Management and Control of Nematode Parasites of Small Ruminants in the Face of Total Anthelmintic Failure

P. J. Waller
Department of Parasitology (SWEPAR), National Veterinary Institute
SE- 751 89 Uppsala, Sweden
Email: Peter.Waller@sva.se

Abstract

Total failure of modern broad spectrum anthelmintics to control nematode parasites of sheep and goats is a reality, of rapidly increasing dimension, on many farms in the tropical / subtropical regions of the world. This is primarily associated with the highly pathogenic, blood sucking parasite, *Haemonchus contortus,* and where it now cannot be controlled by chemotherapy, annual mortalities exceeding 20% of the flock can be expected. Thus sheep and goat enterprises become totally unsustainable, unless major changes in management are effected. These must include a change away from reliance on suppressive anthelmintic treatment and to include several non-chemotherapeutic management options. In situations where livestock numbers need to be preserved and there is no opportunity to increase the grazing area available, then zero grazing with cut-and-carry herbage from uncontaminated pasturelands is the only option. In other circumstances stocking rates need to be substantially reduced, so that short-term rotational grazing can be effectively practiced. This strategy is improved if it is combined with the biological control of the free-living stages of the parasites, using the microfungus *Duddingtonia flagrans*. Monitoring the parasitological status of the animals by faecal sampling sentinel sub-flocks for nematode faecal egg counts, or the use of the FAMACHA procedure, are also valuable tools. Improving overall nutrition of the flock is an important adjunct to control. As a long-term priority, attempts to change the genotype of the flocks to those breeds that have been shown to possess natural resistance to *H. contortus* are worthwhile.

INTRODUCTION

Recently, an exhaustive review was commissioned to prioritise animal health research for poverty reduction in the Developing World, by an international donor consortium consisting of the WHO, OIE, FAO. This report concluded that gastro intestinal parasitism had the highest global index as an animal health constraint to the poor. The highly pathogenic nematode parasite of small ruminants, *Haemonchus contortus*, was singled out as being of overwhelming importance (Perry *et al.* 2002). This blood-sucking parasite is responsible for acute outbreaks with mortalities, particularly in young animals. In Kenya alone, it has been estimated that it causes losses in the order of US$ 26 million each year (Anon. 1999). It is probably the only nematode parasite of sheep and goats that can be accurately diagnosed without the aid of laboratory testing. Signs of acute anaemia are obvious, past history (particularly weather conditions) and discounting other less common conditions that cause anaemia (eg. fasciolosis, theileriosis etc.), will strongly suggest clinical haemonchosis. This parasite has very high biotic potential (egg production by female parasites) and at times when transmission of this parasite is favoured (warm and wet), losses can occur in all classes of animals. On a "worm-for-worm" basis, *H. contortus* is generally considered the most pathogenic parasite of small ruminants (Soulsby, 1986). Although it occurs in mixed infections with other nematode parasites, it invariably dominates the faecal worm egg counts and often approaches 90% of worm egg contamination on pastures under prevailing conditions of high temperature and humidity, which are the norm in the humid tropics / sub tropics.

However it is now apparent that *H. contortus* is becoming more important in the temperate regions of the world, with the apparent change in weather conditions that favour this parasite (Waller *et al.* 2004). Thus much of the problems associated with parasite infections in small ruminants, problems in their control and problems of anthelmintic resistance, relate specifically to this single species of nematode parasite. Detailed economic evaluations repeatedly show that the major losses due to parasites are on animal production, rather than on mortality (Anon. 1991; McLeod 1995). In many instances, these costs exceed the costs of losses due to the major "killer" diseases due to viruses and bacteria (Anon. 1991). Recent estimates of the annual costs of parasites to the sheep industry in Uruguay and South Africa were US$ 41.8 million (Nari *et al.* 1997) and US$ 45 million (I. K. Horak), respectively.

WORM CONTROL: PRINCIPLES AND PRACTICES

The severity of nematode parasitic disease is dictated by the degree of larval pickup, or challenge, from pasture. This is principally determined by the prevailing weather conditions, namely temperature and rainfall. If either of these environmental variables is unfavourable (ie. temperature and/or humidity is too low) then discontinuities in the translation process from egg hatch to infective larval availability on pasture, can occur (Levine 1963). Thus, both temperature and rainfall are important parameters controlling this process in the temperate regions of the world, whereas in the tropics / subtropics, rainfall is the only limiting environmental variable because temperatures are always high enough to facilitate this process. Consequently, in the humid tropics / subtropics, the environmental conditions on pasture are favourable, more-or-less continuously. Whereas in the temperate regions there are often times when "bottlenecks" occur in the larval translation process, which not only reduce larval pickup, but also can be exploited in parasite control programmes (Waller *et al.* 1995).

In contrast to the livestock systems of the temperate regions, where varying degrees of winter housing and /or zero grazing are practiced, ruminant livestock production in the tropics / sub tropics is characterised by all year round grazing on pasture. Thus larval pickup from pasture is more-or-less continuous and all livestock are likely to be infected. Whilst livestock owners in many countries of the tropics / subtropics, lack the financial resources, knowledge, or the will, to treat their animals with drugs, there are also many countries in this region where quite the opposite is the case. In many regions in the tropics / subtropics communal grazing is the norm. Thus there is little, or no, opportunity of individual farmers to practice any form of parasite control, unless there is widespread compliance to the same practices by the whole community.

Anthelmintics: failure and the future?

For livestock producers that can afford it, control of nematode parasites has been based on the use of anthelmintic drugs. However, since the early 1960's there have been only three major classes of broad-spectrum anthelmintics commercially released for the control of nematode parasites of ruminant livestock, namely: the benzimidazoles / probenzimidazoles (BZs), the tetrahydropyrimidines /

imidazothiazoles (most important drug being levamisole: LEV), and the macrocyclic lactones (MLs), or avermectins /mylbemycins. Although there are novel classes of anthelmintic drugs that have been discovered (eg parahequamide, cyclooctadepsipeptides), possibly the greatest constraint in their commercial development are the enormous costs involved (Waller 1997). The international pharmaceutical industry is undergoing unprecedented re-structuring with resultant company mergers and the reorganisation of product portfolios. Apart from the lucrative companion animal and horse market, it is evident that veterinary drugs have been a victim of these "down- sizing" activities. Simply it is a matter of economics. There is more money to be made in human pharmaceuticals – even the cosmetic industry – than providing new drugs for the grazing livestock industries. Therefore, it seems to me to be unlikely that a new anthelmintic drug (class) for use against nematode parasites of food producing domestic livestock will be released onto the market place in the foreseeable future.

Because of the clinical importance of *H. contortus,* and the very high efficiency of the broad spectrum anthelmintics against this parasite (at least in initially), the concept of suppressive drenching of sheep and goats became firmly entrenched in many countries of the tropics / subtropics where this parasite is endemic. Frequent (every 4 – 6 weeks), and often haphazard treatment became commonplace. This has become much more the case since patent protection of all the currently available broad-spectrum anthelmintics has lapsed, resulting in a burgeoning in the marketing of generic anthelmintic products. Quality assurance was an absolute pre-requisite for the parent companies, but now they have to compete on the deregulated market against companies with these "look alike" products. On the face of it, this outcome for the farmers seems to be favourable, with not only a greater range, but also much cheaper products, becoming available. However, many instances of poorly manufactured, or counterfeit, generic products have been reported. This is particularly so in the developing countries, which cannot provide the resources to monitor product quality and to prosecute offenders (Wanyangu *et al*. 1994; Waller *et al.* 1996). Also, as a result of this unfair competition, there are instances of highly reputable companies marketing substandard products in this region of the world (van Wyk *et al*. 1995). Thus in most instances, freeing-up the anthelmintic market in the tropics / subtropics has not been in the farmers best interests. As poor quality products assume a significant market share, then not only do the farmers waste their money, by failing to control parasites in their animals, but they hasten the selection process for anthelmintic resistance.

Recently, the World Organisation for Animal Health (Office International des Epizooties: OIE) commissioned a survey to determine the status of parasiticide resistance in pests of livestock worldwide (Nari and Hansen 1999). Of the 151 member countries, responses were obtained from 77 (55% response). The parasites considered to be of greatest importance to the livestock in each country were in rank order – worms (73% of respondent countries), ticks, mange mites, flies and lice. Control of these pests was almost entirely by the use of chemicals. Resistance had been diagnosed in 55% of the responding countries. Of these, 86% had diagnosed anthelmintic resistance, 50% ixodicide resistance and 31% insecticide resistance. An important note was that these estimates were considered conservative, as 27% of countries mentioned a lack of capabilities, infrastructure, and/or interest in assessing the significance of these problems.

The examples of anthelmintic resistance in nematode parasites of ruminant production systems would form, more-or-less, a uniform gradation along the spectrum from no problem to total failure, which is continuously changing for the worse. The first reports of total chemotherapeutic failure across the entire range of broad-spectrum anthelmintics, was made in 1983 (pre - marketing of MLs) on goat farms in north coastal NSW, Australia, which experienced high levels of summer rainfall (Anon. 1983). Subsequently, van Wyk (1990) cited a number of instances in the high rainfall, or irrigated areas, of South Africa where farmers had to abandon sheep farming because of failure to control worms using chemotherapy. Total failure of the BZs and LEV, plus 70% resistance to ivermectin (IVM), the first of the MLs, was reported in a survey of anthelmintic resistance of sheep farms in the humid Oriental region of Paraguay (Maciel *et al*. 1996). Most recently it has been found that total chemotherapeutic failure to all the three broad-spectrum anthelmintic groups (also to the narrow spectrum, salicylanilide drugs) exist on all the large government managed small ruminant breeding farms in the eastern Malaysian state of Sabah (Chandrawathani *et al*. 2004). Coupled with a similar result on a large government breeding farm on Peninsula Malaysia (Chandrawathani *et al.* 2003b), it seems as though Malaysia has the dubious distinction of being able to declare itself the first country where virtually total anthelmintic failure to control internal parasites of small ruminants is present – at least in the large breeding farms, whose main purpose is to supply sheep and goats to small-holder farmers. Thus in the space of approximately 20 years, the situation of virtually total anthelmintic failure has moved from the individual farm, to district, to region, to state and finally to a country problem.

All the above situations share three important features. Namely, they are all located in the humid tropics / subtropics, where conditions are more-or-less continuously wet throughout the entire year, secondly the major nematode pathogen, *H. contortus*, completely dominates the parasite profile, and thirdly sheep and goat raising was/is attempted to be the sole production system. The experience on Sabah, where total anthelmintic failure has likely to have been present for some years, is that annual mortalities exceeding 20% of the flock can be expected (Chandrawathani *et al*. 2004) – totally unsustainable livestock systems by any assessment!

SOLUTIONS IN THE FACE OF FAILURE

However abandonment of enterprises cited above, is not necessarily the only course of action. I believe that even under such environmental conditions where *H. contortus* flourishes, there are a number of options that could be taken to restore a reasonable measure of small ruminant production and if strictly adhered to, should prove to be sustainable.

Immediate strategies

- Most farms where these problems have been reported have very heavy stocking rates. A reduction of the carrying capacity would provide more ease and flexibility to undertake the following measures.
- Attempt to remove resident worm infections. On the face of it, this maybe a difficult task. However other older classes of drugs with known good efficacy against *H. contortus,* which have not been used should be tried, such as the organo-phosphate anthelmintics (napthalophos: NAP), or phenothiazine (PTZ). These drugs, particularly the former, now play an important role in the management of multiple, high level resistance in nematode parasites of sheep in Australia (Dobson *et al.* 2001)
- In those areas where night housing of stock is a feature and sufficient labour is available, break the infection cycle by preventing grazing of pastures for two months by implementing cut-and- carry for shed feeding of all animals. The pastures selected for cutting should be from a location that has been ungrazed

(thus uncontaminated) by small ruminants for the last two months. Ecological studies in the wet tropics have shown that survival of the free-living stages of *H. contortus* is very short, with the majority of infective larvae disappearing from pasture within 4-6 weeks (Banks *et al.* 1990; Sani and Chandrawathani 1996).

Short term strategies

- Implement and strictly adhere to the short-term rotational grazing strategy, as developed for parasite control in small ruminants in the wet tropics (Barger *et al.* 1994; Sani and Chandrawathani 1996). This requires the subdivision of available pastures into small plots. Animals are then moved around these pastures in quick succession (3 - 4 days grazing only on each plot), returning to their original plot after approximately 30 - 40 days.
- Monitor faecal egg counts on a regular (initially every 4-6 weeks) basis in a sentinel group of young sheep.
- Utilise the FAMACHA system of monitoring presence of anaemia (indirect measurement of *H. contortus* infections) and treat accordingly (Malan and van Wyk, 1992)
- Introduce molasses/mineral feed blocks to improve the general nutrition of the animals. Trial the use of medicated (fenbendazole: FBZ) blocks for one grazing cycle (4 weeks) every 6 months. Previous work has shown that by using a benzimidazole anthelmintic to which resistance has developed, from non-persistent (oral drench) to persistent (daily administration in a feed block) use, can restore anthelmintic efficiency (Knox 1996).
- Consider using biological control with the micro-fungus *Duddingtonia flagrans.* This has been shown to be a useful adjunct to worm control of sheep and goat parasites on Peninsula Malaysia (Chandrawathani *et al.* 2002; 2003a).

Longer term strategies

- Where appropriate and as a long-term priority, attempt to change the genotype of the sheep to those which have been shown to have natural resistance to *H. contortus* infections, such as the Red Maasai, Barbados Black Belly, St. Croix, Florida native sheep (for review Baker 1996).

CONCLUSION

This review focuses on the possible ways forward for owners, or managers, of small ruminant production systems where chemotherapeutic options to control nematode parasites have been exhausted. Whether they abandon such farming enterprises, or attempt to ameliorate the problem, one thing is certain they cannot persist - simply for economic reasons. There are instances where the former option has been taken. In such cases, consigning all animals to the slaughterhouse should occur. This represents a “dead end” for the both the hosts and their parasites. However what often happens is that these animals are sold to other farmers, who unsuspectingly import multiply resistant parasites onto their farm. Such is the case also where government farms pass sheep and goats on to small-holder farmers. It is very important that veterinary advisers are made aware to the problem of anthelmintic resistance in the tropics sub/tropics and aim to prevent this from occurring. Correct diagnosis is important, based clinical signs, history and particularly on faecal nematode egg counts, both pre and post-anthelmintic treatment. In many cases when animals are suffering with “ill thrift”, or diarrhoea, nutritional inadequacies rather than internal parasites is the problem.

However there are alternative solutions to restore parasite control in what appears to be a disastrous situation, but these are not simple or straightforward. They depend on a combination of strategies, none of which will be fully effective if solely relied upon. Such integrated approaches to nematode parasite control in small ruminant livestock are the only way to ensure that reasonable levels of control will occur for the foreseeable future.

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