Article available at http://www.parasite-journal.org or http://dx.doi.org/10.1051/parasite/2007141003

TRENDS AND CHALLENGES IN THE EFFECTIVE AND SUSTAINABLE CONTROL OF *HAEMONCHUS CONTORTUS* INFECTION IN SHEEP. REVIEW

GETACHEW T.*, DORCHIES P.** & JACQUIET P.**

Summary:

Haemonchosis, with its very wide distribution, has become a very important production constraint in sheep farms in tropical, subtropical and temperate regions worldwide. Various intrinsic and extrinsic factors determine the survival of *Haemonchus contortus* and hence the development of the disease in the animal. In general, control of gastrointestinal nematode infestation in sheep relies heavily on anthelmintic treatments. However, the indiscriminate use of these drugs has led to the widespread emergence of drug resistant strains of parasites, that has necessitated the development and use of various parasite control methods such as grazing management, biological agents and vaccines and the selection of resistant breeds of animals, with or without moderate use of anthelmintics. The ultimate goal of such control programs is to enhance productivity, while minimising risks regarding drug resistance and consumer and environmental concerns. This review attempts to highlight the different methods employed in the control of haemonchosis in sheep and the practical limitations associated with both control programs and the internal and external factors associated with the parasite and its microenvironment.

KEY WORDS : *Haemonchus contortus*, sheep, anthelmintic, biological control, breed resistance.

Résumé : MOYENS DE LUTTE CONTRE *HAEMONCHUS CONTORTUS* CHEZ LE MOUTON. REVUE BIBLIOGRAPHIQUE

*L'hémonchose est une infestation parasitaire très répandue chez les petits ruminants et est un facteur limitant important de la production aussi bien dans les régions tropicales que subtropicales, voire tempérées. Divers facteurs intrinsèques ou extrinsèques déterminent la survie d'*Haemonchus contortus *et donc l'épidémiologie de l'infestation. La lutte contre les nématodoses gastro-intestinales du mouton repose principalement sur l'emploi d'anthelminthiques. Cependant, leur emploi à grande échelle a abouti au développement de résistances qui obligent à recourir à d'autres méthodes de lutte par la gestion du pâturage, par l'utilisation de champignon nématophage, ou par la sélection de souches ovines naturellement résistantes à* H. contortus. *L'objectif de ces moyens de contrôle est d'augmenter la productivité, tout en limitant les risques de résistance et les risques potentiels pour l'environnement ou les consommateurs. Cette revue présente les différentes méthodes utilisées pour la lutte contre l'hémonchose et souligne leurs limites, en particulier dans la pratique de l'élevage.*

MOTS CLÉS : Haemonchus contortus, *mouton, anthelminthique, contrôle biologique, race résistante.*

INTRODUCTION

While in temperate regions, the severity of gastrointestinal (GI) parasitic diseases in most livestock farms is now minimised through the seasonal use of anthelmintics and pasture management, the problem still persists in the vast majority of tropical and subtropical regions. Among the GI parasites, *Haemonchus contortus* is the species with greatest pathologic and economic importance. This nematode is a blood feeding abomasal parasite of sheep and goats but can circulate in other ruminant species such as cattle and reindeer (Jacquiet *et al.*, 1998; Achi *et al.*, 2003; Hrabok *et al.*, 2006). The importance of haemonchosis may be explained by: the parasite's ability to produce large numbers of eggs, which results in extensive pasture contamination; the blood-sucking nature of the nematode that causes variable degrees of anaemia, loss of production and mortality in lambs and kids in situations where few or no control measures are used; and its ability to survive adverse climatic conditions through hypobiosis (Gatongi *et al.*, 1998; Waller *et al.*, 2004). The nature of the parasite, host genetic and physiological factors, as well as environmental determinants, greatly influence the degree of infestation and thus appropriate control strategies.

For many years, several methods have been used to reduce the threats resulting from gastrointestinal nematode infestations in general, and haemonchosis in particular, in small ruminants. The use of anthelmintics is the most extensively employed method of control of GI nematodes. However, because of such reasons as emergence of drug resistant strains and problems related to drug residues in food of animal origin and ecotoxicity, a significant amount of research is focusing

* Addis Ababa University, Faculty of Veterinary Medicine, Debre Zeit. P.O. Box 34, Ethiopia.
** UMR INRA/DGER 1225, Interactions hôtes-agents pathogènes, École Nationale Vétérinaire, 23, chemin des Capelles, 31076 Toulouse, France.
Correspondence: Philippe Dorchies
Tel.: +33 5 61 19 38 61 – Fax: +33 5 61 19 39 44.
E-mail: p.dorchies@envt.fr

on alternative or complementary control measures (De Liguoro *et al.*, 1996; Strong *et al.*, 1996; El-Makawy *et al.*, 2006). This review is intended to highlight some of the control strategies and associated challenges encountered in limiting the effects of haemonchosis in sheep.

FACTORS AFFECTING *H. CONTORTUS* POPULATIONS

Intrinsic factors (the parasite)

As for any disease process, the parasite, the environment and the host are in a dynamic interaction, the outcome of which depends on various determinants. *Haemonchus contortus* is a highly prolific, blood-feeding parasite with various strategies to escape adverse climatic conditions and immune reactions of the host. A mature female can produce 5,000-7,000 eggs per day while *Trichostrongylus* species produce only 100-200 eggs per day (Coyne *et al.*, 1991a, b). This allows *H. contortus* an advantage over other parasites in that it can easily contaminate grazing areas and may survive in its small ruminant hosts through frequent and rapid reinfestations. Variations in the degree of infectivity of different *H. contortus* isolates have already been documented. A comparison in infectivity between *H. contortus* isolates from France with those from the West Indies (Guadeloupe island) in two breeds of sheep, namely the Black Belly and the INRA 401, has shown that the latter (sympatric isolate) established better than the former (allopatric isolate) in the Black Belly (Aumont *et al.*, 2003) suggesting that it is important to take into account parasite genetic diversity in different agro-ecological zones.

After being ingested, the infective stage (L3) successively moults to L4 and L5 (immature adult) and then matures to the adult stage in the abomasum. With the exception of the L3, all other stages of development feed on blood resulting in a variable degree of anaemia which results not only from the blood consumed by the parasites but also due to haemorrhage after the parasites detach from their feeding sites. *H. contortus* is known to produce calcium and a clotting factor binding substance known as calreticulin (Suchitra & Joshi, 2005), enabling the parasite to feed easily on host blood and in so doing, cause haemorrhagic lesions. Studies of field parasitism and experimental larval infestations have also identified the morphological and physiological effects of abomasal nematodes: nodule development, mucous cell hyperplasia, superficial epithelial damage, reduced acid secretion and increased serum gastrin and pepsinogen concentrations (Simpson, 1997; Scott *et al.*, 1999). When both internal and external conditions are favourable, the pre-patent period for *H. contortus* in sheep is between two and three weeks. However, in extreme degrees of temperatures and relative humidity, the L4 stage may enter into a phase of arrested development or hypobiosis (Reinecke, 1989; Urquhart *et al.*, 1996, Miller *et al.*, 1998). Hypobiosis usually follows the onset of cold autumn/winter conditions in the northern hemisphere (Waller *et al.*, 2004) or very dry conditions in the subtropics and tropics (Gatongi *et a.*, 1998). This might be an environmental stimulus received by the free-living infective stages prior to ingestion by the host, or it could be an evolutionary parasitic adaptation to avoid adverse climatic conditions for survival of the free-living stages by a significant number of parasites remaining as sexually immature stages in the host until more favourable conditions return. Furthermore, Jacquiet *et al.* (1995) also demonstrated that in some extreme climatic conditions, such as in the desert areas of Mauritania, adult *H. contortus* were capable of surviving for up to 50 weeks in the host which guaranteed the perpetuation of the species from one wet season to another.

Extrinsic factors

The environment

Factors including temperature, rainfall, humidity and vegetation cover, influence patterns of parasite development (Coyne *et al.*, 1992; Krecek *et al.*, 1992; Tembely *et al.*, 1997). In most tropical and sub-tropical countries, temperatures in the environment are permanently favourable for larval development. The ideal temperature range for larval development of many nematode species in the microclimate of the pasture or vegetation is between 22 and 26°C while the optimal humidity is close to 100 %. Desiccation from lack of rainfall kills eggs and larvae rapidly, and is the most lethal of all climatic factors. Wet seasons favour the growth of vegetation which in turn attracts grazing sheep and goats leading, not only to further contamination of pasture, but also providing an opportunity for the existing infective larvae to encounter their favourite hosts. By pasture larval assessment in Ghana (Agyei, 1997) and by the use of tracer lambs in Kenya (Wanyangu *et al.*, 1997), it was found that very few or no *H. contortus* infective larvae were available during dry periods while numbers of larvae were high in the rainy seasons and shortly after. Under optimal conditions (high humidity and warm temperatures), the developmental process for *H. contortus* requires about 7-10 days while in cooler temperatures it may be prolonged. In experiments where larvae were cultured from faecal material under ideal laboratory conditions, only 24 to 44 % of the eggs were found to develop to the third larval stage, 10 to 25 % of the eggs did not hatch after 10 days of incubation while 40 to 55 % of the eggs were assumed to be non-viable (personal observations). Below 5° C, movement and metabolism of L3 is minimal favouring prolonged survival as these larvae are enclosed in a double sheath and thus unable to feed to continuously renew their energy.

Nature of the host

• Host breed and immune status

The pre-patent period of *H. contortus* can vary according to the breed and age of infested hosts. Evidence from different experimental infestations have already demonstrated that the first *H. contortus* eggs appear in the faeces of the susceptible INRA 401 breed of sheep, as soon as days 17 and 21 post infestation, instead of 21 and 28 days in the resistant Black Belly breed (personal observation). Though it is still not clear how natural selection might shape patterns of immuno-responsiveness in terms of type and strength of response, different breeds of sheep express different susceptibility to gastro-intestinal parasitic infestations. In this respect, the Santa Ines (Amarante *et al*., 2004), Barbados Black Belly (Aumont *et al*., 2003; Gruner *et al*., 2003) and Texel (Good *et al*., 2006) breeds of sheep appear to be more resistant to infestation with *Haemonchus contortus* compared with Suffolk and Ile-de-France, INRA 401, and Suffolk breeds respectively. This was shown by reductions in faecal egg count (FEC) and/or worm number, slower worm development and reduced fecundity. Genetic variations in the resistance to *H. contortus* within sheep flocks have also been demonstrated and used in breeding schemes in Australia (Albers & Gray, 1987; Woolaston & Baker, 1996). The development of immunity to gastrointestinal (GI) parasitic infections appears to depend on the host's ability to mobilise both cellular and humoral immune effectors locally at the site of infection and systemically in the blood circulation. *Haemonchus contortus* infestation in sheep is known to elicit a Th2-polarised immune response characterised by Th2 cytokines (Lacroux *et al*., 2006), the recruitment of higher number of eosinophils, mast cells and globule leucocytes (Balic *et al*., 2000, 2006) and the development of local and circulating antibody responses (Schallig *et al*., 1995; Gòmez-Muñoz *et al*., 1999).

• Host age and sex factors

In addition to genetic factors, animals of different ages and sex respond differently to parasitic infections under similar management conditions. Young animals are generally more susceptible to parasitic diseases than mature animals. It is believed that the lower resistance to disease in young ruminants is partly due to immunological hyporesponsiveness, and is not simply a consequence of their not having been exposed sufficiently to pathogens to develop immunity (Manton *et al*., 1962; Colditz *et al*., 1996). Innate immunity, often age-related, is also considered important in many cases. This may be due to physico-chemical differences in the gut environment in adult, compared with young hosts (Mulcahy *et al*., 2004). In four, 12 and 16 months old Black Belly sheep that have never been exposed to helminth infections, we have observed that *H. contortus* faecal egg excretion following primary exposure was markedly affected by the age of the animals, which was in turn strongly associated with an age-dependent increasing level of blood eosinophilia (unpublished observations). The contribution of the stress associated with weaning in delaying the development of protective immune responses to *H. contortus* and *T. colubriformis* has been documented (Watson & Gill, 1991). On the other hand, previous exposure to *H. contortus* infestation could result in enhanced resistance to subsequent homologous infestations. Gauly *et al*. (2002) for Rhön and Merino land lambs, Aumont *et al*. (2003) for Black Belly and INRA 401 lambs, and Gamble & Zajac (1992) for St. Croix and Dorset lambs, reported that animals infested for the second time have demonstrated better resistance. This may be due to the alteration of immunological and physicochemical mechanisms that even though incapable of controlling the primary infection, is nevertheless able to influence the challenge infection.

The phenomenon of the peri-parturient rise (PPR) in nematode egg output is also of great importance in the epidemiology of GI nematodes of sheep. A temporary loss of acquired immunity to *H. contortus* at around the time of parturition and during lactation has been associated with a marked increase in faecal egg count in ewes. Woolaston (1992), Romjali *et al*. (1997) and Tembely *et al*. (1998) have reported that the PPR in FEC started two to four weeks before lambing and continued into lactation in the post-parturition period. This may be related to increased susceptibility to new infestations and enhanced prolificacy of female parasites arising from stress associated to pregnancy, increased milk production and nutritional factors. The inhibition of immunity during lactation places the ewes at a greater risk of parasitic disease and production loss. A significant reduction in haematocrit and serum albumin concentration in post-parturient ewes that had been experimentally infected with *H. contortus* has been reported (Thomas & Ali, 1983). Furthermore, the PPR in FEC could also contribute to increased pasture contamination. Hence, animals in such a physiological state require special attention in order to avoid losses.

• Nutritional status

There is substantial evidence for a beneficial role of a good plane of nutrition in the resistance or resilience of sheep to GI nematode infections. According to Coop and Kyriazakis (2001), nutrition can influence the development and consequences of parasitism in three different ways: 1) it can increase the ability of the host to cope with the adverse consequences of parasitism (resilience); 2) it can improve the ability of the host to contain and eventually to overcome parasitism (resistance) by limiting the establishment, development and fecundity of the parasites; and/or 3) it can directly affect the parasite population through affecting the intake of certain antiparasitic compounds. Haile *et al*. (2004) have demonstrated that parasitic infestation adversely reduced dry matter intake and apparent digestibility in Menz and Horo breeds of sheep and that these were improved by high quality feed supplementation such as cotton seed cake and urea-molasses mixtures. Similarly, highly metabolizable protein diets have been shown to increase resistance of Ile-de-France and Santa Ines lambs against *H. contortus* (Bricarello *et al*., 2005). Well-fed animals can withstand the harmful effects of GI parasitism, can remain reasonably productive and may require less anthelmintic treatments when compared with undernourished animals (Knox *et al*., 2006). The major problem in this respect is that haemonchosis is more prevalent in regions where animal feed resources are very scarce and/or improperly managed and therefore insufficient to satisfy the demand throughout the year.

CONTROL OF HAEMONCHOSIS AND ITS CHALLENGES

The aim of most parasite control strategies is not to totally eliminate the parasites in livestock, but to keep the population under a threshold, above which it would otherwise inflict harmful effects on the host population (Larsen, 2000). Any parasite control method aimed at minimising a given parasitic population must consider the basic disease determinants briefly described above. The relative success or failure of any control strategies can be judged in terms of immediate and/or long term objectives, the ultimate goal being increase production, minimising risks regarding drug resistance and consumer and environment associated problems. Generally, nematode control strategies can be directed against the parasite in the host and/or in the environment.

TARGETING THE PARASITE IN THE HOST

CHEMOTHERAPY AND CHEMOPROPHYLAXIS

Anthelmintic drugs are commonly used either for prophylactic purposes, in which the timing of treatment is based on a knowledge of the epidemiology, or for therapeutic purposes to treat existing infections or clinical outbreaks. Since the advent of modern anthelmintics, tremendous advances have been made in the use of various preparations for different species of animals against diverse spectrum of parasites. The relative success of these drugs depends on their ease of administration, extension of action after administration and period and/or frequency of application based on the epidemiology of the disease problem. In most cases, anthelmintics are administered *per os* in the form of solution, paste or bolus but some of them can be given *via* other routes. In temperate areas, priority is usually given to strategic treatments rather than to a regular interval dosing with anthelmintics. Animals at risk, such as weaned lambs, are often only treated during the first grazing season. In some arid areas where haemonchosis is a problem, first season animals are treated at least twice during the rainy season, four weeks after the onset of the rains and at the end of the rains (Urquhart *et al*., 1996). An additional treatment at the culmination of the wet season may sometimes be necessary. Various drugs have been shown to be successful (almost 100 %) in eliminating *H. contortus* during their early periods of utilisation, and some still remain effective in different parts of the world (Table I). Hence, in the traditional sense of chemotherapy-chemoprophylaxis, we have probably achieved the maximum effect of what is possible from excellent anthelmintics developed by the pharmaceutical industry since 1960, *i.e.* from thiabendazole through levamisole and morantel tartrate, to more advanced benzimidazoles and to the avermectins and milbemycins (Williams, 1997).

For various reasons, however, the efficacy of such valuable and very effective drugs is endangered. Their long term utilisation, inappropriate handling and underdosage may be some of the reasons for their reduced efficacy and for the increasing development of drug resistance. On the other hand, where these drugs are not easily accessible either because of economic reasons or scarcity of veterinary services, as in most parts of Africa, animals die as a result of acute haemonchosis or develop a chronic form of the disease resulting in

Chemical group	Anthelmintics	Prescribed dose
Imidazothiazoles	Levamisole	7.5 mg/kg (Andrews, 2000)
Benzimidazoles	Albendazole	5 mg/kg
	Fenbendazole	5 mg/kg
	Oxfendazole	5 mg/kg (Mckenna & Watson, 1987)
Macrocyclic lactones (avermectins)	Ivermectin	0.2 mg/kg
	Moxidectin	0.2 mg/kg
Salicylanilides	Closantel	10 mg/kg (Uppal *et al*., 1993)

Table I. – List of some recommended drugs against haemonchosis in sheep (Bowman, 1999).

marked loss of body weight and consequent reduced production. This adds another constraint to the already existing poor production performance of small ruminants in such regions.

Risk of drug resistance

Development of drug resistance by populations of *H. contortus* in sheep and goats to repeated applications of benzimidazoles, levamisole and ivermectin, has already been demonstrated (Table II). In most cases where resistance against various anthelmintics has been reported, closantel remained the only efficient drug available, signalling the urgent need to develop alternative measures. *H. contortus* strains resistant to one group of drugs may also be resistant to other groups, which suggests the existence of multiple resistance to the major anthelmintic drugs currently available. In an experimental study, Waruiru (1997) tested the efficacy of closantel, albendazole, levamisole and ivermectin against ivermectin resistant and susceptible isolates of *H. contortus* in sheep. A very impressive result was obtained where all these drugs were almost 100 % effective against ivermectin susceptible isolates, while only closantel proved efficacious on the ivermectin resistant strain. Further alarming findings were also reported, where such resistance in *H. contortus* was found to be inherited as either dominant or recessive traits. According to Le Jambre *et al.* (2000), a completely dominant autosomal trait governs the resistance of *H. contortus* larvae to avermectin while they suggested that in adult worms the expression of resistance was sex-influenced. On the other hand, resistance to levamisole and benzimidazoles has been reported to be inherited as an incomplete recessive autosomal trait (Sangster *et al.*, 1998) and at least two genetic loci (beta-tubulin genes) are involved (Beech *et al.*, 1994). Highly prolific species such as *H. contortus* with short life expectancy of adult worms have a higher risk of developing diverse resistance-alleles due to spontaneous mutations than the less prolific *T. colubriformis* (Silvestre & Humbert, 2002).

Therefore, if effective parasitic treatment with the existing drugs is to continue, more efficient and strategic dosing regimes must be practiced in order to enhance the efficacy or prolong the useful lives of the currently available anthelmintic compounds. Reduction of feed intake before oral anthelmintic treatment slows ruminant digesta flow and premature drug removal (Ali & Hennessy, 1995), whereas administering the normal dose over several hours rather than increasing the amount of drug (Sangster *et al.*, 1991) prolongs availability. Improved drug delivery systems such as the use of chemicals or physical carriers (salts, oils, etc) that reduce drug absorption and metabolism, and that can specifically direct large quantities of active products to the sites of parasite habitat must be adopted (Hennessy, 1997), but these must be cost effective.

Other treatment methods

Alternative treatment measures such as the use of copper oxide wire particles and medicinal plant extracts have long been used against parasitic diseases with varying apparent success. Briefly, administration of 2.5 to 5 gm of copper oxide wire particles in sheep was shown to reduce *H. contortus* faecal egg counts (Knox, 2002). However, besides its limited usefulness, the use of 4 gm of these wire particles in late pregnancy was reported to threaten the life of multiple born offspring (Burke *et al.*, 2005). On the other hand, plant extracts such as condensed tannins, which are secondary tanniferous plant metabolites, have been found to reduce *H. contortus* faecal egg counts and the number of eggs per female worm in goats (Paolini *et al.*, 2003) and the faecal egg counts, worm number and fecundity of *T. colubriformis* in sheep (Athanasiadou *et al.*, 2000). Similarly, flower extracts of *Calotropis procera* have shown excellent anthelmintic activity against *H. contortus* in sheep (Iqbal *et al.*, 2005). Despite the possible existence of a wide variety of plants species potentially able to control gastrointestinal parasites, the difficulty in the selection of potential candidates and extraction of the active ingredients essential for nematode killing without compromising the health of the animal is still a problem which hinders the development of these resources.

	Country	Anthelmintics	Reference
Africa	Ethiopia	Albendazole, tetramizole, ivermectin	Sissay *et al.*, 2006
	South Africa	Almost all groups	van Wyk *et al.*, 1997
Europe	France	Benzimidazoles, levamisole	Chartier *et al.*, 1998
	Great Britain	Benzimidazoles	Coles, 1998
Asia	Malaysia	Benzimidazoles, levamisole, closantel, ivermectin	Chandrawathani *et al.*, 1999
South America	Argentina	Benzimidazoles, levamisole, ivermectin	Eddi *et al.*, 1996
	Uraguay	Benzimidazoles, levamisole, ivermectin	Nari *et al.*, 1996
Australia	Australia	Benzimidazoles, avermectin	Green *et al.*, 1981 Le Jambre *et al.*, 1995

Table II. – Some examples of drugs to which resistant strains of *H. contortus* were reported in different countries.

WHICH WAY FORWARD?

Anthelmintics are not always available to all livestock breeders. When they are easily accessible, their usefulness is increasingly hampered by the development of drug resistance. At present, there appears to be no new chemical class of anthelmintics with a unique mode of action, and hence the chemical active products that are currently available are all that we are likely to have for the foreseeable future (Hennessy, 1997). One recently discovered compound, emodepside, which inhibits pharyngeal pumping of nematodes via latrophilin-like receptors (Harder *et al.*, 2003), is very expensive and is only in use for limited animal species such as cats.

Every available option should be exploited to minimise anthelmintic usage. The FAMACHA system developed by South African researchers could be one of the best methods for reducing the necessity of regular anthelmintic treatments against *H. contortus* infections of sheep thereby minimising both the risk of the development of drug resistance and the cost of treatment. This method is based upon the management of *H. contortus* infestation in sheep and goats, through the clinical identification of developing anaemia in individual animals within a flock (van Wyk & Bath, 2002). Accordingly, trials over several seasons showed that most sheep under severe *Haemonchus contortus* challenge required no or only one treatment over a full summer season in contrast to the usual repeated medication of all animals in the flock. An important feature of the system is that it is easy to use at all levels of the farming community. The visual appraisal of anaemia is linked to an identification chart; therefore literacy is not a requirement and the system can be applied throughout the moist tropics/subtropics of the world where *H. contortus* is endemic (Waller, 1999; van Wyk & Bath, 2002). However, while applying the FAMACHA system, one should not ignore other important parasite infestations that may or may not be accompanied by detectable anaemia.

Apart from the use of chemical medications in livestock, other measures targeting mainly the environment but the host are also in practice in order to address the problem of drug resistance and to accommodate the trend towards organic farming designed to produce consumer and environmentally friendly animal products.

TARGETING THE MICROENVIRONMENT

Grazing strategies

Alternate grazing of different host species (Barger, 1997) and alternation of grazing and cropping are management techniques that can provide safe pasture and give economic advantage when combined with anthelmintics. Studies in the wet tropical climates of several Pacific Island countries showed that peak larval concentrations of *H. contortus* and *Trichostrongylus* species occurred on pasture about one week after contamination, but fell to barely detectable levels within nine weeks (Banks *et al.*, 1990). Based on these results, a rotational grazing system was designed, that has resulted in a significant reduction in faecal egg counts as well as in the number of anthelmintic treatments needed per year. However, in many parts of Africa, communal pastoral systems do not allow for regulated grazing as a means of lowering exposure to infective larvae on pasture. Growing human populations and livestock densities, coupled with the frequent drought in some regions, necessitate unregulated animal movement in search of green pasture and drinking water (Abule *et al.*, 2005). In spite of such prevailing chronic problems, particularly in most African countries, livestock owners should be informed of the benefits of conservation of the relatively abundant forage and water available during the rainy seasons. This would reduce the increased susceptibility to parasites due to malnutrition and subsequently reduce exposure to parasites during the period when pastures are scarce and animals are obliged to graze very close to the ground, which predisposes them to pick up more parasite larvae. Exploitation of refugia through alternate grazing of cattle and sheep (Barger, 1997), or sheep and goats (Sissay *et al.*, 2006) to reduce pasture levels of infective larvae or dilute populations of drug resistant strains of parasites, could be of great value in any management program.

Biological control: use of fungal spores

This is a method in which biological agents can be used to reduce the populations of parasites either on pasture or in the host and by so doing minimise the frequency of anthelmintic usage. One example of biological control against gastrointestinal nematodes is the use of some species of nematophagous fungi with the potential to reduce nematode larval populations on pasture by using these either as their main source of nutrients or as a supplement to a saprophytic existence. There are a number of reviews on this topic by Larsen (2006) and Waller & Faedo (1996). Two groups of such fungi have been identified: there are predacious fungi which produce adhesive or non-adhesive nematode-trapping structures and endoparasitic fungi that infect nematodes or their eggs. Among the endoparasitic fungi, those reported to infect *H. contortus* are *Drechmeria coniospora* and *Harposporium anguillulae* while *Arthrobotrys oligospora* and *A. robusta* are predacious fungi of different species of *Haemonchus* (Larsen, 2000). A significant breakthrough in this area was reported by a number of studies using the species, *Duddingtonia flagrans* (Waller *et al.*, 2001; Fontenot *et al.*, 2003; Chandrawathani *et al.*, 2004; Paraud *et al.*, 2005). This predacious fungus produces three dimensional sticky networks, which tightly traps free-living nematode larvae in the faeces ultimately resulting in their death.

Unlike difficulties associated with the use of other species of fungi, several authors have reported the successful passage of *D. flagrans* chlamydospores in the faeces of sheep after oral drenching (Larson, 2000). Despite its appreciable degree of efficacy, this method of parasite control is still not widely applicable. This may be attributed largely to the requirement for continuous oral or in-feed dosing with fungal spores to achieve the desired level of efficacy (Terrill *et al.*, 2004; Paraud *et al.*, 2005). Also the chlamydospores have a relatively short shelf life (less than one week) in a moist environment, which enables the fungal spores to start to germinate and become vulnerable to degradation during their passage through the animal host (Larsen, 2006).

IMPROVING HOST RESISTANCE

VACCINATION

Control of gastrointestinal parasites by vaccination has been a long-term objective of many parasite research programs. Ideally, vaccines should have a high efficacy and be commercially viable for their proposed use in the livestock sector. A number of GI nematode proteins have been tested as potential vaccine products. In general, these molecules have been divided into two categories. Those termed "natural antigens" or "conventional antigens" are recognised by the host during an infection and are targets of the naturally acquired immune response; the molecules, which are normally not recognised, or which do not induce an immune response during a natural infection but which may serve as targets of the immune response generated against them, are termed "concealed" or "hidden" antigens (Klei, 1997). Natural antigens are constituted mainly of worm surface antigens or excretion/secretion products. Vaccines for *H. contortus* based on natural antigens can generate some level of protection which, although likely to significantly reduce pasture contamination, may not be sufficient to protect young lambs from severe haemonchosis (Newton, 1995).

The majority of concealed antigens of GI parasites described so far are components of epithelial cell surface membranes of the digestive tract of *Haemonchus contortus*. Antibodies directed against these molecules following immunisation and ingestion of blood by the parasites, have proven to be effective in reducing worm burdens (Jasmer & McGuire, 1991; Smith, 1993). In these early studies, a serum transfer experiment suggested that the effector mechanism was serum antibody which bound to the brush border membrane of the parasites intestinal cells; sheep that had acquired immunity to previous *H. contortus* exposure did not recognise the gut membrane proteins, suggesting that these are normally hidden from the host. A more comprehensive review on gut-associated membrane antigens is given by Knox & Smith (2001). One of these molecules, H11, is a 110-kDa integral membrane protein expressed on the intestinal microvilli of the parasitic stages of *H. contortus* and homologues have been identified in *Teladorsagia circumcincta* (Smith *et al.*, 2001). This molecule has been cloned and characterised as an aminopeptidase localised in the brush border of the epithelial cells. The H11 vaccine is apparently effective in all age groups of sheep and against different isolates of *H. contortus* (Jasmer & McGuire, 1991; Newton *et al.*, 1995). Other gut associated antigens such as the 1000kDa *Haemonchus* galactose-containing glycoprotein complex (H-gal-GP) and the 46 and 52 kDa (P46 and P52) glycoproteins have excellent efficacy in reducing FECs (Faecal egg count) and worm burdens (Smith *et al.*, 2000). The cDNAs encoding H11 as well as most of the components of H-gal-GP have been expressed in *E. coli* but, unfortunately, none of these recombinant proteins has been reported to be protective (Knox & Smith, 2001).

Regardless of promising results achieved over the years, especially in terms of vaccine efficacy, we are still waiting for the release of a commercial product. However, its haematophagous nature makes *H. contortus* more prone to gut-associated vaccines compared to other GI nematode parasites; the complex nature of its antigens, involving extensive glycosylation, has probably precluded their molecular cloning at a commercial level. Also, the requirement for various adjuvants and repeated injections that could raise the cost of vaccination, have created considerable difficulties in the realisation of GI nematode vaccines (Klei, 1997; Knox & Smith, 2001).

BREEDING FOR RESISTANCE

The other promising angle, both for the developed and the developing livestock sector, is the selection of breeds or lines of sheep for parasite resistance. There is a sizable body of evidence for the existence of genetic variation in resistance to gastrointestinal nematode parasites both between and within breeds (Gray, 1997) and selection for parasite resistance have been successfully demonstrated in Australia and New Zealand (Barger, 1989; *Bisset et al.*, 1996; Woolaston & Baker, 1996). The benefits of such selection arise from the effects of having fewer and less developed worms or greatly reduced faecal egg counts, which in turn leads to a reduced impact on production, a decreased requirement for chemical control and a reduced contamination of pasture by infective larvae. In this respect, although possibly lacking the productivity and performance capacity of their counterparts in temperate regions, a number of indigenous tropical breeds of livestock have the genetic ability to tolerate or resist disease, a potential developed through natural selection. The long term exposure to GI nematodes in endemic areas coupled with their adaptation to harsh environmental conditions and low levels of nutrition have allowed them to survive in the regions in which they exist. Some examples of relatively resistant breeds have already been given in this text, but it is likely that there are many other, as yet untested, breeds. Similarly, within populations of animals genetically determined differences in parasite resistance has been reported (Woolaston, 1992). Such animals may serve as a potential nucleus for selecting *Haemonchus*-resistant sheep. A number of markers such as FEC, worm burden, peripheral eosinophil count and serum antibody level have been used to identify animals with increased resistance to infection (Douch *et al.*, 1996), and the results using FEC as a marker are promising. However, as a selection trait, FEC has practical limitations and its use may incur production penalties through withholding drench treatment for prolonged periods. Furthermore, FEC is also influenced by the level and composition of a natural nematode challenge and the expression of the immune response (Douch *et al.*, 1996). Moreno *et al.* (2006) have detected a QTL for resistance to *H. contortus* on ovine chromosome 5 in the INRA 401 x Barbados Black Belly back cross lines. The proximal most likely location of this QTL corresponded to the IL-3/IL-4/IL-5 region. As these cytokines are characteristic of Th2 type immune responses (Lacroux *et al.*, 2006), studies of both the cellular and humoral responses will be of paramount importance in the understanding of the mechanism of resistance (Gill, 1991; Schallig *et al.*, 1995; Colditz *et al.*, 1996; Balic *et al.*, 2000).

Hence, there is still much to be done to understand the mechanisms underlying differences both between and within breeds of sheep in terms of their resistance to helminth infections in order to identify the best markers of resistance for use during the selection processes.

CONCLUSION

Haemonchosis with its very wide distribution has become a very important production constraint in sheep farms in temperate, tropical and subtropical regions of the world. Various intrinsic and extrinsic factors determine the survival of the parasite and hence the development of disease in the animal host. The indiscriminate use of anthelmintics has often led to the widespread emergence of drug resistant strains of *H. contortus*. This has encouraged the use of various parasite control methods such as grazing management, biological agents, vaccines and selected breeds with or without moderate use of anthelmintics. The ultimate goal of such control programs is to enhance productivity while minimising the risk of developing drug resistance and addressing consumer and environmentally associated problems. The problem of haemonchosis in sheep is most severe in tropical areas where the potential of livestock production is very high but unfortunately largely unexploited because of lack of knowledge, complex lifestyles and economic reasons. Hence, any proposed control strategy must take into account the practicalities in the successful application of the program and the economic benefits to the livestock owner. Throughout the temperate regions of the world, grazing management combined with the moderate use of anthelmintics has been used to improve the efficiency of parasite control in livestock. In comparison, there are relatively few examples of such schemes in the tropics/subtropics largely due to reasons specific to each agro-ecology. Therefore, intensive epidemiological surveys are required to adapt available grazing management methods to the existing farming systems of the area. Vaccines, "ethnoveterinary" products and biological control agents are unlikely to be commercialised in the near future. Though these could be of great benefit to the large sheep industries of the world and consequently to the consumers, the prospect of such products reaching poor sheep farmers in the tropics/subtropics is questionable for reasons such as lack of veterinary services and availability. In the short term, selection of sheep for resistance to GI parasitism seems to be the most promising and potentially successful answer to the problem of haemonchosis in the tropics and would involve the maximum exploitation of locally available genetic resources. To make further progress however, the mechanisms governing resistance of different breeds of sheep has to be better understood and due consideration should be given to intensifying research efforts in this area.

ACKNOWLEDGEMENTS

The authors would like to thank Professor James Duncan and Doctor Jacques Cabaret for critical reading of this manuscript and their valuable comments.

REFERENCES

ABULE E., SNYMAN H.A. & SMIT G.N. Comparisons of pastoralists' perceptions about rangeland resource utilisation in the Middle Awash Valley of Ethiopia. *Journal of Environmental Management*, 2005, *75*, 21-35.

ACHI Y.L., ZINSSTAG J., YAO K., YEO N., DORCHIES P. & JACQUIET P. Host specificity of *Haemonchus* spp. for domestic ruminants in the savannah in northern Ivory Coast. *Veterinary Parasitology*, 2003, *116*, 151-158

AGYEI A.D. Seasonal changes in the level of infective strongylate nematode larvae on pasture in the coastal savannah regions of Ghana. *Veterinary Parasitology*, 1997, *70*, 175-182.

ALBERS G.A. & GRAY G.D. Breeding for worm resistance: a perspective. *International Journal for Parasitology*, 1987, *17*, 559-566.

ALI D.N. & HENNESSY D.R. The effect of reduced feed intake on the efficacy of oxfendazole against benzimidazole resistant *Haemonchus contortus* and *Truchostrongylus colubriformis* in sheep. *International Journal for Parasitology*, 1995, *25*, 71-74.

AMARANTE A.F.T., BRICARELLO P.A., ROCHA R.A. & GENNARI S.M. Resistance of Santa Ines, Suffolk and Ile de France sheep to naturally acquired gastrointestinal nematode infections. *Veterinary Parasitology,* 2004, *120*, 91-106.

ANDREWS S.J. The efficacy of levamisole, and a mixture of oxfendazole and levamisole, against the arrested stages of benzimidazole-resistant *Haemonchus controtus* and *Ostertagia circumcincta* in sheep. *Veterinary Parasitology*, 2000, *88*, 139-146.

ATHANASIADOU S., KYRIAZAKIS I., JACKSON F. & COOP R.L. Consequences of long-term feeding with condensed tannins on sheep parasitized with *Trichostrongylus colubriformis*. *International Journal for Parasitology*, 2000, *30*, 1025-1033.

AUMONT G., GRUNER L. & HOSTACHE G. Comparison of the resistance to sympatric and allopatric isolates of *Haemonchus contortus* of Black belly sheep in Guadeloupe (FWI) and of INRA 401 sheep in France. *Veterinary Parasitology,* 2003, *116*, 139-150.

BALIC A., BOWLES V.M. & MEEUSEN E.N.T. Cellular profiles in the abomasal mucosa and lymph node during primary infection with *Haemonchus contortus* in sheep. *Veterinary Immunology and Immunopathology*, 2000, *75*, 109-120.

BALIC A., CUNNINGHAM C.P. & MEEUSEN E.N.T. Eosinophil interactions with *Haemonchus contortus* larvae in the ovine gastrointestinal tract. *Parasite Immunology*, 2006, *28*, 107-115.

BANKS D.J., SINGH R., BARGER I.A., PRATAP B. & LE JAMBRE L.F. Development and survival of infective larvae of *Haemonchus contortus* and *Trichostrongylus colubriformis* on pasture in a tropical environment. *International Journal for Parasitology*, 1990, *20*, 155-160.

BARGER I.A. Genetic resistance of hosts and its influence on epidemiology. *Veterinary Parasitology,* 1989, *32*, 21-35.

BARGER I.A. Control by management. *Veterinary Parasitology,* 1997, *72*, 493-500.

BEECH R.N., PRICHARD R.K. & SCOTT M.E. Genetic variability of the beta-tubulin genes in benzimidazole-susceptible and -resistant strains of *Haemonchus contortus*. *Genetics*, 1994, *138*, 103-110.

BISSET S.A., VLASSOFF A., DOUCH P.G.C., JONAS W.E., WEST C.J. & GREEN R.S. Nematode burdens and immunological responses following natural challenge in Romney lambs selectively bred for low and high faecal worm egg count. *Veterinary Parasitology,* 1996, *61*, 249-263.

BOWMAN D.D. Georgis' Parasitology for Veterinarians. 7th Ed., 255-283. W.B. Saunders Company, 1999.

BRICARELLO P.A., AMARANTE A.F.T., ROCHA R.A., CABRAL FILHO S.L., HUNTLEY J.F., HOUDIJK J.G.M., ABDALLA A.L. & GENNARI S.M. Influence of dietary protein supply on resistance to experimental infections with *Haemonchus contortus* in the Ile de France and Santa Ines lambs. *Veterinary Parasitology,* 2005, *134*, 99-109.

BURKE J.M., MILLER J.E. & BRAUER D.K. The effectiveness of copper oxide wire particles as an anthelmintic in pregnant ewes and safety to offspring. *Veterinary Parasitology,* 2005, *131*, 291-297.

CHANDRAWATHANI P., ADNAN M. & WALLER P.J. Anthelmintic resistance in sheep and goat farms on Peninsular Malaysia. *Veterinary Parasitology,* 1999, *82*, 305-310.

CHANDRAWATHANI P., JAMNAH O., ADNAN M., WALLER P.J., LARSEN M. & GILLESPIE A.T. Field studies on the biological control of nematode parasites of sheep in the tropics, using the microfungus *Duddingtonia flagrans*. *Veterinary Parasitology,* 2004, *120*, 177-187.

CHARTIER C., PORS I., HUBERT J., ROCHETEAU D., BENOIT C. & BERNARD N. Prevalence of anthelmintic resistant nematodes in sheep and goats in western France. *Small Ruminant Research*, 1998, *29*, 33-41.

COLDITZ I.G., WATSON D.L., GRAY G.D. & EADY S.J. Some relationships between age, immune responsiveness and resistance to parasites in ruminants. *International Journal for Parasitology,* 1996, *26*, 869-877.

COLES G.C. Drug-resistant parasites of sheep: An emerging problem in Britain? *Parasitology Today*, 1998, *14*, 86-88.

COOP R.L. & KYRIAZAKIS I. Influence of host nutrition on the development and consequences of nematode parasitism in ruminants. *Trends in Parasitology*, 2001, *17*, 325-330.

COYNE M.J., SMITH G. & JOHNSTONE C. A study of the mortality and fecundity of *Haemonchus contortus* in sheep following experimental infections. *International Journal for Parasitology,* 1991a, *21*, 847-853.

COYNE M.J., SMITH G. & JOHNSTONE C. Fecundity of gastrointestinal trichostrongylid nematodes of sheep in the field. *American Journal of Veterinary Research*, 1991b, *52*, 1182-1188.

COYNE M.J. & SMITH G. The development and mortality of the free-living stages of *Haemonchus contortus* in laboratory culture. *International Journal for Parasitology*, 1992, *22*, 641-650.

DE LIGUORO M., LONGO F., BRAMBILLA G., CINQUINA A., BOCCA A. & LUCISANO A. Distribution of the anthelmintic drug albendazole and its major metabolites in ovine milk and milk products after a single oral dose. *Journal of Dairy Research*, 1996, *63*, 533-545.

DOUCH P.G.C., GREEN R.S., MORRIS C.A., MCEWAN J.C. & WINDON R.G. Phenotypic markers for selection of nematode-resistant sheep. *International Journal for Parasitology,* 1996, *26*, 899-911.

EDDI C., CARACOSTANTOGOLO J., PEÑA M., SCHAPIRO J., MARANGUNICH L., WALLER P.J. & HANSEN J.W. The prevalence of anthelmintics resistance in nematode parasites of sheep in Southern Latin America: Argentina. *Veterinary Parasitology,* 1996, *62*, 189-197

EL-MAKAWY A., RADWAN H.R., GHALY I.S. & EL-RAOUF A.A. Genotoxical, teratological, and biochemical effects of anthelmintics drug oxfendazole Maximum Residual Limit (MRL) in male and female mice. *Reproduction, Nutrition, Development*, 2006, *46*, 139-156.

FONTENOT M.E., MILLER J.E., PEÑA M.T., LARSEN M. & GILLESPIE A. Efficiency of feeding *Duddingtonia flagrans* chlamydospores to grazing ewes on reducing availability of parasitic nematode larvae on pasture. *Veterinary Parasitology,* 2003, *118*, 203-2113.

GAMBLE H.R. & ZAJAC A.M. Resistance of St. Croix lambs to *Haemonchus contortus* in experimentally and naturally acquired infections. *Veterinary Parasitology,* 1992, *41*, 211-225.

GASBARRE L.C. Effects of gastrointestinal nematode infection on the ruminant immune system. *Veterinary Parasitology,* 1997, *72*, 327-343.

GATONGI P.M., PRICHARD R.K., RANJAN S., GATHUMA J.M., MUNAYAU W.K., CHERUIYOT H. & SCOTT M.E. Hypobiosis of *Haemonchus contortus* in natural infections of sheep and goats in semi-arid area of Kenya. *Veterinary Parasitology,* 1998, *77*, 49-61.

GAULY M., KRAUS M., VERVELDE L., VAN LEEUWEN M.A. & ERHARDT G. Estimating genetic differences in natural resistance in Rhön and Merino land sheep following experimental *Haemonchus contortus* infection. *Veterinary Parasitology,* 2002, *106*, 55-67.

GILL H.S. Genetic control of acquired resistance to haemonchosis in Merino lambs. *Parasite Immunology,* 1991, *13*, 617-28.

GÓMEZ-MUÑOZ M.T., CUQUERELLA M., GOMEZ-IGLESIAS L.A., MÉNDEZ S., FERNÀNDEZ-PÉREZ F.J., DE LA FUENTE C. & ALUNDA J.M. Serum antibody response of Castellana sheep to *Haemonchus contortus* infection and challenge: relationship to abomasal worm burdens. *Veterinary Parasitology,* 1999, *81*, 281-293.

GOOD B., HANRAHAN J.P., CROWLEY B.A. & MULCAHY G. Texel sheep are more resistant to natural nematode challenge than Suffolk sheep based on faecal egg count and nematode burden. *Veterinary Parasitology,* 2006, *136*, 317-327.

GRAY G.D. The use of genetically resistant sheep to control nematode parasitism. *Veterinary Parasitology,* 1997, *72*, 345-366.

GREEN P.E., FORSYTH B.A., ROWAN K.J. & PAYNE G. The isolation of a field strain of *Haemonchus contortus* in Queensland showing multiple anthelmintic resistance. *Australian Veterinary Journal,* 1981, *57*, 79-84.

GRUNER L., AUMONT G., GETACHEW T., BRUNEL J.C., PERY C., COGNIÉ Y. & GUÉRIN Y. Experimental infection of Black belly and INRA 401 straight and crossbred sheep with trichostrongyle nematode parasites. *Veterinary Parasitology,* 2003, *116*, 239-249.

HAILE A., ANINDO D.O., TEMBELY S., MUKASA-MUGERWA E., TIBBO M., YAMI A., BAKER R.L. & REGE J.E.O. Effects of dietary protein supplementation and infection with gastrointestinal nematode parasites on some nutritional and metabolic parameters in Ethiopian Menz and Horro sheep. *Livestock Production Science,* 2004, *91*, 183-195.

HARDER A., SCHMITT-WREDE HP., KRÜCHEN J., MARINOVSKI P., WUNDERLICH F., WILLSON J., AMLIWALA K., HOLDEN-DYE L. & WALKER R. Cyclooctadepsipeptides-an anthelmintically active class of compounds exhibiting a novel mode of action. *International Journal of Antimicrobial Agents*, 2003, *22*, 318-331.

HENNESSY D.R. Modifying the formulation of delivery mechanisms to increase the activity of anthelmintics compounds. *Veterinary Parasitology,* 1997, *72*, 367-390.

HRABOK J.T., OKSANEN A., NIEMINEN M., RYDZIK A., UGGLA A. & WALLER P.J. Reindeer as hosts for nematode parasites of sheep and cattle. *Veterinary Parasitology,* 2006, *136*, 297-306.

IQBAL Z., LATEEF M., JABBAR A., MUHAMMAD G. & KHAN M.N. Anthelmintic activity of *Calotropis procera* (Ait.) Ait. F. flowers in sheep. *Journal of Ethnopharmacology,* 2005, *102*, 256-261.

JACQUIET P., CABARET J., CHEIKH D. & THIAM A. Experimental study of survival strategy of *Haemonchus contortus* in sheep during the dry season in desert areas of the Mauritania. *Journal of Parasitology,* 1995, *81*, 1013-1015.

JACQUIET P., CABARET J., THIAM A. & CHEIKH D. Host range and the maintenance of *Haemonchus* spp. in an adverse arid climate. *International Journal for Parasitology,* 1998, *28*, 253-261.

JASMER D.P. & MCGUIRE T.C. Protective immunity to a blood-feeding nematode (*Haemonchus contortus*) induced by parasite gut antigens. *Infection and Immunity*, 1991, *59*, 4412-4417.

KLEI T.R. Immunological control of gastrointestinal nematode infections. *Veterinary Parasitology,* 1997, *72*, 507-523.

KNOX M.R. Effectiveness of copper oxide wire particles for *Haemonchus contortus* control in sheep, *Australian Veterinary Journal,* 2002, *80*, 224-227.

KNOX D.P. & SMITH W.D. Vaccination against gastrointestinal nematode parasites of ruminants using gut-expressed antigens. *Veterinary Parasitology,* 2001, *100*, 21-32.

KNOX M.R., TORRES-ACOSTA J.F.J., AGUILAR-CABALLERO A.J. Exploiting the effect of dietary supplementation of small ruminants on resilience end resistance against gastrointestinal nematodes. *Veterinary Parasitology*, 2006, *139*, 385-393.

KRECEK R.C., GROENEVELD H.T. & MARITZ J.I. A preliminary study of the effect of microclimate on the third-stage larvae of *Haemonchus contortus* and *Haemonchus placei* on irrigated pasture. *International Journal for Parasitology,* 1992, *22*, 747-752

LACROUX C., NGUYEN T.H.C., ANDREOLETTI O., PRÉVOT F., GRISEZ C., BERGEAUD J.P., GRUNER L., BRUNEL J.C., FRANCOIS D., DORCHIES P. & JACQUIET P. *Haemonchus contortus* (Nematoda:

Trichostrongylidae) infection in lambs elicits an unequivocal Th2 immune response. *Veterinary Research*, 2006, *37*, 607-622.

Larsen M. Prospects for controlling animal parasitic nematodes by predacious micro fungi. *Parasitology*, 2000, *120*, S121-S131.

Larsen M. Biological control of nematode parasites in sheep. *Journal of Animal Science*, 2006, *84*, E133-E139.

Le Jambre L.F., Gill J.H. & Lenane I.J. Characterisation of an avermectin resistant strain of Australian *Haemonchus contortus*. *International Journal for Parasitology* 1995, *25*, 691-698.

Le Jambre L.F., Gill, J.H., Lenane I.J. & Baker P. Inheritance of avermectin resistance in *Haemonchus contortus*. *International Journal for Parasitology,* 2000, *30*, 105-111.

Manton V.J.A., Peacock R., Poynter D., Silverman P.H., Terry R.J. The influence of age on naturally acquired resistance to *Haemonchus contortus* in lambs. *Research in Veterinary Science,* 1962, *3*, 308.

Mckenna P.B. & Watson T.G. The comparative efficacy of four broad spectrum anthelmintics against some experimentally induced trichostrongylid infections in sheep and goats. *New Zealand Veterinary Journal*, 1987, *35*, 192-195.

Miller J.E., Bahirathan M., Lemarie S.L., Hembry F.G., Kearney M.T. & Barras S.R. Epidemiology of gastrointestinal nematode parasitism in Suffolk and Gulf Coast Native sheep with special emphasis on relative susceptibility to *Haemonchus contortus* infection. *Veterinary Parasitology*, 1998, *74*, 55-74.

Moreno C., Gruner L., Scala A., Mura L., Schibler L., Amigues Y., Sechi T., Jacquiet P., Francois D., Sechi S., Roig A., Casu S., Barillet F., Brunel J.C., Bouix J., Carta A. & Rupp R. QTL for resistance to internal parasites in two designs based on natural and experimental conditions of infection. Proceedings of the 8th World Congress on Genetics Applied to Livestock Production, 2006.

Mugambi J.M., Bain R.K., Wanyangu S.W., Ihiga M.A., Duncan J.L., Murray M. & Stear M.J. Resistance of four sheep breeds to natural and subsequent artificial *Haemonchus contortus* infection. *Veterinary Parasitology,* 1997, *69*, 265-273.

Mulcahy G., O'Neill S., Donnelly S. & Dalton J.P. Helminths at mucosal barriers-interaction with the immune system. *Advanced Drug Delivery Reviews*, 2004, *56*, 853-868.

Nari A., Salles J., Gill A., Waller P.J. & Hansen J.W. The prevalence of anthelmintic resistance in nematode parasites of sheep in Southern Latin America: Uruguay. *Veterinary Parasitology,* 1996, *62*, 213-222.

Newton S.E. Progress on vaccination against *Haemonchus contortus*. *International Journal for Parasitology,* 1995, *25*, 1281-1289.

Newton S.E., Morrish L.E., Martin P.J., Montague P.E. & Rolph T.P. Protection against multiple drug-resistant and geographically distant strains of *Haemonchus contortus* by vaccination with H11, a gut membrane-derived protective antigen. *International Journal for Parasitology,* 1995, *25*, 511-521.

Paolini V., Bergeaud J.P., Grisez C., Prevot F., Dorchies P. & Hoste H. Effects of condensed tannins on goats experimentally infected with *Haemonchus contortus*. *Veterinary Parasitology,* 2003, *113*, 253-261.

Paraud C., Hoste H., Lefrileux Y., Pommaret A., Paolini V., Pors I. & Chartier C. Administration of *Duddingtonia flagrans* chlamydospores to goats to control gastro-intestinal nematodes: dose trials. *Veterinary Research*, 2005, *36*, 157-166.

Reinecke R.K., Kirkpatrick R., Kriel A.M. & Frank F. Availability of infective larvae of parasitic nematodes of sheep grazing on Kikuyu (*Pennisetum clandestinum*) pastures in the winter rainfall area. *Onderstepoort Journal of Veterinary Research*, 1989, *56*, 223-234.

Romjali E., Dorny P., Batubara A., Pandey V.S. & Gatenby R.M. Peri-parturient rise in faecal strongyle egg counts of different genotypes of sheep in North Sumatra, Indonesia. *Veterinary Parasitology*, 1997, *68*, 191-196.

Sangster N.C., Redwin J.M. & Bjorn H. Inheritance of levamisole and benzimidazole resistance in an isolate of *Haemonchus contortus*. *International Journal for Parasitology,* 1998, *28*, 503-510

Sangster N.C., Rickard G.M., Hennessy D.R., Steel J.W. & Collins G.H. Disposition of oxfendazole in goats and efficiency compared with sheep. *Research in Veterinary Science,* 1991, *51*, 258-263.

Schallig H.D.F.H., van Leeunwen M.A.W. & Hendrikx W.M.L. Isotype-specific serum antibody responses of sheep to *Haemonchus contortus* antigens. *Veterinary Parasitology,* 1995, *56*, 149-162.

Scott I., Dick A., Irvine J., Stear M.J. & McKellar Q.A. The distribution of pepsinogen within the abomasa of cattle and sheep infected with *Ostertagia* spp. And sheep infected with *Haemonchus contortus*. *Veterinary Parasitology,* 1999, *82*, 145-159.

Silvestre A. & Humbert J.F. Diversity of benzimidazole-resistance alleles in populations of small ruminant parasites. *International Journal for Parasitology,* 2002, *32*, 921-928

Simpson H.V., Lawton D.E.B., Simcock D.C., Reynolds G.W. & Pomroy W.E. Effect of adult and larval *Haemonchus contortus* on abomasal secretion. *International Journal for Parasitology,* 1997, *27*, 825-831.

Sissay M.M., Asefa A., Uggla A. & Waller P.J. Anthelmintic resistance of nematode parasites of small ruminants in eastern Ethiopia: exploitation of refugia to restore anthelmintics efficacy. *Veterinary Parasitology,* 2006, *135*, 337-346.

Smith W.D., Jackson F., Jackson E. & Williams J. Studies on the local immune response of the lactating ewes infected with *Ostertagia circumcincta*. *Journal of Comparative Pathology*, 1983, *93*, 295-305.

Smith W.D. Protection in lambs immunised with *Haemonchus contortus* gut membrane proteins. *Research in Veterinary Science,* 1993, *54*, 94-101.

Smith W.D., Smith S.K. & Pettit D. Cross protection studies with gut membrane glycoprotein antigens from *Haemonchus contortus* and *Teladorsagia circumcincta*. *Parasite Immunology,* 2001, *23*, 203-211.

Smith W.D., Smith,S.K., Pettit D., Newlands G.F. & Skuce P.J. Relative protective properties of three membrane glycoprotein fractions from *Haemonchus contortus*. *Parasite Immunology,* 2000, *22*, 63-71.

STRONG L., WALL R., WOOLFORD A. & DJEDDOUR D. The effect of faecally excreted ivermectin and fenbendazole on the insect colonisation of cattle dung following the oral administration of sustained-release boluses. *Veterinary Parasitology,* 1996, *62*, 253-266.

SUCHITRA S. & JOSHI P. Characterisation of *Haemonchus contortus* calerticulin suggests its role in feeding and immune evasion by the parasite. *Biochimica et Biophysica Acta*, 2005, *1722*, 293-303.

TEMBELY S., LAHLOU-KASSI A., REGE J.E., SOVANI S., DIEDHIOU M.L. & BAKER R.L. The epidemiology of nematode infections of sheep in a cool tropical environment. *Veterinary Parasitology*, 1997, *70*, 129-141.

TEMBELY S., LAHLOU-KASSI A., REGE J.E.O., MUKASA-MUGERWA E., ANINDO D., SOVANI S. & BAKER R.L. Breed and season effects on the peri-parturient rise in nematode egg output in indigenous ewes in a cool tropical environment. *Veterinary Parasitology,* 1998, *77*, 123-132.

TERRILL T.H., LARSEN M., SAMPLES O., HUSTED S., MILLER J.E., KAPLAN R.M. & GELAYE S. Capability of the nematode-trapping fungus *Dudingtonia flagrans* to reduce infective larvae of gastrointestinal nematodes in goats' faeces in the South-eastern United States: dose titration and dose time interval studies. *Veterinary Parasitology,* 2004, *120*, 285-296.

THOMAS R.J. AND ALI D.A. The effect of *Haemonchus contortus* infection on the pregnant and lactating ewes, *International Journal for Parasitology,* 1983, *13*, 393-398.

UPPAL R.P., YADOV C.L. & BHUSHAN C. Efficacy of closantel against fenbendazole and levamisole resistant *Haemonchus contortus* in small ruminants. *Tropical Animal Health and Production,* 1993, *25*, 30-32.

URQUHART G.M., ARMOUR J., DUNCAN J.L., DUNN A.M. & JENNINGS F.W. Veterinary Parasitology, 19-164, 2nd Ed. Blackwell Science, 1996.

VAN WYK J.A. & BATH G.F. The FAMACHA system for managing haemonchosis in sheep and goats by clinically identifying individual animals for treatment. *Veterinary Research*, 2002, *33*, 509-529.

VAN WYK J.A., MALAN F.S. & RANDLES J.L. How long before resistance makes it impossible to control some field strains of *Haemonchus contortus* in South Africa with any of the modern anthelmintics? *Veterinary Parasitology,* 1997, *70*, 111-122.

WALLER P.J. International approaches to the concept of integrated control of nematode parasites of livestock. *International Journal for Parasitology,* 1999, *29*, 155-164.

WALLER P.J. & FAEDO M. The prospects for biological control of the free-living stages of nematode parasites of livestock. *International Journal for Parasitology,* 1996, *26*, 915-925.

WALLER P.J., FAEDO M. & ELLIS K. The potential of nematophagous fungi to control the free-living stages of nematode parasites of sheep: towards the development of a fungal controlled release device. *Veterinary Parasitology,* 2001, *102*, 299-308.

Waller P.J., Bernes G., Rudby-Martin L., Ljungstrom B.L. & Rydzik A. The epidemiology of abomasal nematodes of sheep in Sweden, with particular reference to over-winter survival strategies. *Veterinary Parasitology,* 2004, *122*, 207-220.

WALLER P.J., RYDZIK A., LJUNGSTRÖM B.L. & TÖRNQUIST M. Towards the eradication of *Haemonchus contortus* from sheep flocks in Sweden. *Veterinary Parasitology,* 2006, *136*, 367-372.

WANYANGU S.W., KARIMI S., MUGAMBI J.M. & BAIN R.K. Availability of *Haemonchus contortus* L3 larvae on pasture at Kiboko: semi-arid warm agro-climatic zone in Kenya. *Acta Tropica*, 1997, *68*, 193-199.

WARUIRU R.M. Efficacy of closantel, albendazole and levamisole on an ivermectin resistant strain of *Haemonchus contortus* in sheep. *Veterinary Parasitology,* 1997, *73*, 65-71.

WATSON D.L. & GILL H.S. Effect of weaning on antibody responses and nematode parasitism in Merino lambs. *Research in Veterinary Science,* 1991, *51*, 128-132.

WOOLASTON R.R. Selection of Merino sheep for increased and decreased resistance to *Haemonchus contortus*: periparturient effects on faecal egg count. *International Journal for Parasitology,* 1992, *22*, 947-953.

WOOLASTON R.R. & BAKER R.L. Prospects of breeding small ruminants for resistance to internal parasites. *International Journal for Parasitology,* 1996, *26*, 845-855.

Reçu le 19 septembre 2006,
Accepté le 13 décembre 2006