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Goat–Nematode interactions: think differently

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Goats (caprine) and sheep (ovine) are infected with the same principal gastrointestinal nematode (GIN) species, which provoke similar pathological changes and economic consequences. However, until now, the majority of data on host–parasite interactions have been accumulated from ovine studies. This article aims to emphasize the need for specific caprine studies. It is hypothesized that, owing to divergent evolutionary processes, sheep and goats have developed two different strategies to regulate GIN infections, respectively, based on immune response versus feeding behavior. Generation of additional comparative data should result in a better understanding of the possible trade-offs between these two basic regulatory processes. Goat studies should also help to avoid past errors in the control of GIN species owing to the lack of relevant information.

Compared threat of helminth parasitism on goats

Worldwide, the goat population is expanding in comparison to sheep. In 2007, it represented approximately 831 million head compared to the 1.09 billion sheep (http://www.fao.org) with more than 90% of the goat population found in Asia and Africa. The usual description of a goat as 'the cow of the poor' underlines its importance in small farming systems. Goat is the most highly consumed meat in the world, and more goats' milk is consumed worldwide than cows' milk. Worldwide, goat production is increasing because of the economic value of goats as efficient converters of low-quality forages into quality meat, milk and hide products for specialty markets.

Helminth parasitism of the digestive tract remains a major threat affecting goat health and production. In contrast to cattle, many of the same species of cestodes, trematodes and nematodes infect goat and sheep (Table 1), although some data suggest the existence of different caprine and ovine strains for some nematode species [1]. Owing to their ubiquitous distribution and high prevalence, infections with gastrointestinal nematodes (GIN) are of major economic importance in goat farming [2]. In developed countries, the main consequences are severe losses of production, whereas in developing countries, some of these GIN species provoke high mortality rates, particularly in kids.

Despite the similar number of goats and sheep in the world and the similar consequences of GIN parasitism in both hosts, the majority of studies on host–nematode interactions and control of GIN species have been carried out in sheep. This discrepancy still occurs, as noted in 2000[1]. The comparison of references on GIN species in goats versus sheep in two databases shows that only 20% to 25% of references relate to caprine studies. The relative dominance of sheep production in developed countries might explain such an imbalance.

With regard to GIN infections, it has been considered for some time that goats are similar to sheep and that results acquired from sheep were also applicable to goats. This was a source of severe consequence for the goat industry. For example, for many years, the registration of anthelmintic (AH) drugs did not discriminate between the two hosts; however, for the past 20 years, experimental evidence has been accumulating illustrating that the lack of direct information from caprine studies can severely impair control programs. Nonetheless, studies on host–parasite interactions in goats remain few and dispersed. We believe that more caprine studies are needed because the generation of comparative data in goats and sheep will help to: (i) understand some basic differences in the regulatory mechanisms controlling GIN infections; (ii) explore some trade-offs between these regulatory processes related either to the host behavior or to the host immune response; and (iii) adapt measures of control to take into account these main differences and their consequences. Therefore, it is important to illustrate the two diverging strategies developed for investigating GIN infections in goats and sheep. Thus, we describe the applied consequences of basic differences for the control of GIN species and how the lack of direct information in goats has led in the past to dramatic errors in the efficacy of control. Lastly, goats provide a model to explore the balance between various regulatory mechanisms of nematode infections.

Key differences between sheep and goats

Following domestication, sheep and goats developed different feeding behaviors (Box 1). Sheep are usually described

[1] Cabaret, J. (2000) Anthelmintic resistance in goats: from fiction to facts. *Proceedings 7th IGA conference, 15-18th May 2000, Tours, France, Institut de l'Elevage / INRA Editor*, pp 793–794.

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Table 1. The main helminth species found in the digestive tract and liver of ruminant

	Cattle	Sheep	Goat
Rumen	*Calicophoron calicophoron*[a]	*C. calicophoron*[a] *Calicophoron daubneyi*[a]	*C. calicophoron*[a] *C. daubneyi*[a]
Abomasum	*Haemonchus placei*[b] *Ostertagia ostertagi*[b] *Trichostrongylus axei*[b]	*Haemonchus contortus*[b] *Teladorsagia circumcincta*[b] *T. axei*[b]	*H. contortus*[b] *T. circumcincta*[b] *T. axei*[b]
Small intestine	*Trichostrongylus colubriformis*[b] *Cooperia oncophora*[b] *Nematodirus helvetianus*[b] *Moniezia benedeni*[c], *Moniezia expansa*[c]	*T. vitrinus, T. colubriformis*[b] *Cooperia curticei*[b] *Nematodirus battus, Nematodirus fillicolis, Nematodirus spathiger*[b] *M. expansa*[c]	*T. capricola, T. colubriformis*[b] *N fillicolis*[b] *N. battus, N. spathiger*[b] *M. expansa*[c]
Large intestine	*Oesophagotomum radiatum*[b] *Chabertia ovina*[b]	*Oesophagotomum venulosum, Oesophagotomum columbianum*[b] *C. ovina*[b]	*O. columbianum, O. venulosum*[b] *C. ovina*[b]
Liver	*Fasciola hepatica*[a] *Dicrocoelium dendriticum*[a] *Echinoccocus granulosus*[c]	*F. hepatica*[a], *D. dendriticum*[a] *E. granulosus*[c], *Taenia hydatigena* (*Cysticercus tenuicollis*)[c]	*F. hepatica*[a] *D. dendriticum*[a] *E. granulosus*[c] *T. hydatigena* (*C. tenuicollis*)[c]

[a]Trematodes.
[b]Nematodes.
[c]Cestodes.

as grazers, preferring to feed on grass and forbs (a broad-leafed plant other than grass). In contrast, goats are classified as browsers or intermediate browsers, ingesting substantial amounts of browse (woody plants, vines and brush) even if other nutritional forage is available[2]. Because feeding is also a source of GIN infective stages, it has been hypothesized that such differences between the two host genera should result in distinct strategies against nematode infections, with major consequences to host–parasite relationships. These two divergent strategies rely on a balance between either the development of an immune response (sheep) or the existence of behavioral responses which limit contact with the infective larvae (L3) present in the environment (goats). These two processes (immune response and behavior) are identified as two general mechanisms contributing to regulation of the dynamics of parasitic infections [3,4]. To some extent, these two strategies correspond to the 'fight or flight' theory applied to parasitic micropredators.

Sheep have long represented the paradigm for host–parasite interactions, where development of an immune response modulates nematode biology and associated pathophysiological consequences [5]. The expression of such immunological mechanisms is shown by the substantial differences usually observed in the levels of infection between young and adult animals. Also, an abundance of experimental results has repeatedly underlined the occurrence of immune processes to regulate challenge infections [5].

In goats, it is suspected that the avoidance of the L3, which are associated with grass, is high because of their browsing behavior [6]. It is also hypothesized that, owing to evolutionary processes, this caprine behavior to feed on a high diversity of plants has led to three other differences which might be involved in the regulation of parasite populations, namely a subdued immune response, a more rapid metabolism of xenobiotics and an ability for self-medication.

Goats' limited contact with GIN species results in subdued immune response

The main differences in the regulatory strategies affecting GIN infections in sheep (facing the parasites) and goats (avoiding the parasites) are supported by a few studies comparing infections in the two hosts when grazing together. Depending on whether the epidemiological surveys were performed on herbaceous pastures or on more ligneous rangelands, major differences were found in the intake or susceptibility of adult sheep versus goats to GIN species. In grazing situations, goats are significantly more heavily infected than sheep [7–10]. By contrast, in rangelands, the reverse situation has been described [11,12]. Such differences have been repeatedly attributed to the browsing rather than grazing behavior of goats [6,10]. However, in both sheep and goats, the distribution of worm populations in the host is aggregated, corresponding to negative binomial distributions [13,14].

It is thought that due to this avoidance of infective L3 by goats, evolutionary processes have led to quantitative or qualitative changes in components of the immune response against GIN species developed by goats compared to sheep [9,15,16]. Although the same cell types occur in the digestive mucosae of the two hosts, the efficacy in limiting worm populations appears much lower in goats [9,16,17].

Several studies have illustrated that both the acquisition and the expression of immune responses against GIN species are less efficient in goats than in sheep [9,10,16,18]. The acquisition of a fully expressed immune response appears delayed in goats (12 months compared with 6 months in sheep) [10,18]. In addition, in dairy goats, similar levels of GIN infections between adult and young animals have frequently been reported in contrast to sheep where adult ewes are usually much less heavily infected than young animals [16,18]. Divergences in the expression of immunity between the two hosts have also been observed. When grazing, a strong regulation of egg

[2] Provenza, F. (2003) Behavioural mechanisms influencing use of plants with secondary metabolites by herbivores. Proceedings of the satellite symposium: "*Secondary compounds and browse utilization*", "*Matching herbivore nutrition to ecosystems biodiversity*" VI International Symposium on the Nutrition of Herbivores. Proceedings of an International Symposium held in Merida, Mexico, 19-24th Oct. 2003. UADY publisher, pp 1–11.

Box 1. Ruminant domestication and patterns of feeding behavior

The first prominent change following domestication of *Capra hircus aegagrus* in the Zagros mountain 10,000 years ago was a reduced body weight, inferring that the diets ingested by the would-be-domestic goats (*Capra hircus hircus*) were less nutritious than those of their wild counterparts [49]. A survey carried out in Spain [50] showed that, although sharing the same heterogeneous environment, domesticated ruminants grazed less and browsed more than their wild counterparts. Wild goats (*Capra pyrenaica*) consumed a diet consisting of 41% browse and 59% herbage, whereas domestic goats (*C. hircus*) consumed 81% browse and 19% herbage. Similarly, the diets of wild sheep (*Ovis musimon*, the ancestor of domesticated sheep) compared with domestic sheep (*O. aries*) contained 80% and 48% of herbage, respectively. In other words, sheep were probably keener on herbage than goats before domestication, and the browsing propensity of goats, as well as the fondness of sheep for forbs, has been strengthened by domestication.

Why and when did that evolution happen? It is hypothesized that the location and quality of pasture available to grazing animals in early times depended on their relative economic importance. The 'primary use' of domesticated livestock was clearly for food. 'Secondary use', that is exploiting animals without killing them, such as use for draft harvesting wool or milk occurred later, from 6500 to 4000 BC [51,52]. As cattle were milked and used for draft and plowing, they were probably well cared for, with the best grass being reserved for them. Small ruminants yielded only meat until approximately 4000 BC, when the wool mutation occurred in sheep and gradually upgraded their economic importance, which peaked probably around 2400 to 1500 BC [52]. In contrast, goat wool (mohair) appeared much later. Outside Turkey, significant flocks of mohair-yielding Angora goats were rare until the end of the 19th century. In other words, because cattle and sheep had much higher economic value than goats, they were probably offered better feed since domestication.

Because sheep digest starch much better than cattle, and because wool was so valuable, wool-producing sheep grazed on unsuccessful drought-stricken barley crops, wheat aftermath or were even fed with barley grain during droughts. In the Ancient Fertile Crescent, crops had to be protected against grazing incursions and goats were kept off crops. Cattle were also important in the domestic economy for people to graze them far from home. If goats produced milk, they were kept in confinement and probably hand-fed with browse, and if not, they were grazed in woodlands. Laws restricting goats, and sheep to a lesser extent, to woodlands and shrub lands also probably contributed to the evolution of foraging preferences in small ruminants.

excretion has been described in flocks of adult sheep. Conversely, in goats, a trend for the accumulation of parasites, correlated with higher and constantly increasing egg excretion has generally been found over the whole grazing period [9,10]. In sheep, the development of an immune response is usually associated with four different consequences for the nematodes, namely a reduction of: (i) L3 establishment; (ii) worm development and growth; (iii) female fertility and egg production; and (iv) persistency of adult worms (Table 2). Based on studies in different caprine breeds, it seems that the immune responses associated with (ii) and (iii) also occur in goats but that reduced larval establishment and expulsion of adult worms are rarely observed (D.M. Patterson, Ph.D. thesis, University of Edinburgh, Edinburgh, UK, 1996) [16,19] (Table 2). Finally, evidence has also been obtained suggesting that after first contacts with GIN species, the ability of goats to control challenge infections is much lower than that of sheep and that the 'immune memory' after AH treatment does not last as long [9,20].

Relationships between contact with plant toxins and detoxification of xenobiotics

Data have illustrated that goats, in comparison to sheep, are better suited to tolerate and detoxify natural toxins, in particular plant secondary metabolites (PSMs) [21,22]. This could be partly explained by the caprine browsing habit resulting in evolutionary processes which have favored the development of physiological and metabolic adaptive mechanisms counteracting the potential toxicity of PSMs[2] [22].

Many experimental studies have shown that these metabolic adaptations to natural PSMs also have consequences for the pharmacology or pharmacokinetics of other xenobiotics, including therapeutic drugs [23]. It has been shown repeatedly that goats metabolize anthelmintics (AH) faster than do sheep and such differences have been described for the three principal broadspectrum AH families [24–26]. Consequently, for years, treating goats at the recommended sheep dose rate has resulted in AH underdosing thus causing a reduced efficacy. This phenomenon might also partly explains why the prevalence of anthelmintic resistance in nematodes is so high in goats compared with sheep [27,28], in particular for multi-resistant nematode strains [29,30]. In practice, understanding these differences has motivated specific recommendations to adapt AH doses in goats to achieve a full efficacy against the GIN species [26,31].

Potential of self-medication in ruminants

Ethnoveterinary and ethnomedical traditions testify to the wide and long-standing knowledge on the potential AH properties associated with some natural plant compounds [32,33]. In the current context of the worldwide spread of resistance to chemical AHs, the potential value of some plants or PSMs (e.g. proteinases, sesquiterpene lactones or tannins) as an alternative method of control of GIN species has recently been the focus of increased attention [34–36].

Evidence of self-medicating behavior has been reported in apes [37,38]. In contrast, the possibility that ruminants might benefit from PSMs and consequently might select plants for this purpose has until recently been the focus of little attention [39–41]. For studies dedicated to zoopharmacognosy in small ruminants, goats seem to represent a unique model because of their ability to feed on a much wider and diverse range of plants than sheep. Goat studies

Table 2. Compared consequences of the expressed immune response against GIN stages of the life cycle in sheep and goats

	Sheep	Goat
Reduction of establishment of infective third-stage larvae	Strongly expressed [53,54]	Weakly expressed [15]
Reduced growth and development	Strongly expressed [53]	Strongly expressed [9]
Reduced female fertility	Strongly expressed [53]	Strongly expressed [55]
Reduced persistence of adult worm populations	Strongly expressed [7]	Weakly expressed [7]

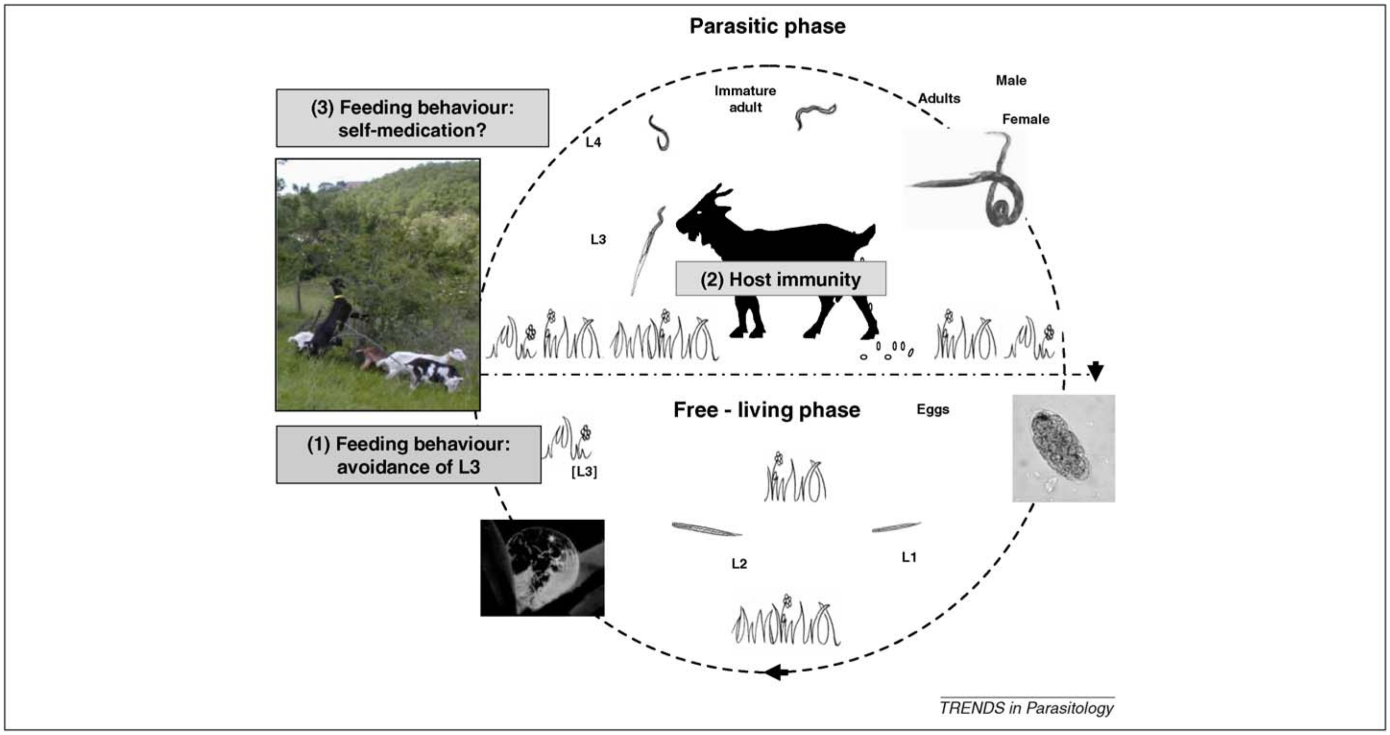

Figure 1. The life cycle of gastrointestinal nematodes (GINs) and modes of regulation. (1.) Owing to the propensity for browsing behavior by goats, avoidance of infective larvae, typically found on grass, reduces the rate of infection. (2.) Immune response affects the different stages of the parasitic phase by four potential processes: **(i)** reduction of establishment of infective third-stage larvae; **(ii)** reduced growth and development; **(iii)** reduced female fertility; and **(iv)** reduced persistence of adult worm populations (Table 2). A low ability to raise an immune response against GINs has frequently been cited in goats. (3.) Consumption of bioactive plants might impair the establishment of larvae and egg excretion by adult worms, but clear-cut evidence of self-medication in ruminants is still missing.

will also help to understand how some adaptive physiological and metabolic mechanisms developed to limit the negative consequences of PSMs can also affect the efficacy of protection against nematodes [25,27].

Browsing goats versus grazing sheep: immune and behavioral regulatory processes

The two reported host strategies (behavior and immune response) are not mutually exclusive. In sheep, despite the predominance of regulatory immune processes, some behavioral mechanisms have been described which contribute to reduced contact with the infective L3, resulting in limited host infections [42,43]. By contrast, in goats, evidence of a continuum in the propensity to browse, with associated consequences for GIN infections, has been found [6]. Results indicative of some degree of immune regulations have been found among goat breeds [16]. Similar to sheep, this has led to exploration of some control methods relying on the development of immune mechanisms, for example genetic selection for resistance to GIN species [19,44] or vaccination [45]. The co-occurrence of behavioral and immune mechanisms in sheep and goats offers the possibility to explore how these regulatory processes interact [46]. In addition, goats offer the possibility to explore the role of a third component, which is the ability of self-medication. Consequently, goats represent a unique model to explore the relationships between the three main processes developed to counteract GIN infections under natural conditions (Figure 1): (i) resistance against nematodes by developing an immune response; (ii) limiting contact with the infective stages by avoidance feeding behavior; and (iii) alleviating worm challenges by self-medication.

Concluding remarks

Comparison of results on the interactions between GIN species and sheep and goats illustrates how the inference of data acquired from one host species compared to a second one can lead to errors; this sometimes causes dramatic consequences in the control of these infections. It also illustrates alternative potential approaches for control. If exploiting the immune response combined with strategic treatments seems an efficient option in sheep, exploiting the feeding behavior, including the potential to self-medicate on natural resources might be as valuable in goats. The previously discussed data also exemplify how holistic approaches are needed and how analysis of the host–parasite relationships should integrate environmental factors such as providing goats with the ability to browse.

A current trend to promote more caprine studies on host–nematode interactions has emerged recently, as illustrated by data produced by the US Southern Consortium for Small Ruminant Parasite Control (http://www.scsrpc.org) or by the recently launched EU Cost Action CAPARA (Goat–Parasite Interactions: from Knowledge to Control) (http://www.capara.org). Hopefully, the expected results of these projects might generate direct data useful for goat industry and might also provide comparative insights on the balance between the various regulatory mechanisms to counteract parasite infections and how they interact. Expected data from such studies might help to better understand not only the interactions between

GIN and goats but also why in other cases of infections with metazoan parasites, for example the nasal bot-fly, *Oestrus ovis* [47]; the small liver fluke, *Dicrocoelium dendriticum* (S. Sotiraki, Ph.D. thesis, Aristotle University, Thessaloniki, Greece, 1999); or the scabies mite, *Sarcoptes scabiei* [48], the caprine ability to develop a fully expressed immune response also seems deficient based on epidemiological or pathophysiological data.

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