

1 Knowing the players- the GI nematodes and 2 what's out there for treatment

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4 Abstract

5 Gastrointestinal nematodes are the most costly and deadly parasites affecting small ruminants. There are 9 genera
6 that cause clinical disease in sheep and goats. Starting in the 1960's, modern chemical anthelmintics were developed
7 to combat these gastrointestinal parasites. Now, there are four major classes of anthelmintics available for use in
8 sheep and/or goats. These proceedings will discuss the parasites that currently affect small ruminants in the United
9 States and the anthelmintics currently labeled to treat these parasites.

10 Keywords

11 Small Ruminant, Parasites, Anthelmintics, Nematodes

12 Gastrointestinal nematodes

13 H-O-T Complex

14 There are three genera that dominate the others in terms of frequency of isolation and presentation of clinical
15 disease. These genera create what is known as the "H-O-T Complex" and include the following:

- 16 • *Haemonchus contortus*
- 17 • *Ostertagia* (now known as *Teladorsagia*) spp.
- 18 • *Trichostrongylus* spp.

19 *Haemonchus contortus*, also known as the "Baber Pole Worm", is one of the deadliest gastrointestinal nematodes.

20 This nematode is a blood-sucking parasite that attaches in the abomasum. This parasite prefers very warm, humid,

21 and wet conditions making late spring, summer, and early fall the peak seasons for infestation. Clinical signs of
22 disease include profound anemia, submandibular edema (bottle jaw), diarrhea, dehydration, poor growth and
23 unthrifty appearance, and death.

24 *Teladorsagia* (formerly known as *Ostertagia*) spp., including *Teladorsagiacircumcincta*, is also known as the
25 “Brown Stomach Worm”. Adults are found in the abomasum and prefer a cooler, drier environment when compared
26 to *Haemonchuscontortus*. Like *Ostertagia* spp. found in cattle, *Teladorsagia* spp. can encyst in gastric glands and
27 undergo a hypobiotic state leading to abomasal damage when adults excyst from these glands. Clinical signs in
28 small ruminants include decreased appetite, diarrhea, malabsorption of nutrients, and an unthrifty appearance
29 *Trichostrongylus* spp., including *Trichostrongyluscolubriformis* and *Trichostrongylusaxeii*, affect small ruminants. *T.*
30 *axeii*, (also known as the “stomach hair worm”) like the previous two gastrointestinal parasites mentioned, is found
31 in the abomasum while *T. colubriformis* (also known as the “bankrupt worm”) is found in the small intestine. These
32 parasites also prefer a cooler, drier environment but will not undergo a hypobiotic state. Clinical signs of
33 *Trichostrongylus* infestation include diarrhea, anorexia, and weight loss as well as damaged abomasal and intestinal
34 mucosa leading to impaired nutrient absorption.

35 All three of the gastrointestinal nematodes found in the “H-O-T Complex” have the same lifecycle. This lifecycle
36 involves the ingestion of the infective L3 larval stage that migrates to either the abomasum or small intestine. Here,
37 the larvae mature to the adult form and start to cause clinical signs of disease. These adults lay eggs that are passed
38 into the feces, hatch, and then mature to the infective larval stage. The pre-patent period for all three of these
39 nematodes is roughly 21 days.

40 *Bunostomum* spp.

41 *Bunostomum* spp., also known as “hookworms”, are not considered a major parasitic concern in sheep and goats in
42 the United States. They do, however, potentially exacerbate other parasitic disease presentation. Like
43 *Haemonchuscontortus*, adult *Bunostomum* suck blood from the host leading to anemia, weakness, and death. The
44 main *Bunostomum* species to affect small ruminants is *B. trigonocephalum* which is not considered a zoonotic
45 pathogen. Sheep and goats can, however, carry *B. phlebotomum* (the hookworm of cattle) which is known to cause
46 cutaneous larval migrans in humans.

47 The lifecycle of *Bunostomum* differs from that of the H-O-T Complex nematodes. Adult hookworms lay eggs in the
48 small intestines and eggs are passed into the environment. These eggs hatch and develop into the infective third-
49 stage larvae. These larvae will penetrate the skin or mucous membranes of the sheep or goat and travel via the
50 bloodstream to the lungs. The larvae will then mature to fourth-stage larvae in the lungs and will be coughed up to
51 the oropharynx and swallowed. Once in the gastrointestinal tract, the larvae will migrate to the small intestines and
52 become adults. The prepatent period for this parasite is nine to ten weeks. Treatment for this parasite includes
53 benzimidazole and imidazothiazole anthelmintics. Macrocyclic lactones and tetrahydropyrimidines are not labeled
54 for treatment of hookworms.

55 *Cooperiaspp.*

56 There are two major *Cooperia* species that affect sheep and goats- *C. curticei* and *C. surnabada*. This
57 gastrointestinal nematode is generally less pathogenic than other nematodes in small ruminants. Clinically, *Cooperia*
58 can lead to unthriftiness, weight loss, and decrease productivity although primary infection is rare. This parasite can
59 contribute to clinical signs seen from other gastrointestinal nematodes.

60 The lifecycle of this parasite is similar to the H-O-T complex parasites. Adults are found in the small intestine and
61 eggs are put into the environment where they hatch. The larvae develop into infective third-stage larvae, are
62 consumed, and migrate to the small intestine. Once there, the larvae become adults in 2-3 weeks and begin to cause
63 clinical disease. All four available classes of anthelmintics can be used to treat *Cooperia*.

64 *Nematodirus spp.*

65 Three species of *Nematodirus* will cause disease in sheep and goats- *N. spathiger*, *N. filicolis*, and *N. battus*. *N.*
66 *battus* is the most pathogenic and causes damage to the mucosa of the small intestine leading to severe diarrhea,
67 decreased appetite, lethargy, dehydration, and death. Although prevalent in the United States, this parasite is more of
68 a concern in Europe.

69 The lifecycle of *Nematodirus* is unique. The egg is passed into the environment and the larvae develop to the third-
70 stage larvae within the egg. These third-stage larvae can remain in the egg over winter and hatch in the spring. These
71 eggs can survive over two years on pasture. Once the third-stage larvae hatch they are consumed by the sheep or
72 goat and migrate to the small intestine where they become adults. Due to the ability to overwinter on the pasture and

73 contaminate the pasture with infective larvae in the spring, *Nematodirus* is of major concern in lambs and kids.
74 Lambs and kids that are beginning to graze on spring grasses (generally around 6-12 weeks of life) are exposed to
75 this hatching parasite. This nematode is also unique diagnostically due to its large egg compared to other
76 gastrointestinal nematodes. Treatment is best achieved by using the benzimidazole anthelmintics.

77 *Oesophagostomum* spp.

78 *Oesophagostomum* spp., also known as “nodule worm” or “nodular worm”, has one main species that affects sheep
79 and goats- *O. columbianum*. The main clinical sign found with this parasite is nodular enteritis. The larvae of this
80 parasite will penetrate the large intestinal mucosa, leading to inflammation and the formation of nodules within the
81 intestinal wall. These nodules can affect peristalsis and lead to diarrhea or constipation, weight loss due to
82 malabsorption, and weakness in the animal. Nodules may lead to rupture of the intestine causing peritonitis.

83 The lifecycle of this parasite starts with eggs being deposited into the environment. The eggs hatch on pasture and
84 larvae grow into the third-stage infective larvae. Third-stage larvae migrate to the small intestine (the ileum) and
85 burrow into the wall of the intestine where they will become fourth-stage larvae. These larvae will either remain in
86 the wall of the ileum or come out of the intestinal wall and migrate to the large intestine where they will become
87 adults. Larvae that remain in the ileum will develop into mineralized cysts. The prepatent period for this parasite is
88 five weeks. All classes of anthelmintics can be used to treat nodular worms.

89 *Strongyloides* spp.

90 *Strongyloides papillosus*, also known as “threadworms”, are typically non-pathogenic in sheep and goats although
91 lambs and kids are more at risk of serious disease. In lambs and kids, these parasites can cause severe diarrhea,
92 dehydration, anorexia and anemia. After initial infection, strong immunity is developed, and animals will have
93 resistance to the parasite.

94 The lifecycle of this parasite is more complicated than other gastrointestinal nematodes. First, female *Strongyloides*
95 spp. can reproduce without the male (a process called parthenogenesis). Also, this parasite has both free living and
96 parasitic generations. The parasitic generation will see male and female larvae hatch from the eggs and develop into
97 the infective third-stage larvae in the environment. The larvae will infect the host either by penetrating the skin of
98 the udder or interdigital space of the foot, or by penetrating the oral mucosa. Once larvae enter the host, it may

99 encyst in the tissue (especially the udder) and can be passed to offspring during lactation. Encysted larvae can
100 survive up to 12 weeks in the musculature of some animals. Alternatively, the larvae that entered via the interdigital
101 space or oral mucosa will travel via the blood stream to the lungs where they are then coughed up and swallowed.
102 Finally, they will migrate to the small intestines to become adults and produce eggs. The free-living parasites,
103 female and male larvae develop into adults on the pasture and produce all female offspring. These larvae develop
104 into infective third-stage larvae and will enter a host. The pre-patent period is roughly 8-14 days. Treatment for
105 *Strongyloides* includes macrocyclic lactones and albendazole. Imidazothiazoles, tetrahydropyrimidines, and
106 fenbendazole will only kill adults and not migrating larvae.

107 *Trichuris* spp.

108 *Trichuris ovis*, also known as “whipworm”, is typically non-pathogenic unless other parasitic infection is present.
109 This parasite will exacerbate clinical signs seen with other parasitic infections. This parasite has a characteristic
110 ovoid egg that is double-operculated. This egg is extremely hardy and survives in the environment for years. Clinical
111 signs, although rare, include diarrhea (sometimes bloody), abdominal pain, unthriftiness, and dehydration.
112 The lifecycle of this parasite differs from other nematodes. The larvae will develop into the infective third stage
113 within the egg and the egg will be consumed by the host. Once in the host, the opercula will be digested and release
114 the larvae which will penetrate the small intestinal epithelium. Over 2-10 days, the larvae will continue to develop
115 then migrate to the cecum where they will become adults. The prepatent period is about 3 months. Infection with
116 this parasite often indicates poor management and/or immunosuppression within the host. Most available
117 anthelmintics can be used to treat this parasite although there has been resistance shown to levamisole.

118 Anthelmintics used against gastrointestinal nematodes

119 There are four main classes of anthelmintics commonly used in small ruminants. These four classes, and
120 the agents that belong in the classes, are as follows:

- 121 • Benzimidazoles- fenbendazole and albendazole (introduced in the 1960's)
- 122 • Macrocyclic lactones- ivermectin (introduced in the 1980's) and moxidectin (introduced in 1997)
- 123 • Imidazothiazoles- levamisole (introduced in the 1960's-1970's))

124 • Tetrahydropyrimidines- pyrantel pamoate and morantel tartrate (introduced in the 1980's)

125 The mechanism of action of these dewormer classes differ. The benzimidazole class directly impacts the energy
126 metabolism of the parasite. These anthelmintics achieve this by binding to beta tubulin, a building block of
127 microtubules which are used for energy metabolism by the parasite. Macrocyclic lactones include ivermectin, an
128 avermectin, and moxidectin, a milbemycin. These compounds cause paralysis and death of the parasite by
129 interfering with GABA-mediated neurotransmission. Moxidectin is known to be more potent than ivermectin and
130 acts on a different neurotransmitter. The imidizothiazoles and tetrahydropyrimidines are both considered nicotinic
131 agonists. This means that they cause a spastic paralysis of the parasite by acting on neurotransmitter receptors that
132 initiate muscle contraction. Both classes mimic acetylcholine.

133 Fenbendazole is relatively safe, even at high doses, and is labeled for goats. Albendazole should not be used within
134 the first 30 days of gestation- it is embryotoxic and may cause early embryonic loss. Albendazole is labeled for
135 sheep and goats, although the label for goats is only for treatment of liver flukes. Ivermectin, if grossly overdosed,
136 may lead to neurologic signs including ataxia and depression and is labeled for sheep. Moxidectin has a much higher
137 margin of safety and is labeled for sheep. Levamisole, on the other hand, has the narrowest margin of safety and
138 may cause depression, hyperesthesia, and seizures. Empirically, it may also cause late term abortions in sheep if
139 used in the last trimester. This product is labeled for sheep. Pyrantel pamoate is not labeled for sheep or goats and
140 therefore not commonly used. Morantel tartrate is labeled for goats and marketed as a top-dress for feed.

141 Conclusion

142 There are many gastrointestinal nematodes of sheep and goats. Many do not play a primary role in disease but can
143 lead to exacerbated clinical signs when co-infection with another parasite is present. The most pathogenic
144 gastrointestinal nematode of small ruminants is *Haemonchus contortus*. There are currently four classes of
145 anthelmintics commercially available to treat gastrointestinal nematodes in small ruminants. Not all these products
146 will uniformly treat all the gastrointestinal nematodes, and each anthelmintic class has a different mechanism of
147 action. It is important to understand and recognize both the gastrointestinal genera of small ruminants and the
148 current treatment modalities available to help producers navigate parasite infection in their sheep and goats.

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