than anthelmintics treatment. Critical tests are extremely time consuming and are really only applicable for parasites of the small and large intestine, since parasites passing the whole length on the intestinal tract tend to be digested and therefore missed.

2. **Controlled Test**

In controlled testing, two groups of animals are similarly infected. One group is then treated with the rest drug, while the other group is left untreated. After a suitable interval, both are killed, the wonns are counted and the percentage efficacy is calculated trom the difference in burdens of treated and control animals. If single inoculations of infective larvae are used rather than trickle infections or naturally acquired infections, the time of treatment can be varied in order to assess anthelmintics activity against different larval stages, killing is carried out after sufficient time has elapsed for surviving larvae to become adult. Controlled tests are preferred to other tests.

3. **Faecal Egg Counts**

Faecal egg counts of infected animals both before and after treatment have been widely used as an indicator of anthelmintics efficacy. Their value in the testing of new drugs is limited for the following reasons:

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1. Drugs may suppress egg production by the worms without killing them.
2. They give no information about the effect of the drug on immature stages.
3. Faecal egg counts are not a reliable indicator of the size of worm burden.
4. They are of greater value in assessing the value of the drug in field outbreaks of parasitic disease.

4. Tests for Arrested Larvae:

For anthelmintics to be evaluated against arrested larval stages, testing must be carried out under conditions that favour the arrest of a high percentage of ingested larvae. This may be done using naturally acquired infections at a specific time of year or using experimental infections where the infective stage has been exposed artificially to conditions likely to cause arrested larval development in the host.

5. Tests for Ovicidal Activity:

Ovicidal activity may be evaluated in vitro by the egg-hatch test as described by Coles and Simpkin (1977). Nematode eggs from fresh (within 4 hours of leaving the host) Faecal samples are incubated *in vitro* in contact with the drug. The percentage of eggs embryonating in the presence of the drug is compared with that of control (no drug). Final demonstration however, must be made by assessing the potential infectivity of eggs passed by treated animals, as some drugs (e.g., Oxfendazole) are ovicidal in animal studies but not in the *in vitro* test. Once a drug has been evaluated by controlled studies in both artificial and naturally acquired infections, the optimum dosage regimen decided and basic toxicological testing done it is then evaluated in, the field in outbreaks of disease and in control programs.

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