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Domestication of ruminant livestock and the impact of nematode parasites: possible implications for the reindeer industry

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Abstract: In a balanced ecological system, both host and nematode parasite populations are firmly controlled by a complex array of interacting factors. However domestication of livestock has tipped the balance in favour of the parasites. This is due to increasing the proportion of susceptible animals in the herd or flock (lactating females and weaned young animals), increasing stocking rate, increasing productivity demands and decreasing the movement of the animals. In contrast with microbial infections, where multiplication takes place entirely within the host, metazoan parasites have both a parasitic phase and a free-living phase. Every worm present has been separately acquired by the ingestion of free-living stages on pasture. Immunity to nematodes develops slowly, it is labile, and its maintenance is dependent upon a good nutritional state of the animal. Consequently, worm parasites are ubiquitous wherever livestock are kept and they impose a constant and often a high infectious pressure on grazing animals. Nematode infections in grazing livestock are almost always a mixture of species. All have deleterious effects and collectively lead to chronic ill thrift. Economic evaluations repeatedly show that the major losses due to parasites are on animal production, rather than on mortality. This paper focuses on the problems of nematode parasites; problems associated with drug use (anthelmintic resistance, environmental impact) and costs of nematode infections for the common ruminant livestock industries (cattle, sheep, goats), with possible analogies for the semi-domesticated reindeer industry.

Key words: domestication, losses, nematodes, parasites.

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Introduction

Few people realise that there are far more kinds of parasitic, than non-parasitic, organisms in the world. Even if viruses and rickettsias, which are all parasitic, as well as the many kinds of parasitic bacteria and fungi are excluded, the parasites are still in the majority (Schmidt & Roberts, 1981). In general, the parasitic way of life has proven to be highly successful, since it has evolved independently in nearly every phylum of animals, ranging from protozoa, to multicellular invertebrates, and even to chordates.

Parasites are organisms that live at the expense of their host and, in doing so, have undergone some degree of evolutionary change, or adaptation, to survive within their hosts (Ebert & Herre, 1996). This is based on immunological phenomena (Maizels *et al.*, 2001). In contrast to the unicellular parasitic organisms (bacteria, protozoa), which are capable of very rapid replication within the host (hours), the metazoan parasites (helminths: nematodes, trematodes, cestodes) must remain in their hosts for a much longer period of time before they can successfully complete their life cycle, which generally takes several weeks. These long-lived helminth parasites are highly accomplished practitioners of immune evasion and manipulation, using strategies honed during their long co-evolutionary interaction with the immune system of their mammalian hosts (Behnke *et al.*, 1992; Allen & Maizels, 1996). Thus, multicellular helminths present very different infection dynamics from the micro-parasites (viruses, bacteria and protozoa) as they do not replicate within the host, and parasite loads increase only as a result of accumulated exposure to infection (Barger *et al.*, 1985; Dobson *et al.*, 1990; Maizels *et al.*, 2001).

Helminth parasites do not outpace the immune system of the host by faster cell division, or rapid antigenic variation (Maizels *et al.*, 1993). Rather, their strategy seems to be one of stealth by defusing aggressive immune reactions and inducing forms of immunological tolerance to permit their long-term survival within their hosts (Dineen, 1963; 1978; Maizels & Lawrence, 1991). Therefore in contrast to the microbial infections where the host recognises their "foreign-ness" and very quickly induces a strong immune response to infection, or following vaccination with efficacies approaching 100% (Emery, 1996), host immunity to worm parasites is slow to develop, is labile and easily destroyed by any form of stress (Cox, 1997). Much research has been done, and is still being conducted, into the mechanisms of naturally acquired immunity to helminth parasites of ruminant livestock, but the final effector mechanisms are not known. Unfortunately from the standpoint of attempting to develop successful helminth vaccines for ruminant livestock, the situation seems complex, involving a combination of local hypersensitivity, cell mediated, antibody and inflammatory responses and is complicated further by the natural unresponsiveness which exists in the young animal and the dam around parturition (Smith, 1999). As a consequence, nematode parasites are ubiquitous wherever livestock are kept and they impose a more-or-less constant infectious pressure on grazing animals.

Effect of domestication on livestock

In a balanced ecological system both host and parasite populations are firmly controlled by a complex array of interacting forces. However domestication of livestock has tipped the balance in favour of the parasites. This is because of the following factors:

Restriction in livestock movement

Reduction in livestock movement to sedentary forms of management is an almost invariable consequence of domestication. Apart from the time taken to complete their life-cycle, another important difference between the microbes and nematodes is the pattern of their life cycles. For microbes, reproduction occurs within the host, whereas for all economically important nematode parasites, their life cycle involves both an obligatory free-living phase on pasture as well as a parasitic phase within the host. Thus every worm present in an animal is derived from its ingestion by the animal through grazing on pasture. In wild ruminant populations (*eg.* African ungulates) movement is primarily dictated by food supply, and characteristically they migrate over considerable geographic ranges. Likewise in nomadic and transhumance herding, animals are typically moved over long distances. Thus in many instances in the above situations, animals leave their faeces, containing the free-living stages of potentially future worm generations, behind them on pasture (Macpherson, 1994; Eckert & Hertzberg, 1994). They return often at a much later date, when these free-living stages are likely to have declined to very low numbers.

Restricting the movement of animals from this otherwise natural migration, or transhumance herding, to more sedentary systems of management, greatly increases the chances of animals being exposed to infection by grazing contaminated pastures. The environmental factors that determine the speed and success of the translation of nematode eggs to infective larvae are temperature and humidity. In the humid tropics and sub/tropics where both of these factors are invariably high, auto-infection (animals being infected by parasites derived from their own contamination) can occur within a few days (Banks *et al.*, 1990). However in milder locations and those where there can be seasonal discontinuities in rainfall, the development of worm eggs to infective larvae tends to be more protracted (Stromberg, 1997), although survival on pasture is also longer (Barger, 1999).

In addition, domestication often forces animals that have a natural tendency to browse on shrubs to a greater-or-lesser extent (*e.g.* camels and goats), to graze on pasture as generally this represents the only available food supply. Such browsing animals have not evolved to be highly resistant to nematode parasite infection (Pomroy *et al.*, 1986), as is the case with some indigenous or "unimproved" breeds of sheep, where the formidable combination of malnutrition, environmental stress and long-term and often massive larval challenge on pasture have imposed the harshest conditions for selection, resulting in survival of the fittest (Baker, 1996).

Although, in general, the semi-domesticated reindeer industries of Fennoscandia still practice herding over extensive areas, these are now often restricted by fencing to lands managed as co-operatives, made up generally of a large number of individual owners who communally graze their animals (Oksanen, 1999). In addition, natural grazing areas for reindeer are progressively diminishing, due to alienation to other priorities for land use. This artificially imposed restriction would mean that animals remain longer, and return sooner, to particular areas of land, thus potentially exposing the herd to greater parasite challenge. Also with the decline in browse available for reindeer, there is a tendency for co-operatives to provide more cultivated pastures as a feed substitute (Kumpula, 2001). Potentially this would also expose the animals to greater parasite pick-up.

Increasing stocking rate

Increasing stocking rate must of course be accompanied by providing more feed to the animals for them to remain productive. In the conventional ruminant livestock systems, such as cattle, sheep and goat production, this is generally achieved by improving pasture production (better pasture plants), often providing fertilizer and additional watering (irrigation) to improve pasture growth. However, enhanced productivity of pasture following application of fertilizer often fails to improve overall animal production (Speedy, 1980), and a commonly held view is that increasing stocking rate leads to increasing levels of parasitism in grazing livestock. This has prompted a number of studies to investigate such a relationship, particularly with studies on sheep in the temperate countries of the world, with mixed results. Although there was no positive correlation between stocking rate and parasitism in a number of studies (Spedding *et al.*, 1964; Cameron & Gibbs, 1966; Downey & Conway, 1968; Waller *et al.*, 1987), these were based on assessments of performance in young lambs up to weaning or marketing at around 3 – 4 months of age when the effects of parasites would have been too early to have any marked effect. However equally a number of studies have shown a direct relationship between increasing stocking rate and increasing parasitism of livestock (Zimmerman, 1965; Downey, 1969; Southcott *et al.*, 1967; 1970; Beveridge *et al.*, 1985; Brown *et al.*, 1985; Thamsborg *et al.*, 1996).

The impact of increasing stocking rates in relation to increasing risk of internal parasitism does not necessarily translate to the reindeer industry, but certainly more feed is now being provided at times of nutritional stress (generally winter) to keep the increasing numbers of animals alive. Within the last several decades, the increasing numbers of reindeer has clearly exceeded carrying capacity in parts of Norway and Finland (Kojola & Helle, 1993; Kumpula *et al.*, 2002; Moen & Danell, 2003). In attempts to offset this feed shortage, increased supplementary feeding is being practiced (Helle & Kojola, 1993). However, increasing numbers of animals naturally puts greater grazing pressure on pastures and in turn potentially results in greater parasite pickup of the animals.

Increasing number of susceptible animals

Profitability of any grazing livestock industry is largely driven by product output. This translates into raising more animals on any given area to produce more meat, fibre and hides. Thus man-made changes to herd, or flock structure result in more reproducing females and their progeny. For ruminant livestock, both the lactating female and the young animal (< 1 year of age) are the most susceptible to nematode infections (Dineen & Outteridge, 1984). The so called "periparturient relaxation of resistance" to worm infection is well known in sheep, goats and cattle (Connan, 1976; Barger, 1993). There is no maternal transfer of immunity (via placenta, or milk) to nematodes in the young ruminant (Meeusen, 1996). So actively growing, but worm naïve, young animals are particularly susceptible to infection in their first year of life (Stear & Murray, 1994). For example, the age at which young sheep acquire natural resistance to nematode infections is usually 7-10 months (Gibson & Parfitt, 1972, Dobson *et al.*, 1990), but this can be delayed by insufficient exposure to infection (Stewart &

Gordon, 1953; Gibson *et al.*, 1970), or by poor nutrition (Abbott *et al.*, 1985a; 1985b).

Increasing productivity demands

Coupled with the pressure of increasing reproductive rate, livestock producers also strive for increasing the amount of animal product, such as meat, milk and wool from their herds or flocks. Depending on the age and metabolic condition of animals, they allocate food resources (*i.e.* energy and/or various nutrients) among their body functions (Coop & Kyriazakis, 1999). Such body functions include the usual ones such as maintenance, growth and reproduction, but also additional functions that are a direct consequence of parasite infection. Studies on the patho-physiology of internal parasite infection show a metabolic drain caused by increasing endogenous loss of protein (Symons & Jones, 1975) and a reduced efficiency in the utilization of metabolisable energy due to parasite infection (Sykes & Coop, 1976). Clearly the increase in parasite challenge associated with contemporary livestock production systems must come at a price with regards to animal productivity, particularly at times of sub-optimal nutrient supply, when the animal has to prioritise the allocation of scarce nutritional resources.

Nematode host specificity

Alternate grazing between sheep and cattle can be a very effective form of parasite control for both livestock species, provided that the grazing alternations are linked with the seasonal troughs in larval availability on pasture. From a practical standpoint, cross-transmission of parasites from one host to the other is of little consequence. In the temperate regions of the world, excellent control of parasites from both species of livestock can occur from very infrequent pasture interchange (Barger & Southcott, 1978) and if the timing is epidemiologically precise, pasture changes need not be accompanied by anthelmintic treatment (Donald *et al.*, 1987). However, care must be exercised in simply transferring such schemes to the tropics and subtropics, without first conducting ecological studies on the free-living stages of parasites in these environments. Similar benefits may result from interchange grazing, but the grazing intervals will, almost certainly, need to be shorter. Also control of *Haemonchus contortus* may prove difficult. In the more temperate regions this species can cycle in calves but they rapidly acquire natural immunity to become refractory to infection by 12 months of age (Southcott & Barger, 1975). In the tropics this age resistance is slower to, or may never, develop. For example, in Paraguay there was no indication that cattle had acquired significant immunity after two years of grazing (Benitez-Usher *et al.*, 1984).

With domestication, it is inevitable that reindeer have come into closer contact with other species of domestic livestock. This is quite evident in the distribution range of reindeer in Fennoscandia, particularly so with sheep and goats in the Norwegian reindeer herding regions. A number of parasite species, considered to have domestic ruminants as their definitive hosts, have been reported in reindeer, particularly *Teladorsagia(Ostertagia) circumcincta* of sheep. It has been suggested that *T. circumcincta* represents a cryptic species complex, which may also be the case for *Ostertagia gruehneri,* which has been reported in roe deer (Dallas *et al.*, 2000; O. Halvorsen, pers.comm.).

The only reasonably comprehensive assessment of cross-transmission between parasites of reindeer and other livestock species has been done with the brain-worm *Elaphostrongylus* spp*.,* which is also found in moose. This parasite is responsible for severe outbreaks of meningo-encephalitis after warm and moist summers (Handeland & Slettbakk, 1994). However, it has been established that different species of this parasite are found in reindeer and moose and these parasites are specific to their hosts (Steen *et al.*, 1997).

Also with domestication comes the opportunity for greater contact with the companion animals (dogs, cats) of man. In this regard, reindeer can play an important role with parasite zoonotic disease; that is, parasites of animals that can infect man. The two most significant are the dog tapeworm, *Echinococcus granulosus,* where the intermediate (cystic) phase, referred to as "hydatids", has been a major problem in the reindeer herding communities (Skjenneberg, 1959; Huldt *et al.*, 1973) and toxoplasmosis caused by the protozoan *Toxoplasma gondii* of cats. Human infections of *T. gondii* are particularly serious if they occur during pregnancy and may result in abortion or congenitally acquired disorders, which primarily affect the central nervous system. Toxoplasmosis has recently emerged as a potentially serious disease in reindeer (Oksanen *et al.*, 1996) and has been associated with increased corral feeding of reindeer and by implication, increased contact with cat faeces (Oksanen *et al.*, 1997).

Chemotherapy

There has been a continual battle by livestock owners to control worm parasites in their flocks, or herds, that have come with the changes associated with domestication. This battle has relied almost entirely on the use of chemotherapy, namely anthelmintics, or known colloquially as "de-worming" compounds. Over the last 50 years there have been some remarkable developments in anthelmintic discovery and development. Now there exists a seemingly formidable array of very highly effective, very safe compounds with a very wide spectrum of activity to control internal parasites of livestock (McKellar, 1997), but the broad spectrum drugs fall into just 3 groups or classes, namely:

- *Group 1:* the benzimidazoles / probenzimidazoles
- *Group 2:* the imidazothiazoles / tetrahydropyrimidines
- *Group 3:* the avermectins /milbemycins (or macrocyclic lactones)

Anthelmintic resistance

For anthelmintics used to control nematode parasites of small ruminants (sheep and goats), high levels of resistance now exist to two (Group 1 and 2) of the three main broad-spectrum anthelmintic groups (Waller, 1994; 1997a). However resistance to the only remaining group, the macrocyclic lactones, is now rapidly increasing in the most economically important nematodes of sheep and goats (Sangster, 1999). There are now instances, such as in Malaysia, southern Brazil, Paraguay and South Africa, where farmers abandoned farming of sheep and goats because of uncontrolled parasitic disease with annual mortalities exceeding 20%, due to total anthelmintic failure (van Wyk, 1990; Maciel *et al.*, 1996; Chandrawathani *et al.*, 2004).

Resistance in cattle nematodes appears to be spreading, but the reports are localised isolations. Most concern surrounds ivermectin resistance that has now been reported in *Cooperia* spp. in several countries in the southern Hemisphere (Coles, 2002). The macrocyclic lactone anthelmintics are so widely used for parasite control in cattle that the treatment failure because of resistance would be serious indeed.

The macrocyclic lactone drugs are exceedingly potent and their spectrum of activity, which includes not only nematode parasites but also arthropod pests, thus they are commonly referred to as endectocides. With the additional advantage of being administered by injection, these drugs (particularly the forerunner, ivermectin) have been a great boon to the semi-domesticated reindeer industry of Fennoscandia. The use of injectable ivermectin in this region is widespread. For example in Finland, estimates show that approximately two-thirds of the total overwintering reindeer population are treated with this drug (Nieminen, 1984; 1989). Concerns have been expressed that because of the almost exclusive use of ivermectin by reindeer owners, resistance may emerge in any of the target parasite species (Waller, 1990). Although the frequency of ivermectin treatment of reindeer is low, with the majority of animals treated with ivermectin only once per year (Oksanen *et al.*, 1992), this is more-or-less synchronous with the gathering of animals in early winter at the time when free-range grazing ceases and the larval stages of the warble fly (*Hypoderma tarandi*) have not penetrated the hide of the animals. Such strategic use of anthelmintics, even when the frequency of treatment is very low, can impose a powerful selection for resistance as the timing is chosen to coincide with a very high proportion of the parasite population being present in the animals. Field evidence to this effect comes from the very rapid selection for ivermectin resistance in the nematode parasite of sheep, *T. circumcincta,* following just two treatments / year (during summer) in the Mediterranean climatic conditions of Western Australia (Besier, 1997).

Drug resistance in any organism, including worms, is genetically determined and every time a drug is used there is the possibility to select for those individuals in the targeted pest population that are resistant. If the proportion of the population that escapes exposure to drug selection (refugia) is very small, then those individual parasites that survive treatment will have an enormous survival advantage to pass on resistance genes to their progeny (Dobson *et al.*, 2001). Although the chances of this occurring within parasite populations of reindeer might seem remote, the threat will always be present, particularly if ivermectin alone remains the drug of choice.

New anthelmintics classes?
It is unlikely that an entirely novel anthelmintic class, or group, will become commercially available in the foreseeable future. This is because of the high development costs, high risks and the expected poor return on investment to the pharmaceutical industry (Waller, 1997b). Irrespective of this, resistance is mainly a problem in the Developing World and with sheep and goat industries, which account for a relatively small share of the parasiticide market (Waller, 1997c). Thus there is little commercial incentive for drug companies to search for new active anthelmintic compounds for the ruminant livestock industry, let alone proceed with these down the development track towards marketing a new commercial product.

Anthelmintics and the effects on the environment
Apart from the avermectins, there has been very little published information on the impact of excreted anthelmintics, or their metabolites, on the environment (Waller, 1993). However, the effect of ivermectin excreted in the dung of treated animals still remains an issue of continued controversy (Herd *et al.*, 1993, Wiktelius, 1996; Edwards *et al.*, 2001). There is no doubt that this drug has profound effects on the larval stages of certain coprophilic arthropods (Steel, 1997), but limited information is available on the effects of this drug on either micro-organisms, or saprophytic nematodes in the external environment. To address this latter issue, recent environmental impact studies on the use of ivermectin bolus in young cattle in Sweden have focused on soil nematode dynamics (Yeates *et al.*, 2002; 2003). Additionally, the influence of ivermectin on cattle dung pat disintegration over three grazing years was studied (Dimander *et al.*, 2003). The results of all these Swedish investigations showed that there was no effect on total numbers, diversity, or functional groups of soil nematodes. Also there was no delayed breakdown of dung pats from ivermectin bolus treated cattle.

Arthropods are only part of the diverse array of organisms that play a role in dung breakdown. It is also important to note that these arthropods are highly sensitive to the prevailing weather conditions (ideally suited to warm moist conditions) and are only attracted to freshly deposited dung. On this basis, it can be assumed that dung beetles and coprophilic flies play an insignificant role in the destruction of dung of reindeer treated with ivermectin in early winter. Breakdown of such dung has been observed to be slow and does not occur until the thaw of the following spring (Nilssen *et al.*, 1999). In addition to abiotic factors (eg. sun, rain, frost and wind), soil nematodes and micro-organisms are primarily responsible for this activity (Stark *et al.*, 2000). No long-term studies have been conducted on the effect of ivermectin residues in dung and surrounding soil on these latter organisms. Species diversity has been shown to be much less in extreme environments, such as in the arctic region, than in more temperate climates. This makes these former environments particularly sensitive to any man-induced changes. On this basis, it is of fundamental importance to conduct environmental impact studies on the effect of any chemical use that would ultimately end up in the arctic environment. This particularly applies to any chemical, such as ivermectin, that has been shown to have detrimental effects on non-target organisms in more equitable environments.

Costs of worm parasites
There are instances where livestock production systems are so ecologically out-of- balance that parasites have the potential to overwhelm their hosts unless they are kept in check by frequent drug treatment. Such systems are unsustainable. The inevitable penalty for suppressive anthelmintic treatment is the development of very high levels of resistance across the entire range of available anthelmintics, with the ultimate consequence that farmers are forced into abandoning their livestock enterprises (van Wyk, 1990; Maciel *et al.*, 1996). The costs of parasites to such livestock producers are obvious.

Although the vast majority of livestock production enterprises never reach the above extremes, worm infections occur in all grazing livestock, are almost always mixtures of species and collectively may lead to chronic ill thrift. In many cases this is not obvious to the livestock owner. However, these sub-clinical, or hidden costs of nematode parasite infection, particularly in young ruminants, can be substantial (Perry & Randolph, 1999; McLeod, 1995).

Recently an exhaustive review was conducted (Perry *et al*., 2002) to prioritise animal health research for poverty reduction in the Developing World on behalf of the major donors and international partners in improving animal health in these regions, such as the Food and Agriculture Organisation (FAO), the World Organisation for Animal Health (OIE) and the World Health Organisation (WHO). The report concluded that nematode parasite infections had the highest ranking in the global index of animal health constraints confronting the poor owners of livestock. *H. contortus,* the highly pathogenic nematode parasite of sheep and goats, was singled out as being of overwhelming importance.

Attempts to estimate the costs of parasites in reindeer have been made. For example, infestations by the larval stages of warble flies (*H. tarandi*) and throat bots (*Cephenemyia trompe*) were estimated to cause in the order of 15-30% lost production to the Swedish (Nordkvist, 1967) and Soviet (Saval'ev, 1968) reindeer industries. Notwithstanding the fact that these estimates were made more than 30 years ago, before the advent of the macrocyclic lactones, it is difficult to understand how these workers could partition the costs of larval stages of arthropods from concurrent nematode infections. Irrespective of whether or not one considers these estimates to be no more than wild guesses, it is probable that worm infections in semi-domesticated reindeer have increased in their prevalence and intensity since this time. Therefore by analogy with other livestock industries the costs of parasite infections to the reindeer industry would be very significant.

Conclusion

Domestication of ruminant livestock has disturbed the ecological balance, which has evolved between the animals and their parasites. As a consequence of imposing sedentary grazing systems, increasing stocking rate, modifying the age distribution, increasing productivity demands within livestock populations, parasites now have much greater opportunities. These man-made changes have increased the exposure pressure of parasites on their livestock hosts. As a consequence, parasite-induced productivity losses, and in certain circumstances mortalities, can be enormous (Chandrawathani *et al*., 2004). For those livestock owners who can afford it, the use of anthelmintic drugs has been the mainstay for control. But the development of resistance by nematode parasites to these drugs, concerns about the effect of drug residues in animal products and the environment have necessitated a complete re-evaluation of parasite control in contemporary livestock grazing systems (Waller, 1997b; 1999). Coinciding with this have been economic evaluations and these show that internal parasitic infections are the greatest infectious disease problems that currently face the domestic livestock industries.

By analogy, the same is likely to apply to the semi-domesticated reindeer industry. Most of the parasitological studies on reindeer have been restricted to the wild populations on Svalbard and in South Norway (Halvorsen & Bye, 1999), which of course differ considerably from the management and environment of the semi-domesticated reindeer of Fennoscandia. Current studies on parasite population dynamics, control options and their environmental impact (Hrabok *et al*., 2003) will provide answers to some of these issues of concern regarding the management of reindeer in semi-domesticated situations.

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