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Mini Review

Bovine Genital Campylobacteriosis - A Review

Abstract

Bovine genital campylobacteriosis (BGC) is a true venereal disease of cattle. This disease results in infertility, embryonic and fetal death, metritis, salpingitis, pyometra, and abortion in cattle, and sheep and goats as well. The causal agent of BGC, is *Campylobacter fetus*. This organism is found worldwide and causes significant economic losses in endemic areas where appropriate management has not been instituted.

Review

Bovine genital campylobacteriosis (BGC) also termed bovine venereal campylobacteriosis (BVC) or Vibriosis is considered one of the two true venereal diseases of cattle [1-4]. Trichomoniasis caused by *Tritichomonas fetus* is considered the other true venereal disease of cattle [2,3]. The causal agent of the sexually transmissible disease, BGC, is *Campylobacter fetus* [1-4]. However, after further examination of *Campylobacter fetus* by microbiologist a division was made into two closely related subspecies: *C. fetus subsp. venerealis* and *C. fetus subsp. fetus* [4]. An additional subspecies of *venerealis* was identified as biotype *intermedius* (*C. fetus venerealis intermedius*) [5,6]. This biotype has also been shown to causes fertility issues in cattle [5,6]. The main causative agent of BCG is considered to be *C. fetus subsp. venerealis* (CFv) and infection is often manifested as infertility, embryonic and fetal death, metritis, salpingitis, pyometra, and abortion [2,3,6-8]. Abortions can occur at any time but are most commonly detected at 4 to 6 months of gestation [8]. Significant economic losses occur with infected herds especially in endemic areas [2,6,8]. Campylobacteriosis is a disease of socio-economic and public health significance and is a list B notifiable disease of the World Organization of Animal Health (OIE) [6]. Campylobacteriosis exists worldwide including Latin-America, Africa, Asia, North America, Europe, and NewZealand [6-10]. The prevalence of CFv in some countries is still questionable due to lack of reporting and reliable testing [9,10]. Bovine infections with *C. fetus subsp. fetus* (CFf) do occur but are considered to be much more sporadic in occurrence in comparison to sheep. Oral transmission of CFf occurs resulting in colonization the intestines of cattle and sheep leading to enteritis and abortion mostly in sheep and sporadically in cattle [6,8].

C. fetus venerealis is a comma shaped microaerophilic, gram-negative rod. It often times has an "S" shape and has been described as having "spiral" or "seagull" shape [6]. The bacteria are well adapted to surviving in the low oxygen environment of the epithelial folds found in the prepuce of older bulls [11]. Isolation and identification of the agent, *C. fetus venerealis*, is the prescribed test for international trade according to the OIE [6]. The OIE details appropriate reporting, and testing for *C. fetus*. In order for *Campyloacter* to be detected on

culture, the sampler needs to be cultured at 37°C for at least three days in a micro-aerobic atmosphere [6]. Most culture media contain the antifungal, cycloheximide, but due to its potential toxicity it is often replaced by amphotericin B [6]. The recommended selective medium for isolation of *C. fetus* is Skirrow's [6]. Skirrow's medium is a blood-based medium with 5–7% (lysed) defibrinated blood and contains the selective agents: polymyxin B sulphate (2.5 IU/ml), trimethoprim (5 µg/ml), vancomycin (10 µg/ml), and cycloheximide (50 µg/ml) or amphotericin B [6]. Additional discrimination between species and subspecies requires additional biochemical or molecular methods. The vaginal mucus from a cow that recently aborted can be tested via a vaginal mucus agglutination test or an ELISA. The ELISA can detect antibodies to IgA. Immunofluorescence may also be used to identify the organism from genital discharges of bulls, cows and heifers, but it will not differentiate between different subspecies [6,8]. Utilization of PCR for diagnosis has provided a way to easily differentiate between subspecies. However, not all PCRs are alike and so there have been mixed results [9-12]. The development of a new real-time quantitative polymerase chain reaction (qPCR) test has shown to be very reliable and was used to diagnose CFv infection in a Canadian cattle herd [11]. This qPCR was verified with repeated culture, phenotypic characterization of the organism and DNA sequencing. Obviously, a reliable practical field test for CFv would prove to be very useful but currently is not available.

Transmission of the organisms occurs most often during natural mating. However, transmission can also occur during artificial insemination with contaminated semen [1,6]. During natural exposure bulls are infected by carrier cows and or carrier bulls infect cows during coitus. During coitus contaminated semen gains entrance to the vagina and can live in the cervical mucus from three weeks to three months. During artificial insemination, the contaminated semen is placed within the uterus and / or very close to the internal cervical os and readily establishes uterine infection. The organism can grow and thrive on the penis and prepuce of the bull with the correct microenvironment. Specifically, CFv is confined to the epithelial surface of the gland penis, prepuce, and the urethra [1]. It has been reported to live in the crypts of the prepuce [1-3,6]. However, Strickland et al., 2010 [13], reported following numerous preputial biopsies from a number of bulls, that there was insufficient

gross or histological evidence to term these areas “crypts”. Hence, it was suggested that the term “mucosal folds” be a utilized to more accurately describe these areas. Bulls do have numerous folds of the mucosa which seem to assist in the creation of the correct micro-environment on the prepuce, penis and urethra that allows for growth and sustainability of *CFv*. Chronic infections can be established within the prepuce and without causing observable signs which is seen most often in older bulls [1-3,6,8]. The chronic carriers propagate the disease within the herd. Some bulls, especially younger bulls, the infection may be transient and they may clear the infection but can become re-infected at a later date.

Susceptible females that are bred by *CFv* carrier bulls can have customary conception rates [2,8]. However later in gestation, vaginitis, cervicitis, and then endometritis and salpingitis develops resulting in embryonic and fetal death at approximately seven to ten weeks of development [2,8]. Infected cows or heifers will develop a mucosal immune response approximately three to five months after the onset of infection. Most often this mucosal immune response will result in clearance of *CFv* from the uterus and oviducts [8]. The re-establishment of normal fertility along with temporary immunity can follow along with resistance to subsequent infection. However, the immunity is somewhat short lived and lasts for approximately two years [2,6]. Persistent infections of *CFv* can occur when convalescing females re-acquire a vaginal infection.

Diagnosis is made through collection of cervical mucus from infected cows and heifers often collected at three weeks to three months post infection. Culture results, vaginal mucus agglutination tests, fluorescent antibody tests can all be questionable so confirmatory PCR is being looked to as a more reliable diagnostic of herd infection [8,11,12]. Also, if cervical mucus sampling is not completed in estrus but in metestrus false positives can occur at a higher rate [8,12]. Diagnosis in the bull is performed most often via a preputial scraping or preputial wash performed twice one week apart or testing of contaminated semen via culture, fluorescent antibody and PCR [6,12]. It is imperative that *CFv* should be inoculated into Clark’s media or Skirrow’s media soon after collection of the sample to allow for maximum survival of the organism [6,8]. The organism can survive for only a short period of time, approximately six to eight hours following collection. However, if the sample is placed in Clark’s media for transportation and / or culture it will allow for a longer period of survival up to 48 hours.

Whole herd treatment of *CFv* is considered to be impractical due to the lack of overt clinical signs at the initiation of the disease process [8]. However if elected, bulls may be treated by administering one to two treatments of streptomycin given subcutaneously at a dose of 20 mg/kg along with administration of a topical suspension containing five grams of streptomycin to the prepuce and penis for three consecutive days but resistant strains have been reported [8]. Hence, prevention of venereal diseases in the herd is the most practical approach to dealing with *CFv* as well as *T. foetus* [1,2]. Control measures include utilization of artificial insemination with non-contaminated semen, testing and culling of infected animals, and vaccination of all bulls, cows and heifers [2,6,8,14,15]. Utilization of artificial insemination exclusively for two breeding seasons is

suggested in infected herds due to the fact that *CFv* has been isolated from cows for greater than six months after calving [8]. However, total use of artificial insemination is impractical in range cattle. Hence, most producers utilize management, culling problem cattle and use of virgin bulls, and vaccination as their primary means of prevention and control [8].

The recommendations for vaccination by the OIE includes vaccination of all infected herds, all breeding animals, bulls, cows and heifers should be vaccinated twice prior to the breeding season except in countries that have been determined to be free of *C. fetus*. Vaccination is prohibited in *C. fetus* free countries [6]. In order to stimulate effective immunity, it is imperative to induce IgA in the vagina and IgG in the uterus [2,6,14]. Hence, cows and heifers are often administered an additional vaccine in the middle of the breeding season to enhance their immunity. Vaccination reduces the length of the infection but carrier-cows have been known to harbor the infection from one season to the next and have the potential to infect susceptible bulls [6,14,15]. Also, it has been suggested that bulls should be given double the dose of vaccine at each of two vaccinations annually to assist in terminating established infections [6,14]. However, in non-infected herds the bulls should at least be vaccinated initially with two doses given 3-4 weeks apart with the last dose approximately 30 days prior to the start of the breeding season [6,8].

There has been controversy in use of vaccines and the efficacy of them especially in bulls. Vaccination against *C. fetus* subsp. *venerealis* has been reported to be protective and even curative for the bull and cow [4,14,16]. Although, other studies have conveyed that prevention of infection utilizing commercial vaccinations has had questionable efficacy [8,14]. A recent study by Cobo et al., 2004 [14], evaluated an experimental vaccine containing *Campylobacter fetus* and *Tritrichomonas foetus* antigens compared to commercial vaccine utilizing subcutaneous and intravaginal administration routes. It was found that heifers vaccinated with the experimental vaccine had an increased clearance rate of both pathogens, higher pregnancy rates and higher systemic immune responses during and after breeding. Hence, it was determined that the experimental vaccine was superior to the commercial vaccine with both bovine venereal campylobacteriosis and trichomonosis were tested. So, vaccination especially for *C. fetus* has been found to beneficial [2,6,8,14]. It is important that vaccines contain specific antigens, the thermolabile ‘H’ flagellar antigens and the thermostable ‘O’ somatic antigens, the capsular ‘K’ antigens and four to five heat-labile glycoprotein immunogens which are shared by many *C. fetus* subsp. *venerealis* and *C. fetus* subsp. *fetus* strains [6,14].

For those countries free of *C. fetus* such as the member countries of the European Union or wanting to decrease the incidence or to become *C. fetus* free the OIE has outlined management protocols that include importation of breeding females, bulls and semen [17]. All animals need to be accompanied by an international veterinary certificate stating that all animals were virgins and kept in a *C. fetus* negative herd where there have been no cases of *C. fetus*. If the animals are bred then the vaginal mucus or semen, or preputial smegma need to be tested negative for *C. fetus* prior to importation.



Additionally, imported semen must come from A-I Centers that are free of *C. fetus*. Artificial insemination is a tool for control and management of *Cfv*. Countries that are free of *C. fetus* do not usually employ vaccination in management protocols due to the possibility of masking disease outbreaks. It is important in maintaining free status to quickly identify disease in the population and prevent the disease from spreading further. Screening tests which have a high sensitivity are implemented as the first line of testing in control and eradication programs. Tests which have a high specificity are necessary in the second line of testing to determine which animals are false positive in those testing positive on screening tests. The positive predictive value depends on the prevalence of the disease in the population so the probability of disease among subjects with positive tests will be higher.

References

1. Eaglesome M, Garcia M (1992) Microbial agents associated with bovine genital tract infections and semen. Part I. *Brucella abortus*, *Leptospira*, *Campylobacter fetus* and *Trichomonas foetus*. *Vet Bull* 62: 743–775.
2. Bondurant RH (2005) Venereal diseases of cattle: Natural history, diagnosis, and the role of vaccines in their control. *Vet Clin North Am Food Anim Pract* 21: 383–408.
3. Skirrow S, BonDurant R (1998) Bovine trichomoniasis. *Vet Bull* 58: 591–603.
4. Clark B, Dufty J, Monsborough M (1968) Experimental *Vibrio fetus* (venerealis) infection in heifers. The immunising properties of killed organisms injected subcutaneously. *Aust Vet J* 44: 110–114.
5. MacLaren AP, Agumbah GJ (1988) Infertility in cattle in south-west Scotland caused by an “intermediate” strain of *Campylobacter fetus* subspecies *fetus* (formerly *Campylobacter fetus intestinalis*). *Br Vet J* 144: 29–44.
6. OIE; http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.04.05_BGC.pdf Chapter 2.4.5.
7. Cipolla A, Paolicchi F, Poso M, Morsella C, Casaro A, et al. (1998) Lectin-binding sites in uterus and oviduct of normal and *Campylobacter fetus* subspecies *venerealis*-infected heifers. *Eur J Histochem* 42: 63–70.
8. Truyers I, Luke T, Wilson D, Sargison N (2014) Diagnosis and management of venereal campylobacteriosis in beef cattle. *BMC Veterinary Research* 10: 280
9. Sanhueza JM, Heuer C, Jackson R, Hughes P, Anderson P, et al. (2014) Pregnancy rates of beef cattle are not affected by *Campylobacter fetus* subsp. *venerealis* real-time PCR-positive breeding sires in New Zealand. *NZ Vet J* 62: 237–243.
10. Hosseinzadeh S, Kafi M, Pour-Teimouri M (2013) PCR detection of *Campylobacter fetus* subspecies *venerealis* in smegma samples collected from dairy cattle in Fars, Iran. *Vet Res Forum* 4: 227–231.
11. Waldner C, Hendrick S, Chaban B, Garcia Guerra A, Griffin G, et al. (2013) Application of a new diagnostic approach to a bovine genital campylobacteriosis outbreak in a Saskatchewan beef herd. *Can Vet J* 54: 373–376.
12. Chaban B, Chu S, Hendrick S, Waldner C, Hill (2012) Evaluation of a *Campylobacter fetus* subspecies *venerealis* real-time quantitative polymerase chain reaction for direct analysis of bovine preputial samples. *Can J Vet Res* 76: 166–173.
13. Strickland L (2010) Surface Architectural Anatomy of The Penile and Preputial Epithelium of Bulls. Thesis 2010.
14. Cobo ER, Morsellac C, Canoc D, Cipollac A, Camperoc CM (2004) Immunization in heifers with dual vaccines containing *Trichomonas foetus* and *Campylobacter fetus* antigens using systemic and mucosal routes. *Theriogenology* 62: 1367–1382.
15. Sanderson M, Gnad D (2002) Biosecurity for reproductive diseases. *Vet Clin Food Anim* 18: 79–98.
16. Yaeger MJ, Holler LD (2007) Bacterial causes of bovine infertility and abortion. In: Younquist R.S., editor. *Current Therapy in Large Animal Theriogenology*. 2nd ed. Philadelphia; W.B. Saunders Company 391.
17. OIE (2015) http://www.oie.int/fileadmin/Home/eng/Health_standards/tahc/2010/chapitre_bovine_genital_campylobacteriosis.pdf. Chapter 11.3 of the Terrestrial Animal Health Code.