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Complete Anthelmintic Resistance Observed in U.S. Meat Goats

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Summary

The objective was to examine fecal-egg-count (FEC) reduction in meat goats entered into the University of Maryland (2008 to 2016) or Eastern Oklahoma State College (2014 to 2017) buck test. Weaned-buck kids from private farms in 21 United States were entered into the Western Maryland Pasture-Based, Meat-Goat Performance Test in Keedysville (Maryland; 2008 to 2016), or the Oklahoma Forage-Based, Meat-Goat Buck test at Eastern Oklahoma State College, Wilburton (Oklahoma; 2014 to 2017) in early summer. The buck tests examined growth and response to natural parasite infection on a pasture-based diet in a common environment. Between 18 and 84 goats were enrolled each year. All goats were dewormed upon arrival with moxidectin (0.4 mg/kg), albendazole (20 mg/kg) or fenbendazole (10 mg/kg), and levamisole (12 mg/kg). Feces were collected directly from the rectum to determine FEC on day of arrival (Day 0 or FEC_1) and 10 days to 13 days later (FEC_2). The FECR ($1 - (FEC_2/FEC_1) \times 100$) was calculated for 300 observations and 137 observations for the Maryland and Oklahoma tests, respectively, and analyzed using PROC GLM of SAS. The range in FEC_1 among years was between 813 eggs/g ± 519 eggs/g and 3014 eggs/g ± 454 eggs/g (year, $P = 0.005$), and 14 eggs/g ± 151 eggs/g and 1036 eggs/g ± 178 eggs/g (year, $P < 0.001$) for FEC_2 in the Maryland test. The LS mean for FECR was 82.1% ± 4.7% and ranged between 60% and 96%. Year was significant, but not linear ($P < 0.001$). The highest FECR was in 2009 (99.2% ± 4.5%), but the lowest was in 2010 (48.2% ± 5.3%). In the Oklahoma test, FEC were 2311 ± 457 (year, $P = 0.08$) and 426 ± 142 (year, $P < 0.001$) eggs/g on Days 0 and 10 days to 13 days later, respectively. The FECR was 73.4% ± 5.8% (year, $P < 0.001$), and ranged between 47.6% and 98.6%. The highest FECR was in 2015 (91.4% ± 7.7%) and the lowest was in 2014 (48.9% ± 5.2%). In both buck tests, the FECR was as low as 48% indicating a dire problem for the goat industry.

Key Words: *Anthelmintic Resistance, Gastrointestinal Nematodes, Goats*

Introduction

There were more than 2.1 million meat goats reported in the United States in 2016 on close to 119,000 farms (USDA, 2017). Total non-predatory goat deaths in 2015 were 382,367 of which 24.8% were associated with parasites and 16.1% and 21.3% additional losses were due to "found dead" or "unknown", respectively, of which a proportion could be associated with parasites (USDA, 2017). The USDA equated this to more than $8.7 million in losses, not including cost of treatments or labor. The Pacific and Northeast regions had the lowest losses, but gastrointestinal nematode (**GIN**) parasites can be found in these regions as well as throughout the United States and worldwide (Zajac, 2006). Anthelmintic resistance is highly prevalent in goats (Howell et al., 2008; Kaplan and Vadyashankar, 2012; Crook et al., 2016), originally reported in the United States about 30 years ago (Uhlinger et al., 1988; Craig and Miller, 1990) creating difficulty in GIN parasite management. Current information provided by the American Consortium for Small Ruminant Parasite Control (**ACSRPC**, *www.wormx.info*) includes deworming with multiple classes of anthelmintics, but on an as-needed basis (anemia, hypoproteinemia, etc.; Kaplan, 2017). However, goats in the Southeastern United States have experienced anthelmintic resistance to multiple anthelmintic classes for more than 10 years (Zajac and Gibson, 2000; Kaplan et al., 2005), calling into question the practicality of anthelmintic combinations in meat goats. Therefore, the objective of this study was to determine the efficacy of such combinations for treatment of gastrointestinal nematodes on a subset of the population of meat goats across the Midwest, Southeastern, and Eastern United States, weaned buck kids entering buck performance tests.

Materials and Methods

Weaned-buck kids from private farms were entered into the Western Maryland Pasture-Based, Meat-Goat Performance Test in Keedysville (Maryland; 2008 to 2016) or the Oklahoma Forage-Based Meat, Goat-Buck test at Eastern Oklahoma State College, Wilburton (Oklahoma; 2014 to 2017) in early summer. In the Maryland test, 18 states were included, and in the Oklahoma test, 15 states were included (Table 1). Between 18 goats and 84 goats were enrolled each year, which came from 13 to 38 farms. The buck tests examined body weight changes over time and response to natural GIN infection on a pasture-based diet in a common environment. In some years of the MD test, goats were supplemented with 225 g/day per goat of a grain product or by-product dependent on forage quality. All goats were orally dewormed upon arrival with moxidectin (0.4 mg/kg; Cydectin®; Boehringer Ingelheim Vetmedica, Inc., St. Joseph, Mo., USA), albendazole (20 mg/kg; Valbazen®; Zoetis Inc., Kalamazoo, Mich., USA) or fenbendazole (10 mg/kg; Safe-Guard®; Intervet/Merck Animal Health, Madison, N.J., USA), and levamisole (12 mg/kg; Prohibit®; Agri Laboratories, Ltd., St. Joseph, Mo., USA). Feces were collected directly from the rectum to determine fecal egg count (**FEC**) using a modified McMaster's method with a sensitivity of 50 eggs/g (Whitlock, 1948) on day of arrival (Day 0 or $\mathbf{FEC_1}$) and 10 days to 13 days later ($\mathbf{FEC_2}$). For the Maryland test, 2014 was omitted from the data set because the second fecal sample was collected on day 6.

The FEC reduction (**FECR**) was determined on each goat by the following equation: $1 - (FEC_2/FEC_1) \times 100$. The FEC_1 was used rather than a control or untreated group of goats (Cole et al., 1992), since all goats were dewormed. If FEC_1 was less than 200 eggs/g, that animal was deleted from the analyses because of poor sensitivity (Maryland, n = 119; Oklahoma, n = 17). If FEC_2 was greater than FEC_1, then FECR was considered to be 0. If the FECR percentage is less than 95% and the lower 95% confidence limit for the reduction is less than 90%, the GIN population was considered resistant. There were 300 observations and 137 observations used for the Maryland and Oklahoma tests, respectively (Table 1). For each goat test, data were analyzed using general linear models (SAS; SAS Inst., Inc., Cary, N.C., USA) with year in the model to determine FECR, as well as FEC_1 and FEC_2. State was initially included in the model, but because four states in each of the MD and OK tests had fewer than four observations, it was removed from the final model, and was not a significant variable ($P > 0.12$). The proportion of goats with a FECR > 90% were calculated for each year.

Table 1. The number of goats entered into the Western Maryland Pasture-Based, Meat-Goat Performance Test in Keedysville (MD; 2008-2016) or the Oklahoma Forage-Based, Meat-Goat Buck test at Eastern Oklahoma State College, Wilburton (OK; 2014-2017) from each state listed. State was initially included in the model to analyze fecal egg count reduction, but because four states in each of the MD and OK tests had fewer than 4 observations, it was removed from the final model, and was not a significant variable ($P > 0.12$).

State	MD	OK
Alabama	10	3
Arkansas	-	3
Delaware	18	-
Georgia	-	15
Illinois	26	13
Indiana	9	1
Iowa	-	6
Kansas	14	30
Kentucky	62	6
Maryland	48	-
Missouri	7	5
Mississippi	3	6
North Carolina	18	1
New Jersey	6	-
Ohio	2	-
Oklahoma	6	22
Pennsylvania	6	-
Tennessee	18	4
Texas	-	18
Virginia	43	-
Vermont	1	-
West Virginia	3	4
Total	300	137

Results

Maryland Test

The range in FEC_1 among years was between 813 eggs/g ± 519 eggs/g and 3014 eggs/g ± 454 eggs/g (year, $P = 0.005$), and in FEC_2 was between 14 eggs/g ± 151 eggs/g and 1036 eggs/g ±

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178 eggs/g (year, $P < 0.001$; Fig. 1A). The overall least squares (**LS**) mean and standard error (**SE**) of FECR was 82.1% ± 4.7% and ranged between 60% and 96%. Year was significant, but not linear ($P < 0.001$; Fig. 1B). The highest FECR was in 2009 (99.2% ± 4.5%), and the lowest was in 2010 (48.2% ± 5.3%). Gastrointestinal nematodes were considered resistant (FECR % < 95% and lower 95% confidence limit < 90%, data not shown) in 2008, 2010, 2011, 2013, 2015, and 2016. The percentage of goats with a FECR > 90% were 78.1, 97.4, 25.0, 63.1, 94.4, 69.2, 67.2, and 38.2 in 2008, 2009, 2010, 2011, 2012, 2013, 2015, and 2016, respectfully.

Oklahoma Test

The overall LS mean and SE of FEC_1 was 2311 ± 457 (year, $P = 0.08$) eggs/g, and FEC_2 was and 426 ± 142 (year, $P < 0.001$; Fig. 2A) eggs/g. The overall LS mean and SE of FECR was 73.4% ± 5.8% (year, $P < 0.001$), and ranged between 47.6% and 98.6%. The highest FECR was in 2015 (91.4% ± 7.7%) and the lowest was in 2014 (48.9% ± 5.2%; year, $P < 0.001$; Fig. 2B). Mean FECR analyzed by year indicated GIN resistance for each year. The percentage of goats with a FECR > 90% were 28.2%, 83.3%, 73.0%, and 55.3% in 2014, 2015, 2016, and 2017, respectfully.

Discussion

Information generated by the ACSRPC (*www.wormx.info*) suggests that using multiple anthelmintic combinations to deworm small ruminants will help to reduce the development of anthelmintic resistance. In both buck tests, the FECR after such combination treatment was effective in a relatively large proportion of goats in most years examined. However, FECR was as low as 48%, suggesting diligence needed in the control of GIN for goats. Anthelmintic resistance was recorded for GIN populations in all years in both goat tests.

The observed efficacy to anthelmintic treatment will be variable both within and between goats depending on the amount of variability in the response to treatment; the true efficacy is always unknown (Martin et al., 1989; Vidyashankar et al., 2012). The overdispersed distribution of GIN in animals on the same farm and differences in GIN intensity among farms can result in large differences in pre-treatment values among animals, and technical variation in FEC analyses, goat breed differences, spatial differences among farms, and differences in sampling time all contribute to variability in FEC results (Vidyashankar et al., 2012). In addition, small sample size after removing goats with low or zero pre-treatment FEC also increases variability. While goat producers were encouraged not to deworm goats before the test began, it is possible that some goats were treated, which could influence the FECR test that would have used pre-selected worms that did not represent a normal population (Coles et al., 1992).

Fig. 1. Distribution of fecal egg count (FEC) and FEC reduction (FECR) of goats entered into the Western Maryland Pasture-Based, Meat-Goat Performance Test in Keedysville (MD; 2008-2016). Panel A: least squares means FEC determined on day 0 (white stack) or 10 to 12 days later (black stack). Panel B: FECR with lower and upper borders of the box that represent the 25th and 75th percentiles, respectively. Mean (dashed line) and median (solid line) values are presented within the box. Whiskers above and below the box indicate the 90th and 10th percentiles and the circles represent individual values outside of this range. Values within each box represent the number of animals included each year.

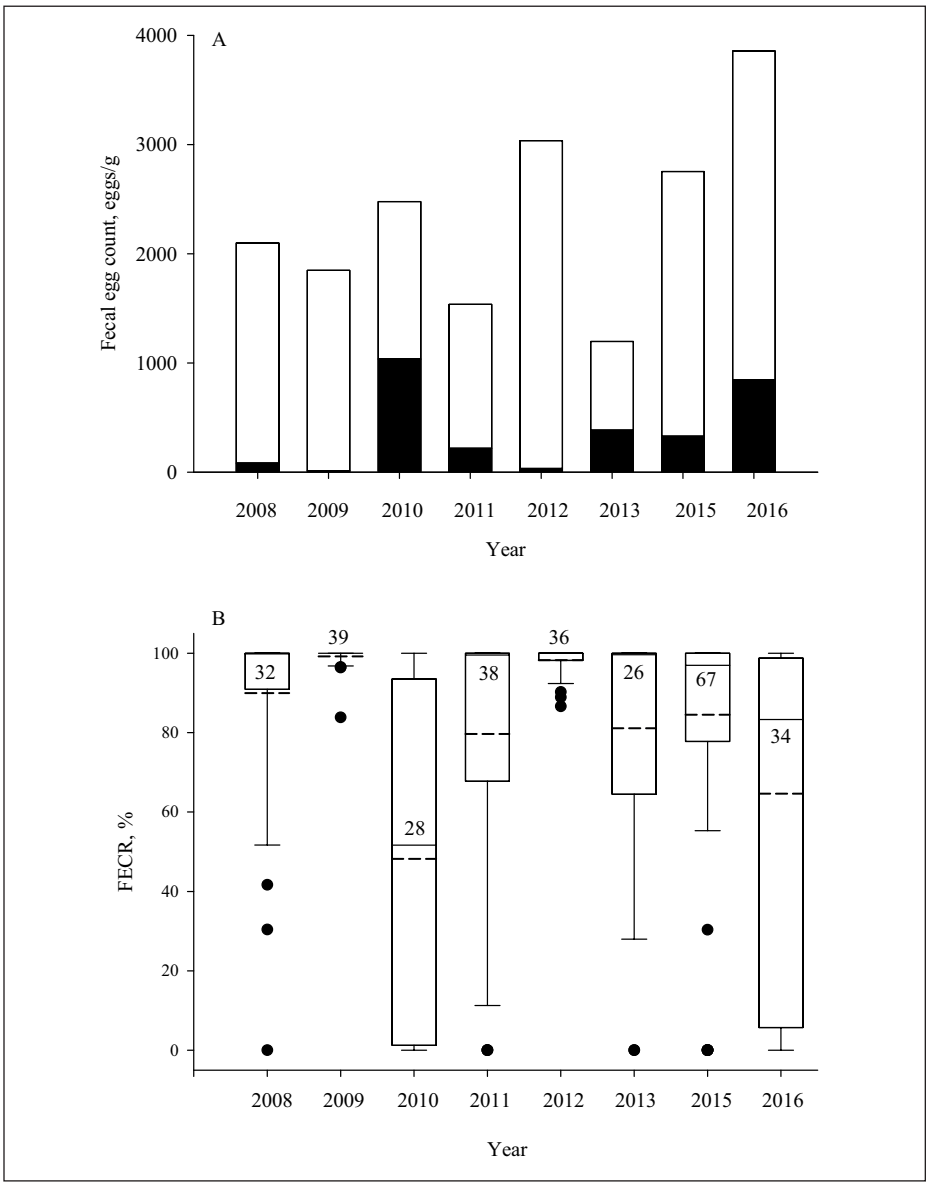
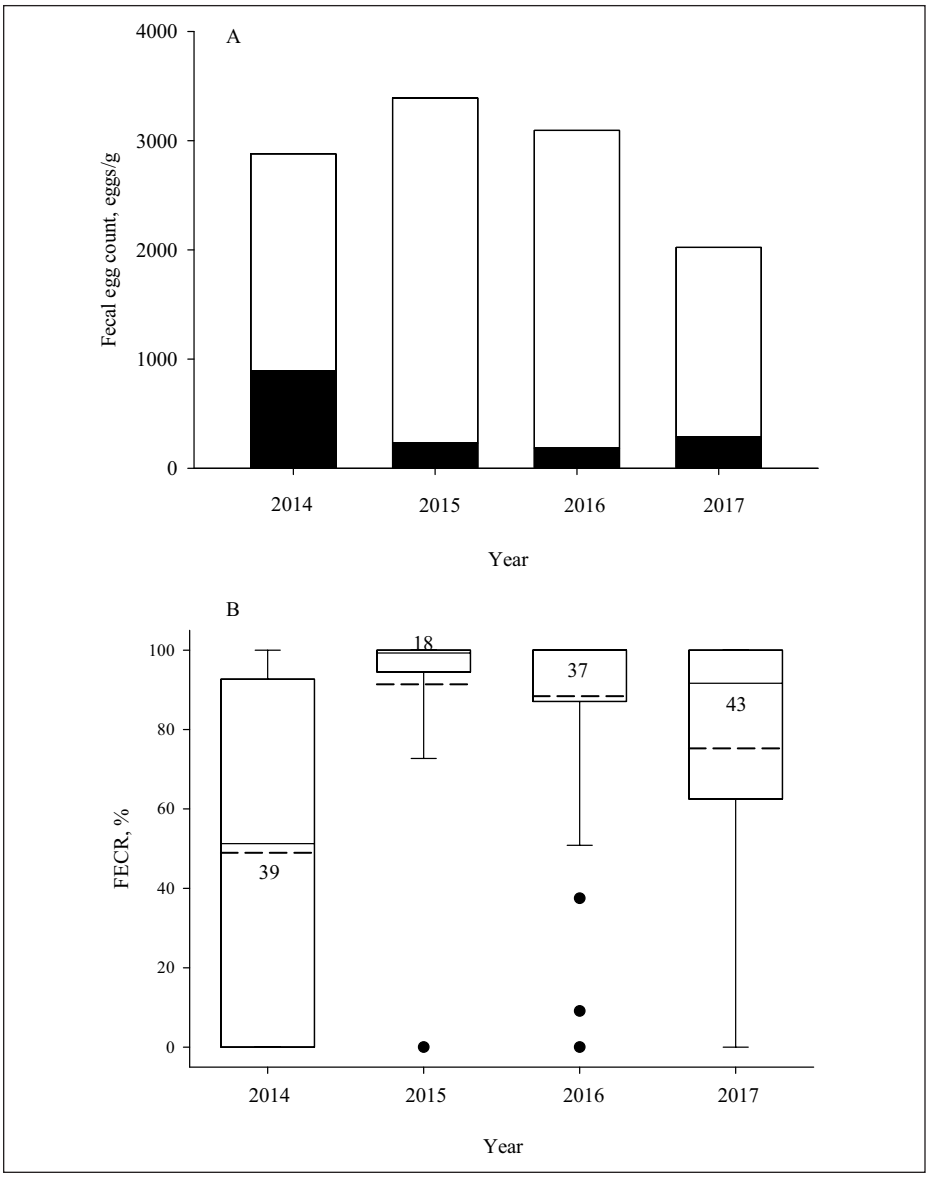


Fig. 2. Distribution of fecal egg count (FEC) and FEC reduction (FECR) of goats entered into the Oklahoma Forage-Based, Meat-Goat Buck test at Eastern Oklahoma State College, Wilburton (OK; 2014-2017). Panel A: least squares means FEC determined on day 0 (white stack) or 10 to 12 days later (black stack). Panel B: FECR with lower and upper borders of the box that represent the 25th and 75th percentiles, respectively. Mean (dashed line) and median (solid line) values are presented within the box. Whiskers above and below the box indicate the 90th and 10th percentiles and the circles represent individual values outside of this range. Values within each box represent the number of animals included each year.



Thus, any of these factors could have contributed to differences in FECR among years, such as observing a high FECR one year and low the following year (Maryland, 2009 to 2010 and 2012 to 2013). It was the aim of the buck tests to minimize differences. Several farms contributed goats in multiple years (between 1 and 7), often the same farms, but not always. The attending veterinarian at the Oklahoma test and small ruminant specialists were tasked with deworming goats, minimizing differences in procedures among years. Even in farms that provided goats in multiple years, FECR was often variable among years (data not shown), but some farms observed good FECR (above 90%) within 10 percentage units among years. Because the number of observations or goats was low (most farms submitted three or fewer goats per year), a statistical comparison was not possible. Variability among farms could range from complete anthelmintic resistance to reduced development of anthelmintic resistance by practicing selective deworming and using caution in bringing new goats with resistance on farm (maintaining refugia). Again, based on the study design, it is not clear whether variable FECR among years was due to poor management of dewormers on some farms, or chance.

Goat producers can (and should) determine herd anthelmintic resistance by conducting a FECR test on naturally infected animals. Rather than administering anthelmintic to all goats as in the current study, a proportion should remain untreated (Coles et al., 1992). These untreated goats allow both a comparison of the change in FEC over time, which is not static, and a comparison with the treated animals. Efficacy will be higher in equations that consider untreated goats as it accounts for increases in FEC in these goats (Miller et al., 2006). When post-treatment FEC is high, as in the current study, improving the calculated efficacy does not matter since anthelmintic resistance is evident and using the animal as its control is acceptable (Vidyashankar et al., 2012). As an alternative to the FECR test, producers can opt to collect feces from a representative group of animals in the herd and submit the pooled sample to an in vitro larval development assay (information for U.S. farmers can be found at *www.wormx.info*).

It is not known if any new classes of anthelmintics will be available in the United States in the near future. However, if such new anthelmintics do become available, it will not offer the goat industry a resolution to anthelmintic resistance as resistance will most likely develop as has occurred with monepantel in Uruguay (Mederos et al., 2014) and the Netherlands (Van den Brom et al., 2015). In addition, due to cost of development and limited return on investment, new anthelmintics for control of small ruminant GIN will be limited (Kaplan and Vidyashankar, 2012).

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Conclusion

While FECR varied among years, the data suggest a high prevalence of poor efficacy of anthelmintic treatment. Goat producers should practice alternatives to minimize GIN infections and the need for deworming in order to maintain sustainable goat production due to the threat of anthelmintic resistance. Producers that rely on grass production systems that favor GIN development as represented in these buck tests must practice smart use of anthelmintics and employ alternatives in order to stay viable. Most of the goats entered into the two goat tests come from grass-based-farm systems, and under the conditions of this study, displayed substantial multi-anthelmintic resistance.

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