# Trichomoniasis

<sup>1</sup>Julie Gard Schnuelle, DVM, PhD, DACT, Professor,
<sup>1</sup>Sue Hudson Duran, RPH, MS, PhD, DICVP, Professor Emeritus
<sup>1,2\*</sup>Soren Rodning, DVM, MS, DACT, Extension Veterinarian and Associate Professor,
<sup>3</sup>Misty Edmondson, DVM, MS, DACT, Associate Alabama State Veterinarian,
<sup>1</sup>Thomas Passler, DVM, PhD, ACVIM, Associate Professor,
<sup>1</sup>Jessica Rush, DVM, MS, DACT, Assistant Professor

<sup>1</sup>Auburn University
<sup>2</sup>Alabama Cooperative Extension System
<sup>3</sup>Alabama Department of Agriculture and Industries

\*Corresponding author: Julie Gard Schnuelle 1500 Wire Road

# Abstract:

Bovine trichomoniasis is a venerealy transmitted disease of cattle. The organism responsible for Trichomoniasis in cattle is the extracellular protozoa *Tritrichomonas foetus*. This protozoan is an obligate parasite of the reproductive tract of cattle. The epithelial surfaces of the bull's penis and prepuce including the distal urethra. Infected bulls are often asymptomatic carriers of *T. foetus*. Most bulls become chronically infected with *T. foetus* after breeding an infected cow, and these infections often become chronic in nature and rarely clear regardless of time. Currently there is no approved treatment for Trichomoniasis in cattle but new therapies are being tested with promising results.

Keywords: Bovine Trichomoniasis, Tritrichomonas foetus, bovine venereal disease

## Introduction:

The profitability of the beef cattle industry relies on efficient reproduction. The production of calves for replacements and for meat is necessary for replenishing the herd. Additionally, the production of calves for meat is the crux of the beef cattle industry. The efficiency of cow-calf operations are drastically effected by Tritrichomonas foetus (*T. foetus*) infections.<sup>1-4</sup> Bovine Trichomoniasis is a sexually transmitted disease caused by T. foetus. Tritrichomonas foetus can result in producing a chronic carrier state in a bull.<sup>5</sup> Infected bulls are often asymptomatic carriers of T. foetus and, if older than four years of age, rarely spontaneously resolve the infection.<sup>1,5,6</sup> It is has been reported that young bulls exposed to this organism may be able to resist infection, clear infection or experience a transient infection.<sup>2,3,5</sup> Infected bulls are capable of transmitting the organism to a cow during coitus.<sup>4</sup> The organism can be found in an infected bull's sheath on the penis and prepuce.<sup>5</sup> There is an absence of penile or preputial lesions and does not seem to affect semen quality or libido.<sup>2,5</sup> Since there are no noticeable clinical signs when a bull is infected with T. foetus, it is imperative to utilize appropriate diagnostic tests to determine a bull's *T. foetus* status prior to introducing him into the herd.<sup>6,7</sup> Most bulls become chronically infected with T. foetus after breeding an infected cow, and these infections are thought to become chronic in nature and rarely clear regardless of time.<sup>5</sup> Tritrichomonas foetus can cause a myriad of reproductive issues in the female such as transient infertility, early embryonic death, metritis, pyometra, and sporadic abortions.<sup>2</sup> This organism is an obligate protozoan parasite that lives on the surface of the epithelial folds of the bull's penis and prepuce.<sup>1-5, 7-11</sup> Disease involving *T. foetus* is specific to cattle. Bulls efficiently transmit this protozoan to cows and heifers during breeding. The organism moves from the vagina and into the uterus during estrus. economic losses in the hundreds of millions of dollars in the US alone.<sup>2</sup> Because bulls are unable to eliminate T. foetus from the penis and prepuce, once a bull is infected, it is considered to have a life-long infection.<sup>1-4,5</sup> Currently there is no approved treatment for Trichomoniasis in cattle.

# **Literature Review:**

Bovine Trichomoniasis has been known to exist for over 80 years with the first reported case in the United States in Pennsylvania in 1932.<sup>12</sup> Following this time, Trichomoniasis has been diagnosed throughout the United States and worldwide.<sup>1,4,5,8,11,13-19</sup> More cases of Trichomoniasis

have been reported in recent years.<sup>18,19</sup> The increased incidences/reporting is probably linked to increased cattle movement, drought conditions and more intensive management. It can also be related to improved detect through the use of better diagnostic testing methods avaliable, specifically the polymerase chain reaction (PCR).<sup>6,7,20</sup> Regardless of the cause, the increased prevalence of Trichomoniasis has prompted many states within the U.S. to enact rules and regulations regarding the sale and movement of animals potentially infected with *T. foetus*, making prevention and control of Trichomoniasis very important especially for every cow-calf operation and all dairy operations utilizing clean up bulls. According to National Animal Health Monitoring System (NAHMS) over 51.5% of dairies utilize bulls opening the door to *T. foetus* infections with resultant fetal loss.<sup>21</sup> Dairy cows already have low conception rates, first service conception rates of 18 to 30% are considered normal, Hence prevention of Trichomoniasis is imperative.

Infected bulls are often asymptomatic carriers of *T. foetus* and, if older than 4 years of age, rarely spontaneously resolve the infection.<sup>1,5</sup> It is thought that young bulls exposed to this organism may be able to resist infection, clear infection or experience a transient infection.<sup>2,3,5</sup> Infected bulls are capable of transmitting the organism to a cow during coitus.<sup>4,5</sup> The organism affects can be found in an infected bull's sheath on the penis and prepuce, but causes no penile or preputial lesions and does not affect semen quality or libido.<sup>2,-4,5,10</sup> Since there are no noticeable clinical signs when a bull is infected with T. foetus, it is imperative to utilize appropriate diagnostic tests to determine a bull's *T. foetus* status prior to introducing him into the herd.<sup>6,7,20</sup> Most bulls become chronically infected with T. foetus after breeding an infected cow, and these infections are thought to become chronic in nature and rarely clear regardless of time.<sup>5,8,9</sup> Bulls with trichomoniasis do tremendous reproductive damage by infecting cows and heifers during the breeding season. The organism moves ascends from the vagina through the cervix during estrus and colonizes the entire reproductive tract within a couple weeks.<sup>2,3</sup> Cows and heifers very rarely show any evidence of current infection such as vaginal discharge.<sup>2,3,10</sup> Low conception rates and irregular inter-estrus intervals are often the first signs of infection with pyometra and abortion occurring in less than 5% of infected animals.<sup>2,3,10</sup> Infertility due to early embryonic or fetal death is the most economically damaging clinical sign and occurs in a much larger percentage of infected cows. Early embryonic death results in irregular return to estrus, which can easily go

unnoticed in a large herd. Unlike the bull, the cow is capable of mounting an effective immune response to *T. foetus*<sup>10,22</sup> but usually takes a long period of time to clear the infection, 2 to 6 months. *Tritrichomonas foetus* does not usually prevent conception, but often results in death of the embryo or fetus most commonly reported between gestational days 15 to  $80.^{23}$  Reproductive loss is most often the result of the immune response so it is an economically devastating disease. There is a very small percentage of cows that will abort in the second or even third trimester and it has been estimated to be about 1% or less of pregnant cows will maintain infection throughout gestation and deliver a live calf.<sup>24</sup> This scenario is very damaging due to the chance of reinfection of the herd in the following breeding season.

The major economic consequences associated with *T. foetus* are: reduced calf crop due to early embryonic loss or abortion, reduced weaning weight due to delayed conception, and culling and replacement of infected cattle.<sup>2,10</sup> The result is that more cows will calve later in the calving season than desired, which results in extreme variations in weaning weights in addition to a reduced calving percentage. A late-calving cow will continue to calve late in subsequent years, thus sacrificing valuable growing time for her calf before sale. Therefore, less days of gain means fewer pounds to sell and this is compounded yearly. In herds with new infections, the results can be devastating, with long, drawn-out calving seasons and maybe only a 50-70% calf crop.<sup>10</sup> In herds where Trichomoniasis has gone undetected for a period of time, the results may be less dramatic because of temporary herd immunity. In such cases, the calf crop may only be reduced 5-10%; however, this loss is still enough to have a substantial economic impact on feeder calf breakeven price and profit per brood cow. The economic impact attributed to direct, secondary and indirect losses are approximated at \$300 million to \$650 million in just one state alone.<sup>18,19,25</sup>

Metronidazole is the primary drug utilized to treat Giardia and Trichomoniasis in humans and companion animals.<sup>9</sup> The use of Metronidazole in food producing animals is prohibited.<sup>9</sup> A recent study by Love et al., 2017, cured a Trichomoniasis positive bull using Metronidazole intravenous solution for a total dosage of 60 mg/kg for two treatments 24 hrs apart.<sup>9</sup> In the study by Love et al., it was argued that the studies performed in mice where flawed and that Metronidazole does not pose such a risk in induction of cancer.<sup>9</sup> The biggest roadblock to

Metronidazole use in cattle is probably the potential for adding to resistant strains that already exist in humans. Approximately 5% of strains of *Trichomoniasis vaginalis* in humans are already resistant to Metronidazole.<sup>26</sup> Additionally, Metronidazole is an important antibiotic in treatment of *Clostridium difficle* infections in humans and anything that will potential add resistance to this serious toxin forming bacteria is most likely not going to be taken off the prohibited list.<sup>26,27</sup> Hence, in vitro culture trials have been performed to identify approved food animal drugs that might be utilized for treatment of Trichomoniasis.

At Auburn University College of Veterinary Medicine in vitro trials showed promising results with total kill of the *T. foetus* within the culture environment utilizing benzimadazoles.<sup>28,29</sup> The next logical step is in vivo trials. It is necessary to determine if these preparations when placed topically to the prepuce and the penis of naturally infected *T. foetus* positive bulls could result in a complete kill of the *T. foetus* organisims. The impact of this research has the potential to provide a cure for bulls chronically infected with *T. foetus*. A cure for *T. foetus* would result in a significant reduction in economic losses due to fetal wastage and culling of *T. foetus* positive bulls. The intent is to develop an FDA approved treatment for *T. foetus* infection. Additional information needs to be gathered assessing biofilm formation. This information will allow for the development of more effective treatments if the formulations utilized in this study are not successful in eliminating the T. foetus infection in these bulls.

Until effective, approved therapies are proven to be effective for bovine Trichomoniasis prevention and control measures are necessary. Infection with *T. foetus* does not always induce an effective local immune response in bulls.<sup>8,30</sup> However, Cobo *et al.* recently noted that immunoglobulins directed against *T. foetus* appeared in the preputial secretions of bulls vaccinated with *T. foetus* antigens.<sup>8,30</sup> This Cobo *et al.* study also demonstrated that TrichGuard<sup>®</sup> prevented colonization of the preputial and penile mucosa.<sup>8,30</sup> However, this study used an experimental challenge with only a single dose of *T. foetus*. TrichGuard<sup>®</sup> is the only commercially available vaccine for *T. foetus* in the United States. Thus, assessment of the ability and impact of TrichGuard<sup>®</sup> to prevent or reduce transmission of *T. foetus* from infected heifers to vaccinated bulls is necessary. Vaccination is important in minimizing the detrimental effects of *T. foetus* infections in cattle. However, the only vaccine currently available in the United States to protect against *T. foetus* are inactivated and require an initial subcutaneous dose followed by a booster dose two to four weeks later. The booster dose should be administered at least four weeks prior to the breeding season. For continued benefits, annual revaccination four weeks prior to the breeding season is recommended. Vaccination against *T. foetus* increases the number of calves produced in infected herds. A recent study showed 80% of vaccinated heifers were *T. foetus*-negative within two weeks after a 15-day breeding cycle, as compared to 80% of non-vaccinated heifers still infected four weeks after a 15-day breeding cycle.<sup>30,31</sup> In addition, 60 % of non-vaccinated heifers remained infected 10 weeks following a 15-day breeding cycle.<sup>30,31</sup> Hence, a vaccinated cow or heifer that is subsequently infected with *T. foetus* will clear the infection sooner and either maintain her pregnancy or be ready to rebreed weeks or months sooner than a non-vaccinated animal. Vaccination programs can decrease the severity of clinical signs but are unable to completely prevent abortion within a herd.<sup>10</sup> In a recent vaccine trial by Edmondson et al., 2017, naïve heifers were vaccinated and subsequently challenged with *T. foetus.*<sup>10</sup> Embryonic or fetal loss was detected in 9/19 (47%) vaccinated heifers and 10/14 (71%) sham vaccinated heifers (p = 0.153).<sup>10</sup>

Veterinarians throughout the United States are reporting more cases of Trichomoniasis in recent years. It may be a result of increased cattle movement and weather conditions. The increase in the reporting of clinical cases of Trichomoniasis may be directly correlated to the increase in awareness of it and a longer diagnostic test for the disease. Testing has been key in the initiation and the development and implementation of control programs within the U.S. Texas, since 2009, Colorado, Alabama and a number of others states including Kansas the most current state have developed programs specifically regarding the sale and movement of animals potentially infected with T. foetus,. These programs have made prevention and control of Trichomoniasis a focus for cattle producers and especially for those that are primarily cow-calf operations. The current rule in Alabama is states that all virgin and non-virgin bulls 18 months of age and older entering the state of Alabama must be tested negative for Trichomoniasis within the 30 days prior to entry into the state. The testing requirements mandate that Bulls shall be negative to one official Polymerase Chain Reaction (PCR) which was cultured of 48 hrs prior to testing. All bulls tested must be identified with official USDA approved ear tag, registry brand or registry tattoo. Any bull comingled with cows between testing and importation into Alabama must be retested. All bulls entering the state must be accompanied by a Certificate of Veterinary Inspection (CVI)

containing the date of test, name of the lab used for testing, complete address of consignor and consignee, a complete description of the bull including official identification and signature of an accredited veterinarian. The following animals may be exempt from Trichomoniasis testing: Exhibition and rodeo bulls that are temporally in the state for the purpose of an event with no comingling with female cattle and will be leaving the state after the event, Bulls consigned directly to slaughter, bulls being transported through Alabama in interstate commerce and not offloaded to be comingled with female cattle. Virgin bulls under 18 months of age as determined by breed registry records or the absence of permanent central incisor teeth in wear. Virgin bull(s) must be accompanied by a CVI containing any and all identification, age, signed by an accredited veterinarian and a statement on the CVI declaring that the bull(s) is virgin and less than 18 months of age. Other states have their similar but specific rules. The Texas regulations for Breeding bulls more than 12 months of age entering Texas are outlined according to the Texas Animal Health Commision: Breeding bulls from any other state must have a CVI and a negative PCR Trich test within 30 days prior to entry.<sup>33</sup>

### **Summary:**

The efficiency of cow-calf operations are drastically effected by *T. foetus* infections. In naïve herds, 80 percent to 90 percent of females exposed to the organism becoming infected. Infected females often conceive but lose the fetus.<sup>2,10</sup> The calf crops are severely affected and may be reduced 50 percent or even more.<sup>2, 10</sup> The economic impact attributed to direct, secondary and indirect losses are approximated at \$300 million to \$650 million.<sup>18,19</sup> Currently, there are not any approved therapeutics that can legally be utilized for treatment of *T. foetus* in cattle. Vaccination programs can decrease the severity of clinical signs but are unable to completely prevent abortion within a herd. Current studies are ongoing to treat T. *foetus* in bulls and the results have been promising. However, the best insurance is to test all bulls prior to breeding season, good biosecurity and quarantine with new replacements.

# **Reference List:**

1. Abbitt B Meyerholz GW: *Trichomonas foetus* infection of range bulls in South Florida. *Vet Med Sm Anim Clin* 74: 1339-1342, 1979.

2. Anderson ML, Barr BC Conrad PA: Protozoal causes of reproductive failure in domestic ruminants. *Vet Clin North Am Food Anim Pract* 10: 439-461, 1994.

3. BonDurant RH: Diagnosis, treatment, and control of bovine trichomoniasis. *Compend Contin Educ Pract Vet* 7: S179-188, 1985.

4. BonDurant RH, Anderson ML, Blanchard P, Hird D, Danaye-Elmi C, Palmer C, Sischo WM, Suther D, Utterback W Weigler BJ: Prevalence of trichomoniasis among California beef herds. *J Am Vet Med Assoc* 196: 1590-1593, 1990.

5. Parsonson IM, Clark BL Dufty J: The pathogenesis of Tritrichomonas foetus infection in the bull. *Aust Vet J* 50: 421-3, 1974.

 McMillen L , Lew AE: Improved detection of Tritrichomonas foetus in bovine diagnostic specimens using a novel probe-based real time PCR assay. Vet Parasitol. 2006;141(3-4): 204-215.

7. Cobo ER, Favetto PH, Lane VM, Friend A, VanHooser K, Mitchell J BonDurant RH: Sensitivity and specificity of culture and PCR of smegma samples of bulls experimentally infected with Tritrichomonas foetus. *Theriogenology* 68: 853-60, 2007.

8. Cobo ER, Corbeil LB, Gershwin LJ BonDurant RH: Preputial cellular and antibody responses of bulls vaccinated and/or challenged with Tritrichomonas foetus. *Vaccine* 28: 361-70, 2009.

9. Love D, Fajt VR, Hairgrove T, Jones M, and Thompson JA. Metronidazole for the treatment of Tritrichomonas foetus in bulls. *BMC Veterinary Research*, (2017) 13:107:1-6.

 Misty A. Edmondson, Kellye S. Joiner, Jennifer A. Spencer, Kay P. Riddell, Soren P. Rodning, Julie Gard, M. Daniel Givens. Impact of a killed tritrichomonas foetus vaccine on clearance of the organisms and subsequent fertility of heifers following experimental inoculation. Theriogenology, March 2017(90);245-251.

Fitzgerald PR: Bovine trichomoniasis. *Vet Clin North Am Food Anim Pract* 2: 277-282, 1986.

12. Emmerson M: Trichomoniasis in cattle. J Am Vet Med Assoc 34: 636-640, 1932.

 Erasmus JA, De Wet JAL, Van der Merwe HE Pienaar GCJ: Bovine trichomoniasis in the North Western Cape Province, Western Transvaal, and the Orange Free State. *J S Afr Vet Assoc* 60: 51-52, 1989.

14. Johnson AE: Incidence and diagnosis of trichomoniasis in western beef bulls. *J Am Vet Med Assoc* 145: 1007-1010, 1964.

15. Mickelsen WD, Paisley LG Anderson PB: Survey of the prevalence and types of infertility in beef cows and heifers. *J Am Vet Med Assoc* 189: 51-54, 1986.

16. Riley DE, Wagner B, Polley L Krieger JN: PCR-based study of conserved and variable DNA sequences of *Tritrichomonas foetus* isolates from Saskatchewan, Canada. *J Clin Microbiol* 33: 1308-1313, 1995.

17. Wilson SK, Kocan AA, Gaudy ET Goodwin D: The prevalence of trichomoniasis in Oklahoma beef bulls. *Bov Pract* 14: 109-110, 1979.

18. Jones, L. Infection Can Result in Significant Losses in Cattle Herds, Georgia Department of Agriculture, 2018.

19. Tritrichomonas foetus Infection in Female Beef Cattle with Abortion in Wyoming, USA, Journal of Medical Microbiology Case Reports, 2015.

 Mutto AA, Giambiaggi S, Angel SO. PCR detection of *Tritrichomonas foetus* in preputial bull fluid without prior DNA isolation. Vet Parasitol 2006;136(3-4):357-61.

21. National Animal Health Monitoring System: Dairy https://www.aphis.usda.gov/animal\_health/nahms/dairy/downloads/dairy14/Dairy14\_dr\_PartI.pdf]

22. Skirrow SZ BonDurant RH: Immunoglobulin isotype of specific antibodies in reproductive tract secretions and sera in *Tritrichomonas foetus*-infected heifers. *American Journal of Veterinary Research* 51: 645-653, 1990.

23. Roberts SJ: Infectious diseases causing infertility in cows: in (ed): *Veterinary Obstetrics and Genital Diseases*. Ann Arbor, MI, Edward Bros., Inc, 1986, pp 447.

24. Skirrow S: Identification of trichomonad-carrier cows. *J Am Vet Med Assoc* 191: 553-554, 1987.

25. Seeking Harmonization of Trichomoniasis Regulatory and Testing Standards, National Institute for Animal Agriculture, April 2014.

26. Cudmore SL, Delgaty KL, Hayward-McClelland, Petrin DP, Garber GE. Treatment of Infections Caused by Metronidazole-Resistant *Trichomonas vaginalis*. Clinical Microbiol Rev. 2004;17(4): 783–793. doi: 10.1128/CMR.17.4.783-793.2004.

27. Mitteregger D, Aberle SW, Makristhasis A, Walochnik J, Brozek W, Marberger M, Kramer G. High detection rate of Trichomonas vaginalis in benign hyperplastic tissue. Med Microbiol Immunol. 2012;201(1):113-6.

28. L.A. Niehaus, K.S. Joiner, A.S. Lovelady, C. Armstrong, M.A. Edmondson, J.A. Gard, S.H. Duran, Efficacy of Various Topical Formulations against Tritrichomonas foetus. Proceedings of the International Society of Veterinary Hospital Pharmacists Meeting. June, 2013, Raleigh, NC.

29. Koziol JH, Edmondson MA, Duran SH, Passler T, Gard JA, Joiner K, Wolfe DF. In vitro efficacy of anti-protozoal compounds as a novel treatment of Tritrichomonas foetus. Clinical Theriogenology, 2017; 9(4):539-543.

30. Cobo ER, Corbeil LB, Gershwin LJ, et al. Preputial cellular and antibody responses of bulls vaccinated and/or challenged with Tritrichomonas foetus. Vaccine 2010;28:361-370.

31. J. Hall MR, Kvasnicka WG, Hanks D, Chavez L Sandblom D: Improved control of trichomoniasis with *Trichomonas foetus* vaccine. *Agri Pract* 14: 29-34, 1993.
32. Kvasnicka WG, Hanks D, Huang J, Hall MR, Sandblom D, Chu H, Chavez L Acree WM: Clinical evaluation of the efficacy of inoculating cattle with a vaccine containing *Tritrichomonas foetus Am J Vet Res* 53: 2023-2027, 1992.

33. Texas Animal Health Commission Regulationshttp://www.tahc.state.tx.us/news/brochures/TAHCBrochure\_TrichRegulations.pdf.