# Effects of Label Dose Permethrin Use in Yearling Angus Beef Bulls on Reproductive Function and Testicular Histopathology

## A.S. Leaflet R2958

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### Summary and Implications

To eliminate the potential for insect borne diseases and improve productivity in cow-calf operations, many producers use pour-on pyrethroids. However, popular press literature has identified potential links between use of pyrethroids and reproductive function failures in bulls. While literature in mice and rats have reported potential endocrine disruption of sex steroids resulting from pyrethroid exposure, effects of pyrethroid use on bull fertility is still questionable. The objective of this study was to measure reproductive parameters in peripubertal Angus bulls using a commonly used pyrethroid pour-on. We hypothesized that use of a pyrethroid pour-on at labeled dose would have limited effects on semen and testicular characteristics. Results from this study revealed pyrethroid-treated bulls had greater spermatozoa head and midpiece abnormalities compared to controls, resulting in higher primary morphological abnormalities. Although some morphological semen parameters appear to be negatively affected by use of pyrethroid administration in bulls, biological relevance of this result needs to be further elucidated as the ability to pass a breeding soundness exam was not affected. Moreover, further research should be conducted to determine the effects of pyrethroid pour-ons on fertility when used with other pyrethroids such fly tags or perimeter sprays. Based on these results, pour-on pyrethroid use in yearling bulls is still recommended for label dose administration.

### Introduction

Pyrethroids are potent insecticides that are used in common cattle topical pour-ons, fly tags, and perimeter sprays. Pyrethroid use is heavily based on the diminished general toxicity in mammalian species compared to previously used organophosphates. Recent popular press publications have stimulated uncertainties and fears for producers and veterinarians using pyrethroids on beef bulls and potential effects on reproductive health.

Previous research on this topic has been limited and variable in beef cattle. To date, research has utilized different products and applications, and most trials have involved limited numbers with a large variance in breed type and or age. While standard BSE parameters and steroid (testosterone) concentrations have been previously assessed, effect of pyrethroids on testicular histopathology has not been evaluated in the bovine.

The objective of this study was to study the effects of a commonly used commercial pyrethroid based pour-on product, permethrin, on yearling beef bull reproductive parameters and testicular histopathology. It was hypothesized that a single use of a pour-on pyrethroid would have limited detrimental effects on reproductive factors.

### Materials and Methods

Purebred Black Angus yearling beef bulls (n=60; 365 ± 17 d of age; 1118 ± 62 lb.; 6.3 ± 0.4 BCS) were assigned to either 1) a saline control (CON; n=30) or 2) a permethrin pour-on treatment group (PYR; n=30). The PYR bulls received a label dose of permethrin (Ultra Boss®, Intervet/Merck Animal Health, Summit, NJ) for lice and fly control. Because all bulls weighed more than 1000 lbs., all received the maximum label dose of 30 mL. The CON group received the same 30 mL volume of saline. Both products were administered on the topline of the bulls. Treatment groups were housed 1 pen per treatment to avoid cross-contamination.

Prior to treatment, initial body weight (BW) body conditioning scores (BCS), and coccygeal blood samples were collected. At that time, all bulls were subjected to an industry standard breeding soundness exam (BSE). The BSE consisted of general physical exam, scrotal circumference (SC) measurement, external palpation of sex organs (scrotum, testes, and epididymis), internal palpation of accessory sex glands, visual assessment of penis and prepuce, and collection of semen sample.

Semen was collected via electroejaculation into a plastic collection bag and was immediately transferred to a warming plate (37°C). A small drop of ejaculate was placed on two warmed slides with one receiving a coverslip to assess progressive motility and one being stained with Eosin-Nigrosin for morphology. Progressive motility was analyzed by a blinded, boarded theriogenologist and morphology was analyzed using high power magnification (100X) and phase contrast modalities.

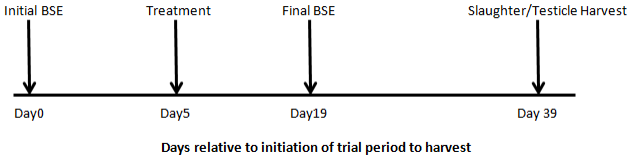
One hundred sperm cells were assessed for morphological analysis. Morphological abnormalities were classified as primary or secondary and broken down by head, midpiece, proximal droplet, coiled tail, distal droplet, bent tail, and tail-less sperm defects.

Testosterone concentrations were analyzed in plasma using via commercial radioimmunoassay (RIA) kit.

After initial BSE on d 0, bulls were treated on d 5 and were subjected to duplicate BSE on d 19. A 14 day window between treatment and final BSE was based on previous research reports that indicate that the largest morphological alterations occur approximately 2 weeks after pyrethroid treatment.

On d 39, bulls were slaughtered and 1 testicle was randomly selected for harvest. Within 1 hour of collection, testicles were processed (breadloafed) and submerged in 10% neutral buffered formalin. Histology samples from three standard locations were analyzed by a blinded, boarded pathologist. Testicular degeneration was scored on a 0-4 scale (0=normal, 1= rare, 2= mild, 3=moderate, and 4=severe degeneration). Seminiferous tubule diameter was also measured for 10 random tubules using computerized software. The experimental design is illustrated in Figure 1.

**Figure 1. Experimental Design**




Data was analyzed using SAS 9.3 with the MIXED and GLIMMIX procedures for continuous and binary data, respectively. Days of age was used as a covariate in the model for all reproductive parameters.

**Results and Discussion**

Performance parameters were not different between treatments. (Table 1). Motility in both treatments numerically decreased post-treatment (Table 2), but this is likely attributed to a considerably lower ambient temperature at second collection. Pyrethroid-treated bulls had greater differences in head and midpiece abnormalities compared to controls, resulting in greater primary abnormalities ($P < 0.05$, Table 5). Nonetheless, the differences were minimal and did not change the outcome for satisfactory breeder status (Table 3).

Previous research has reported a decrease in testosterone concentration of bulls treated with pyrethroids. However, no significant change in testosterone concentration was noted in this experiment (Table 2).

Seminiferous tubule degeneration was not different as a result of treatment (Table 4); however, numerical impacts may be noteworthy, particularly as degeneration score had a positive correlation with primary abnormalities ($P = 0.008$; r = 0.35) and a negative correlation with normal sperm cells ($P = 0.001$; r = -0.43, data not shown).

In conclusion, these data indicate that a single use of permethrin at label dose in yearling Angus bulls results in minimal detrimental effects on semen morphology, but not to a degree that impacts the ability of those bulls to pass a standard BSE. Further research may be warranted to evaluate the effects of label dose pyrethroids use on post-BSE fertility.

**Table 1. Performance parameters of yearling Angus bulls treated with a pyrethroid pour-on.**

| | Treatment[1] | | | |
|---|---|---|---|---|
| Parameter | CON | PYR | SEM | *P*-Value |
| Body weight, lbs | | | | |
| Initial | 1128 | 1118 | 13.4 | 0.60 |
| Final | 1225 | 1214 | 14.1 | 0.60 |
| Change | 94 | 92 | 4.9 | 0.85 |
| Average daily gain,[2] lbs | 4.93 | 4.86 | 0.258 | 0.85 |
| Body condition score[3] | | | | |
| Initial | 6.10 | 6.30 | 0.087 | 0.11 |
| Final | 6.02 | 6.20 | 0.115 | 0.28 |
| Change | -0.07 | -0.10 | 0.764 | 0.78 |

[1] Labeled dose and route of pour-on pyrethroid (PYR; Ultra Boss®) sterile saline (CON).
[2] Calculated by final weight minus initial weight and divided by 19 days of trial period.
[3] Based on industry standard (1-9) body condition scoring technique.

**Table 2. Reproductive parameters of yearling Angus bulls treated with a pyrethroid pour-on.**

| | Treatment[1] | | | |
|---|---|---|---|---|
| Parameter | CON | PYR | SEM | *P*-Value |
| Scrotal circumference, cm | | | | |
| Initial | 35.5 | 35.5 | 0.42 | 0.99 |
| Final | 36.6 | 36.8 | 0.44 | 0.77 |
| Change | 1.1 | 1.3 | 0.14 | 0.18 |
| Testosterone, ng/ml | | | | |
| Initial | 6.17 | 8.44 | 0.824 | 0.06 |
| Final | 6.55 | 7.21 | 0.699 | 0.51 |
| Change | 0.22 | -1.22 | 0.816 | 0.22 |
| Sperm motility, % | | | | |
| Initial | 71.8 | 76.6 | 2.95 | 0.27 |
| Final | 56.3 | 66.8 | 4.15 | 0.09 |
| Change | -12.9 | -10.1 | 4.78 | 0.69 |

[1] Labeled dose and route of pour-on pyrethroid (PYR; Ultra Boss®) sterile saline (CON).

**Table 3. Breeding Soundness Exam (BSE) classification results of yearling Angus bulls treated with a pyrethroid pour-on.**

| | Treatment[1] | | |
|---|---|---|---|
| BSE classification | CON | PYR | *P*-Value |
| Satisfactory classification, % (no./no.)[2] | | | |
| Initial | 63.3 (19/30) | 43.3(13/30) | 0.17 |
| Final | 65.5 (19/29) | 70.0(21/30) | 0.72 |
| Downgraded[3] | 16.7 (3/18) | 7.7 (1/13) | 0.82 |

[1] Labeled dose and route of pour-on pyrethroid (PYR; Ultra Boss®) sterile saline (CON).
[2] Percent of bulls with satisfactory BSE standards (≥ 30% motility and 70% normal sperm morphology).
[3] Percent of bulls classified as satisfactory at initial BSE, but non-satisfactory on final BSE.

**Table 4. Testicular histopathology of yearling Angus bulls treated with a pyrethroid pour-on (34 days post treatment).**

| | Treatment[1] | | | |
|---|---|---|---|---|
| Histopathology parameter | CON | PYR | SEM | *P*-Value |
| Tubular diameter[2], µm | 153.1 | 153.2 | 2.18 | 0.99 |
| Degeneration score[3,4] | 1.4 | 1.9 | 0.24 | 0.19 |
| None/rare[5], % | 51.9 (14/27) | 48.3(14/29) | | 0.72 |
| Mild or greater[6], % | 48.1(13/27) | 51.7(15/29) | | 0.72 |
| Moderate or greater[7], % | 14.8 (4/27) | 31.0 (9/29) | | 0.19 |
| Severe degeneration[8], % | 3.7 (1/27) | 17.2 (5/29) | | 0.17 |

[1] Labeled dose and route of pour-on pyrethroid (PYR; Ultra Boss®) sterile saline (CON).
[2] Average of 10 random seminiferous tubules from each animal.
[3] Degeneration scoring: (0) = normal or no degeneration, (1) = scattered and rare degeneration, (2) = mild degeneration, (3) = moderate degeneration, (4) = severe degeneration.
[4] Three different sections (proximal, middle, and distal) of testicles used to average the degeneration score.
[5] Includes degeneration scores (1) and (2).
[6] Includes degeneration scores (2), (3), and (4).
[7] Includes degeneration scores (3) and (4).
[8] Includes degeneration score (4).

**Table 5. Semen morphology of yearling Angus bulls treated with a pyrethroid pour-on.**

| | Treatment[1] | | | |
|---|---|---|---|---|
| Semen morphology, % | CON | PYR | SEM | *P*-Value[2] |
| Normal | | | | |
| Initial | 69.9 | 64.7 | 2.72 | 0.19 |
| Final | 78.5 | 73.7 | 2.43 | 0.17 |
| Change | 8.9 | 9.5 | 1.78 | 0.80 |
| Abnormal | | | | |
| Initial | 30.1 | 35.3 | 2.72 | 0.19 |
| Final | 21.5 | 26.3 | 2.43 | 0.17 |
| Change | -8.9 | -9.5 | 1.78 | 0.80 |
| Primary defects | | | | |
| Initial | 15.8 | 15.4 | 2.63 | 0.91 |
| Final | 10.7 | 15.4 | 2.21 | 0.15 |
| Change | -5.1 | -0.08 | 1.71 | 0.04 |
| Head defects | | | | |
| Initial | 2.8 | 1.4 | 0.39 | 0.02 |
| Final | 1.0 | 1.6 | 0.21 | 0.04 |
| Change | -1.9 | 0.2 | 0.37 | < 0.001 |
| Midpiece defects | | | | |
| Initial | 4.7 | 3.8 | 1.21 | 0.63 |
| Final | 1.8 | 3.4 | 0.46 | 0.02 |
| Change | -3.0 | -0.4 | 1.14 | 0.12 |
| Proximal droplet | | | | |
| Initial | 3.7 | 6.1 | 1.62 | 0.31 |
| Final | 4.0 | 6.4 | 1.67 | 0.32 |
| Change | 0.3 | 0.3 | 0.98 | 0.99 |
| Coiled tails | | | | |
| Initial | 4.6 | 4.6 | 0.86 | 0.97 |
| Final | 4.0 | 4.0 | 0.78 | 0.98 |
| Change | -0.4 | -1.0 | 0.64 | 0.47 |
| Secondary defects | | | | |
| Initial | 14.3 | 18.6 | 1.5 | 0.05 |
| Final | 10.7 | 10.9 | 1.09 | 0.90 |
| Change | -3.9 | -7.7 | 1.75 | 0.13 |
| Distal droplets | | | | |
| Initial | 1.5 | 0.8 | 0.37 | 0.24 |
| Final | 1.8 | 1.2 | 0.38 | 0.26 |
| Change | 0.5 | 0.4 | 0.50 | 0.85 |
| Bent tails | | | | |
| Initial | 5.9 | 5.8 | 0.70 | 0.89 |
| Final | 5.8 | 5.2 | 0.76 | 0.60 |
| Change | -0.02 | -0.7 | 0.83 | 0.57 |
| Tailless sperm | | | | |
| Initial | 6.9 | 12.6 | 1.20 | 0.002 |
| Final | 3.1 | 4.5 | 0.61 | 0.12 |
| Change | -4.3 | -8.2 | 1.32 | 0.05 |

[1] Labeled dose and route of pour-on pyrethroid (PYR; Ultra Boss®) sterile saline (CON).
[2] ($P \leq 0.05$) considered statistically significant.