1.1. Gastrointestinal nematode infection in sheep

The major species of nematodes infecting the gastrointestinal tract of ruminants belong to the family *Trichostrongylidae.* This family includes the genera *Teladorsagia*, *Cooperia, Haemonchus, Trichostrongylus* and *Nematodirus* (Schnieder, 2006). These nematodes have a simple direct life cycle consisting of an egg stage, five larval stages and an adult stage (Figure 1.1). They do not need an intermediate host. The life cycle of a nematode can be divided into two phases, the free-living phase in the external environment and the parasitic phase in the host (Waller, 1998). After the adult worms mate, the females lays eggs in the abomasum or the small intestine of the infected animal, which are excreted with the faeces and contaminate the pastures. The eggs hatch into the first stage larvae (L1), which develop and moult for the first time to the unsheathed second larval stage (L2). Without casting the sheath they moult to the sheathed third larval stage (L3) (Schnieder, 2006). The first and second larval stages have the ability to feed on soil microbes and bacteria but they are not able to move. Whereas, the third stage larvae are active and can crawl onto the grass leaves to be taken up by grazing animals (Waller, 1998; Schnieder, 2006). Under ideal conditions of temperature and humidity, the development from the hatching of the eggs to the third larval stage takes about 4 to 6 days. Exceptionally for *Nematodirus* spp., this development takes more than two months.

The parasitic phase starts after the ingestion of infective larvae (L3) by the host. These larvae lose their sheath in the host to become parasitic L3 and migrate to their host organ (abomasum or small intestinal). The larvae enter the gastric glands where they moult for the third time to the fourth larval stage (L4) and emerge back into the lumen of the gastrointestinal tract. After another moulting, the L4 develop into immature adults (L5). Afterwards, they become mature adults **(**Schnieder, 2006; Sutherland and Scott, 2009**)**. The adult stages of nematodes survive in the lumen of the gastrointestinal tract of ruminants. The prepatent stage, which is the period from the infection of the host until the first eggs are excreted with the faeces, is about 3 weeks. The fecundity of adult female worms ranges form 40 for *Nematodirus* spp. (Coyne *et al.,* 1991) to over 5000 eggs per day for *H. contortus* (Le Jambre, 1995).

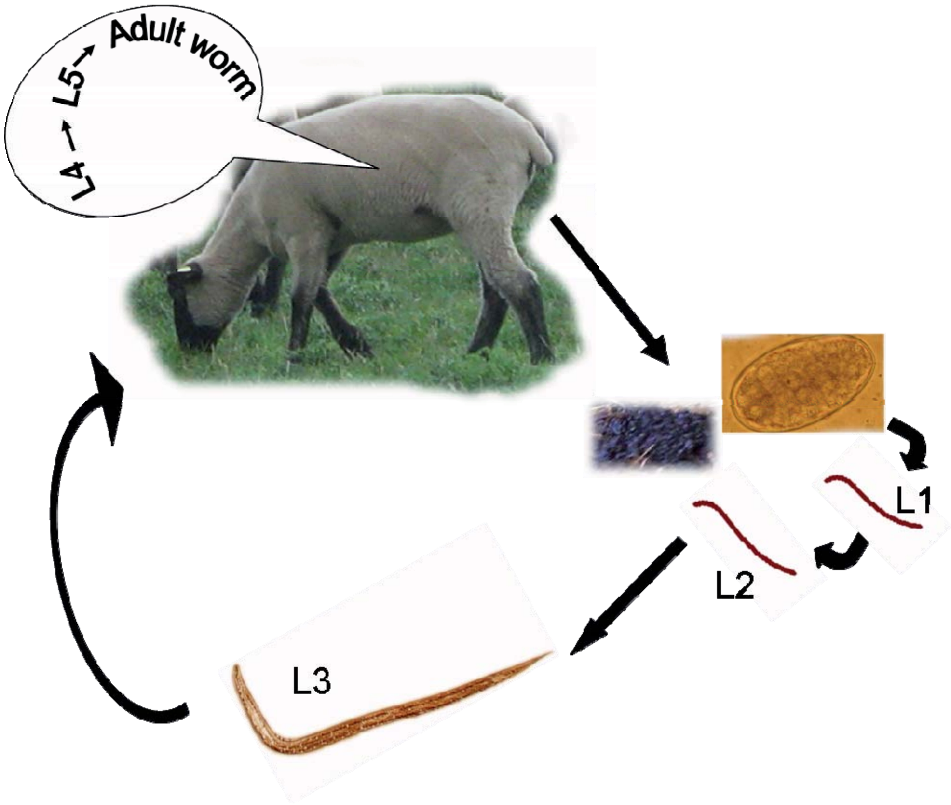

Fig. 1.1 The life cycle of gastrointestinal nematodes

Infections with gastrointestinal nematodes cause severe economic losses in the sheep industry (Davies *et al.*, 2005). Beside the direct costs of these infections including anthelmintic drugs and veterinary services, indirect costs are caused. These are due to reduced performances of clinically and sub-clinically infected animals. Infections with gastrointestinal nematodes in the field are usually mixed infections and involve several different species of nematodes. Its impact on the animals is mainly influenced by the intensity of the infection and the physiological status of the host. Growing lambs and periparturient ewes are most susceptible to the infection by nematodes (Shubber *et al.*, 1981; Bishop and Stear, 2001). The common clinical symptoms of the infection with gastrointestinal nematodes are anorexia, diarrhea, emaciation, anaemia. Heavy infections may cause the death of infected animal (Steel *et al.*, 1982; Behrens, 2001).

Resistance and resilience explain the responses of the host animal to parasitic infections. Woolaston and Baker (1996) defined resistance as "the ability of a host to initiate and maintain responses to suppress the establishment of parasites and/or eliminate the parasite load", and resilience as "the ability of the host to maintain a relatively undepressed production level under parasite challenge". Faecal egg counts (FEC) is used worldwide to measure host animal resistance against gastrointestinal nematode infections and to estimate the breeding value of host resistance (Rahmann and Seip, 2006; Stear *et al.*, 2007). Resilience can be assessed by comparison between the performance of nematode-infected and non-infected animals (Albers *et al.*, 1987).

Table 1.1 Prevalence of gastrointestinal nematode infections in sheep reported by different authors from various regions in Germany

Region	**Prevalence of GIN %**	**Author**
Taunus	80	SCHNEIDER (1942)
Württemberg	95	FORSTNER (1960)
Bayern	99	GRÄNZER *et al.* (1979)
Hessen	51	BENESCH (1993)
Oberbayern	100	REHBEIN *et al.* (1996)
Bonn	54	SCHWENK (1998)
Schwäbische Alb	100	REHBEIN *et al.* (1998)
Sachsen-Anhalt	100	GRZONKA *et al.* (2000)
Niedersachsen	71	MORITZ (2005)

Most studies focussing on nematode infestations in Germany have reported a moderate to high prevalence of infection in sheep (Table 1.1). The predominant nematode species were *Teladorsagia* spp., *Haemonchus contortus, Trichostrongylus* spp. *Nematodirus* spp. and *Cooperia* spp. (Benesch, 1993; Rehbein *et al.,* 1996).

1.2. Strategic control of gastrointestinal nematodes

There are several ways of controlling nematodes in either the host animal or in the environment to which the host animal or the parasite is exposed. In the following, the most widely used control methods will be described.

1.2.1. Anthelmintic treatments

The traditional method to control the gastrointestinal nematodes is the use of chemical dewormers. In most farms in Germany, the animals are usually treated two or more times per year. The major two treatments take place at the beginning of the grazing season and at the end of the summer. Some farmers treat their animals additionally at the end of the grazing period before the animals return to the barns. The treated animals are generally moved to clean pasture, if it is available, to minimise the re-infections. There are three major classes of anthelmintics that are widely used for the control of nematodes in small ruminants: Benzimidazoles, Avermectins / Milbemycins and Imidazothiazoles / Tetrahydropyrimidines (Kaplan*,* 2004; Hale, 2006). However, the frequent use of these compounds has caused resistance to the anthelmintics in numerous nematode species. Recently, a new chemical class of synthetic anthelmintics (the Amino-Acetonitrile Derivatives) was discovered **(**Kaminsky *et al.*, 2008). Nematode resistance to this anthelmintic has not yet been observed.

1.2.1.1. Anthelmintic resistance (AR)

The anthelmintic resistance was defined by Prichard *et al.* (1980) as: “Resistance is present when there is a greater frequency of individuals within a population able to tolerate doses of a compound than in a normal population of the same species and is heritable”. The use of anthelmintics may inevitably lead to AR (Alvarez-Sanchez *et al.*, 2006). The parasites can become resistant to an anthelmintic in a very short period of time. The period between the approval of an anthelmintic and the first report of its resistance varied from 3 to 9 years (Kaplan 2004). The phenomenon of AR in gastrointestinal nematodes of small ruminants is world wide observed (Fleming *et al.*, 2006). Resistance being developed by nematodes of sheep was first reported in Germany by Bauer *et al.* (1987) and Düwel *et al.* (1987).

1.2.1.2. Targeted selective treatment

In practice, if an animal population is infected by nematodes all the animals will be treated. In the selective treatment approach only those animals are treated that require the treatment most. Thus, highly susceptible or infected animal, which are responsible for the heavy environmental contamination with nematode eggs, will be drenched. Through this approach the frequency of anthelmintic treatments and the excessive exposure of the worms to the anthelmintics can be sustainably reduced. This in turn will slow down the spread of AR (Hoste *et al.*, 2002; Gallidis *et al.*, 2009). Worms that have not been exposed to the drugs are supposed to be in refugia and are, therefore, still susceptible to the anthelmintics (Jackson *et al.*, 2009; Kenyon *et al.*, 2009). As the proportion of larvae in refugia increases, the development of AR decreases extensively.

The identification of animals, which are suspected to be highly infected with nematodes, relies mainly on the faecal eggs count (FEC). However, this method is time consuming and also cost-intensive. That led to looking for simpler, cheaper and safe indicators of nematode infections, such as scoring mucosal colour (FAMACHA$^{©}$), scoring body condition as well as dag score (van Wyk and Bath, 2002; Broughan and Wall, 2007; Riley and van Wyk, 2009; Bath and van Wyk, 2009).

1.2.2. Grazing management

The management of pastures basically aims to reduce the extent of infections and re-infections by reducing the intake of infective larvae of the grazing animals from the pasture. To obtain a safe pasture, grazing be must inhibited for 6 months during cold weather or for 3 months during hot, dry weather (Fleming et al; 2006). Michel (1985) classified strategies of the grazing management as following: preventive grazing is based on raising worm-free animals on a clean pastures; evasive grazing relies on the movement of animals to a clean pasture just before the infectious larvae are evolved on the original pasture; diluting grazing exploits the concurrent grazing of susceptible animals with a greater population of relative resistant animals of the same or different species in order to reduce the contamination of the pasture with parasite eggs. However, these strategies can be only applied if a large pasture size is available.

Barger (1997) suggested that the control of nematodes based on the grazing management may be unsustainable when considered in isolation. Nevertheless, the use of this strategy combined with anthelmintic treatments probably will be more effective in parasite control. However, it may not reduce AR.

1.2.3. Dietary supplementation

The importance of nutrition for the control of nematodes is firstly expressed as the influence of a parasite on host metabolism and secondly as the effect on resistance or tolerance of the host against the parasites (Coop and Kyriazakis, 1999). The infection with gastrointestinal nematodes reduces the feed intake and at the same time the efficiency of feed utilization, whereas the main impact of the infection is the loss of endogenous protein in the form of whole blood, plasma, sloughed epithelial cells and mucus (Coop and Holmes, 1996; Knox *et al.*, 2006). In young animals, infections may also disrupt the absorption of some minerals, e.g. phosphorus, calcium, copper and magnesium (Sykes and Greer, 2003).

Many studies reported that sheep show a higher resilience when fed a high level of metabolizable protein. The negative impact of the infection on weight gain and wool growth as well as on blood parameters such as hematocrit, total serum protein and albumin concentrations was smaller in animals supplemented with high protein levels when compared to animals supplemented with low protein levels (Abbott *et al.*, 1988; van Houtert *et al.*, 1995; Coop and Holmes, 1996; van Houtert and Sykes, 1996). In the case of protein scarcity, a high level of protein can also improve the resistance of the parasitised host animals (Coop and Kyriazakis, 2001). Through higher protein supplementations the immune response of infected sheep can be increased resulting in reduce the infection parameters (van Houtert *et al.,* 1995b; Datta *et al.,* 1998; Steel, 2003).

However, the effect of the protein supplementation on the resistance of sheep against GIN is less pronounced than the effect on the resilience, especially in breeds which are relatively resistant to nematode infections (Coop and Kyriazakis, 1999). Since the ruminants are known to use plants with low protein contents and less degradable fibres effectively, protein supplementation as an alternative or supportive strategy to control GIN in sheep seems to be relatively uneconomical.