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REPRODUCTIVE DISORDERS CAUSED BY *CORYNEBACTERIUM PSEUDOTUBERCULOSIS* IN GOATS: A Review

Catarina Nunes Bittencourt[1], ORCID: 0000-0002-5518-1772
Lorena S. C. Nogueira[2], ORCID: 0009-0004-1107-749X
Laura N. F. Costa[3], ORCID: 0000-0002-4792-5655
Jackeline de Oliveira Costa [4], ORCID: 0009-0003-4203-7119
Ana Karina da Silva Cavalcante[5], ORCID: 0000-0002-7166-6673

ABSTRACT

Goat farming is a significant activity in Northeastern Brazil, characterized by family-based and subsistence farming, with low levels of technology and technical assistance. Technological issues, especially those related to animal health, impact the productivity and profitability of goat farming. Caseous lymphadenitis (CL) is an infectious contagious disease with worldwide distribution, caused by the bacterium *Corynebacterium pseudotuberculosis*, and is one of the main diseases compromising herd health, affecting both male and female goats and sheep regardless of breed or age, though it is most commonly found in animals over one year of age. The disease generally lacks specific symptoms; however, it results in low animal productivity and reproductive efficiency, as it is a chronic condition. With an estimated clinical prevalence of 50% in Brazil, especially in Northeastern Brazil, CL affects the reproductive efficiency of goats, as it may cause infertility in females, in addition to hormonal imbalances. Investigating the impacts of CL on reproduction and seeking alternatives to minimize losses, such as pharmacological control of the estrous cycle, are essential for improving herd conditions.

Keywords: Reproductive efficiency; Caseous lymphadenitis; Lymph nodes; Estrus repetition.

[1]State University of Bahia (UNEB), Graduate Program in Agroecology and Territorial Development, Juazeiro, Bahia, Brazil. E-mail: cati.bittencourt@gmail.com.
[2]Federal University of Recôncavo da Bahia (UFRB), Cruz das Almas, Bahia, Brazil. E-mail: lorenasacramento81@gmail.com.
[3]Arnaldo Horácio Ferreira University Center (UNIFAAHF), Luís Eduardo Magalhães, Bahia, Brazil. E-mail: nicoletifilipin@gmail.com.
[4]Federal University of Bahia (UFBA), Graduate Program in Environmental and Technological Science, Salvador, Bahia, Brazil. E-mail: jackelineooliveira@gmail.com.
[5]Federal University of Recôncavo da Bahia (UFRB), Center for Agricultural, Environmental, and Biological Sciences, Professional Master's Program in Agricultural Defense, Cruz das Almas, Bahia, Brazil. E-mail: karina@ufrb.edu.br.

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INTRODUCTION

According to Farias et al. (2019), goat farming is one of the main sources of income in Northeastern Brazil; however, it presents low levels of technology, technical assistance, and prophylactic management, as it is, in most cases, a subsistence farming activity.

Various technological obstacles in goat production systems in Northeastern Brazil result in low zootechnical and profitability indices. Among these obstacles, animal health stands out, as in an increasingly demanding market, the lack of sanitary control of herds leads to losses due to decreased production, herd depreciation, and the creation of trade barriers (Souza Neto, 1987; Nogueira Filho et al., 2008; Pinheiro et al., 2009).

Caseous lymphadenitis (CL), commonly known as “cheesy gland”, in english (or "mal-do-caroço", in portuguese), is caused by the bacterium *Corynebacterium pseudotuberculosis*. It is an infectious contagious disease with worldwide occurrence, affecting sheep and goats and, occasionally, humans. It has been identified as an endemic problem in Brazil, with an estimated clinical prevalence of approximately 50% in Northeastern Brazil, an important production area in the country, especially for meat goats and sheep (Nóbrega, 2010; Bezerra et al., 2017).

The disease can affect reproductive organs and reduce the reproductive efficiency of goats; however, the mechanism of action remains unclear, as does the economic impact caused by the repetition of one or more estrus cycles. *C. pseudotuberculosis* has also been shown to cause hormonal imbalances in non-pregnant goats, which may be the cause of infertility observed in seropositive females within a herd (Othman et al., 2014; Abdullah et al., 2020).

Thus, it is necessary to investigate the possible effects of caseous lymphadenitis on reproduction, as well as to seek alternatives to minimize the losses resulting from this pathology, with pharmacological control of the estrous cycle being a possible solution.

LITERATURE REVIEW

Goat farming in Brazil and worldwide

Goat farming extends across all continents and shows a significant annual growth rate. In 2017, the global goat population amounted to approximately 1 billion and 45 million animals, with an increase of about 49 million animals by 2019. China and India hold approximately 282 million goats globally, while Brazil’s goat population is approximately 11,301,481 (FAO, 2019).

The majority of Brazil's goat population is concentrated in Northeastern Brazil, with around 7.6 million head, distinguishing itself as a major producer of meat goats. Bahia ranks first nationally, with a herd of 2.4 million animals, followed by the states of Piauí, with 1.85 million head, and Pernambuco with 1.4 million head (FAO, 2019; IBGE, 2017), due to the high adaptability of these animals to climatic conditions (Nogueira Filho et al., 2008).

Despite the size of herds in these regions, their productivity remains low due to various factors, such as irregular rainfall, which affects food production, increases mortality rates, reduces weight gain, and lowers utilization rates. Another significant factor contributing to low productivity in goat farming is the general lack of technology adoption among producers. In recent years, improvements in small ruminant farming systems have been noted due to the increasing consumer market demand for meat and milk. This activity is essential for rural communities as it generates higher income, improves the economic conditions of small producers, and ensures their subsistence (Pedrosa et al., 2003).

Thus, goat farming is a highly important activity in the agriculture of Northeastern Brazil’s semi-arid region, although still unorganized, as it contributes to the region's economic growth, generates income, increases food supply, and leads to an improved quality of life for the population.

Sex hormones and the estrous cycle in goats

The goat species is characterized as seasonally polyestrous, meaning that females can exhibit multiple estrous cycles within a given season, responding to photoperiod and associated with good nutritional and health conditions. In tropical regions, where climatic variations are minimal and average temperatures remain higher throughout the year, females may cycle year-round, entering anestrus during periods of drought and scarcity (Delgadillo et al., 2004; Hafez, 2004).

The estrous cycle in goats lasts, on average, 21 days, varying from 17 to 25 days, and culminates in ovulation at the end of each cycle. The estrus phase, when the female is receptive to copulation, lasts approximately 36 hours (Delgadillo et al., 2004; Hafez, 2004).

Estrogen and progesterone (P4) are the main hormones responsible for maintaining the reproductive tract in mammals, sexual responses, and the development of the estrous cycle. Estrogen is secreted by the theca interna cells of ovarian follicles, while progesterone is produced by the corpus luteum. However, both hormones have hormonal precursors secreted by the hypothalamic-pituitary-gonadal complex to enable local release. Any dysregulation in the secretion of these hormones may cause an imbalance in the mechanisms of the estrous cycle, potentially leading to reproductive failure (Hafez, 2004; Khuder, 2012).

The corpus luteum begins to develop during the ovulation phase, 24 to 36 hours after the onset of estrus. It is a transient gland responsible for the synthesis and secretion of P4. In goats, the corpus luteum may remain active for up to 16 days, or, in the case of fertilization, it remains functional to support embryonic development and maintain pregnancy until its completion (Hafez, 2004; McIntosh & Smith, 1994). A study by Arashiro et al. (2010) revealed a positive correlation between corpus luteum development and serum P4 levels in healthy goats.

Caseous Lymphadenitis

Caseous lymphadenitis is a chronic disease caused by the bacterium *Corynebacterium pseudotuberculosis*, which commonly affects small ruminants, leading to production losses due to the high morbidity rate within herds, weight loss, increased mortality among younger animals, and decreased reproductive performance. This drastically reduces the pregnancy rate of the herd (Williamson, 2001; Pépin & Paton, 2011) and induces infertility as the disease progresses to a chronic stage (Latif et al., 2016).

It is an infectious and contagious disease with a chronic and debilitating nature, characterized by the formation of granulomas in superficial lymph nodes, organs, and internal lymph nodes. It has high morbidity rates within herds and is often subclinical. The disease has a worldwide distribution and, in Brazil, occurs primarily in Northeastern states, although it is present in herds throughout all regions of the country (Faccioli-Martins et al., 2014; De Sá et al., 2018).

Once affected, animals may experience reductions in meat, milk, and wool productivity, reproductive failures, as well as carcass condemnation at slaughter and depreciation of hides (Dorella et al., 2006; Camargo et al., 2010; Duno et al., 2016).

Epidemiology

Many countries have studied the prevalence of this disease, especially those where this activity is developed for subsistence farming, as in Northeastern Brazil. Souza et al. (2011) showed that this was the most prevalent disease in goats and sheep in the region. Guimarães et al. (2011) reported that various control programs were implemented in the region; however, due to the subclinical nature of the disease and the inefficacy of antibiotics against the microorganism, there were challenges in executing these programs. Even so, prophylactic measures are recommended, such as caution when introducing new animals into the herd and culling affected animals.

Farias et al. (2018) evaluated the seroprevalence of C. pseudotuberculosis in five states of Northeastern Brazil (Rio Grande do Norte, Paraíba, Ceará, Piauí, and Sergipe) and found a prevalence of 88.5% (193/218), suggesting that the agent is widespread in the evaluated herds. The highest prevalence was observed in the state of Rio Grande do Norte (94.5%) and the lowest in the state of Sergipe (70.3%).

Etiological agent

The etiological agent of caseous lymphadenitis is a facultative intracellular macrophage bacterium, non-capsulated, non-sporulating, non-motile, and aerobic. These characteristics allow the agent to survive in the environment for extended periods (Dorella et al., 2006; Souza et al., 2011).

The bacterium was first isolated in 1888, when it was identified in a cow with an atypical case of lymphangitis. Subsequently, the bacillus was also identified in an abscess in the kidney of a sheep. Years later, the bacterium was named *Bacillus pseudotuberculosis* ("false tuberculosis" in Greek) due to the similarity of its clinical lesions to the nodular lesions caused by tuberculosis. In 1894, the microorganism was fully described, and due to its similarities with the diphtheria bacillus in terms of morphology and cell wall composition, it was classified within the genus Corynebacterium (Faccioli-Martins et al., 2014; Dorella et al., 2006). This microorganism belongs to the CMNR group of Actinobacteria, which includes the genera Corynebacterium, Mycobacterium, Nocardia, and Rhodococcus. These genera have a complex lipid layer in their cell wall structure and the ability to multiply within macrophages. These microorganisms share similar cell wall characteristics, such as thickness, the presence of mycolic acids, and saturated and unsaturated fatty acids (Belchior et al., 2006).

There are two known and identified virulence factors: phospholipase D and mycolic acid. Phospholipase D is an enzyme capable of causing lysis and destruction of host cell membranes, facilitating the invasion and spread of the microorganism within the host organism. Therefore, it is considered an important exotoxin of the pathogen and, moreover, a determining factor in the virulence and development of caseous lymphadenitis (Baird & Fontaine, 2007). Another relevant aspect is the cell wall coating composed of mycolic acids, which increase the bacterium's resistance and pathogenicity (Oliveira, 2013). These acids have a cytotoxic effect on phagocytic cells, preventing their destruction and allowing the pathogen to survive within the host's intracellular environment (Williamson, 2001; Souza et al., 2011; Faccioli-Martins et al., 2014).

Transmission

The primary route of transmission of the disease is through direct contact between healthy and infected animals during confinement, with the latter considered sources of infection for the herd, as they shed the microorganism through oronasal discharge, purulent secretion from ruptured abscessed lymph nodes, and occasionally through milk (Pugh, 2005).

According to Baird and Fontaine (2007), animals, especially those in production, can become infected by ingesting

contaminated feed. Animals without clinical symptoms but with pulmonary lesions may be responsible for transmitting the disease through aerosols.

Transmission can be facilitated by small superficial wounds on abscesses (Solanet et al., 2011). The disease is primarily characterized by bacteria-induced caseous necrosis in the lymph glands (Santana-Jorge et al., 2016).

Regarding environmental viability, the bacterium can survive up to eight months in soil, four months in shearing sheds, and two months in hay and contaminated materials. Poor sanitation of facilities significantly contributes to this spread (Radostits et al., 2000). According to Alves et al. (1997), the thorny vegetation present in Northeastern Brazil constitutes a high-risk factor for the spread of the agent by causing skin lesions in sheep and goats.

Pathogeny

Shortly after infecting the host, C. pseudotuberculosis is phagocytosed by macrophages at the site of infection. However, due to the characteristics of its cell wall, which protect the agent from phagocytosis, this response is ineffective, as the bacterium is able to resist digestion by cellular enzymes. Thus, it remains as a facultative intracellular parasite of the macrophages (Baird & Fontaine, 2007; Collett et al., 1994).

The pathogen multiplies within the macrophages, causing cell lysis (Bogdan et al., 1997) and is able to survive inside the phagocytes for more than 48 hours (Bastos et al., 2012).

Subsequently, the microorganism migrates through the bloodstream or lymphatic circulation (Williamson, 2001), affecting various internal organs, such as mediastinal lymph nodes, lungs, liver, kidneys, subcutaneous tissues, mammary glands, and reproductive organs (Othman et al., 2016), thereby characterizing the visceral form of caseous lymphadenitis (CL). In the cutaneous form, there is infection of subcutaneous tissue and formation of abscesses in the lymph nodes, which can be palpated externally. Both forms may coexist in the same individual (Baird & Fontaine, 2007; Grosso et al., 2020).

Depending on the location of the abscesses, the disease may interfere with chewing, food-seeking behavior, locomotion, and lactation (Radostits et al., 2000; Santarosa et al., 2014). The visceral form of CL affects organs such as the liver, lungs, and spleen, as well as mediastinal and mesenteric lymph nodes (Guedes et al., 2015).

Mahmood et al. (2016) investigated the effects of *C. pseudotuberculosis* on buffalo fertility and, based on their findings, suggested that the bacterium and its exotoxin caused adverse effects on serum testosterone concentration, semen quality, and scrotal circumference in the animals studied. According to the authors, the main influence of CL on fertility may be associated with the chronicity of the disease, which damages the reproductive system.

Othman et al. (2016) investigated the histopathological changes in the reproductive organs and lymph nodes of non-pregnant goats experimentally infected with *C. pseudotuberculosis* via intradermal, intranasal, and oral routes. Their findings indicated that the bacterium can lead to infertility resulting from lesions in the uterus and ovaries, as the animals exhibited elevated concentrations of estrogen (E2) and progesterone (P4), a predisposing factor to infertility, as hormonal imbalances impair ovulation and embryo implantation. According to Foster (2012), the abnormal elevation of P4 can be interpreted by the organism as a signal of pseudopregnancy, potentially resulting in hydrometra or mucometra in the uterus, which hinders follicular development and ovulation.

Othman et al. (2016) attributed the observed hormonal changes to histopathological conditions in the ovaries. In this study, all goats inoculated with the bacterium developed histopathological lesions in the reproductive organs, with leukocyte infiltration in the lumen of ovulatory follicles, generalized congestion, and necrosis of ovarian stromal cells. Abdullah et al. (2020) identified the presence of inflammatory cells, vascular congestion, degeneration, and necrosis in the uterine myometrium. In the ovaries, they observed mild to moderate lesions, such as degeneration and necrosis..

Clinical signs

The clinical signs of caseous lymphadenitis (CL) may manifest in two clinical forms: external and internal (which may occur simultaneously). In the internal form, abscesses develop primarily in internal lymph nodes but also in organs such as the kidneys, lungs, liver, spleen, and uterus, potentially impairing organ function and causing obstructions in vital passages, such as the larynx, pharynx, and blood vessels. In the external form, animals commonly exhibit affected superficial lymph nodes, which are sensitive to palpation and have abscesses that rupture, releasing infectious material into the environment (Pépin & Paton, 2011; Grosso et al., 2018).

Animals with abscesses in superficial lymph nodes are considered clinically infected; however, some animals may present the visceral (or internal) form without showing clinical symptoms (Ribeiro et al., 2013) but still shed the bacterium, contaminating the environment in which they live (O'Reilly et al., 2008).

The most commonly affected lymph nodes are the pre-parotid and pre-scapular nodes, which are visible due to their fluctuant nature. Internally, granulomas may form in the mediastinal lymph nodes, causing respiratory symptoms such as chronic cough (Ribeiro, 1997).

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Economic impact of Caseous lymphadenitis

Caseous lymphadenitis (CL) causes a range of losses to global and Brazilian goat farming, with significant impacts on rural economies (Meyer et al., 2002; Guimarães et al., 2011). Characterized by the formation of encapsulated caseous necrotic lesions, CL leads to substantial losses for goat producers in various countries due to reduced meat, wool, milk, and hide yields; decreased reproductive efficiency; delayed growth; lower weight gain; premature culling of animals; and the sale of animals at prices below market value (Souza et al., 2011).

CL is the leading cause of carcass condemnation in sheep at slaughterhouses in Australia (Arsenault et al., 2003). It presents a significant challenge to goat farming, necessitating the implementation of biosecurity measures to control the disease and maintain its prevalence at acceptable levels (Guimarães et al., 2011).

In 2004, the National Health Program for Goats and Sheep (PNSCO) was established by the Ministry of Agriculture, Livestock, and Supply through Normative Instruction No. 87, dated December 10, 2004. The program aims to conduct epidemiological and sanitary surveillance for diseases affecting goats and sheep, with actions defined by the Department of Animal Health (DDA/DSA/MAPA) and implemented by State Official Services and private veterinarians. The objective is to ensure that the goat and sheep farming production chain meets the sanitary safety requirements necessary for market access, as well as food safety, through actions such as: epidemiological and sanitary surveillance for diseases in goats and sheep; reducing the risk of contagious disease spread among these species within the state; protecting herds from the introduction of exotic diseases; and contributing to public health promotion and environmental conservation.

Zoonotic potential

Caseous lymphadenitis is a zoonosis primarily affecting individuals who come into contact with infected animals, meaning it is associated with occupational exposure through contact with purulent material present in abscesses (Radostitis et al., 2000; Yeruham et al., 2004), as well as through contact with or ingestion of contaminated dairy products. The occurrence of the disease in humans is rare or unreported.

Faccioli-Martins et al. (2014) described some scientifically reported cases in countries with large numbers of animals, such as Australia and New Zealand, while few cases have been observed in other countries, including the United States, France, Panama, and Spain.

In Australia, Pell et al. (1997) reported ten cases of caseous lymphadenitis in humans, most of which were related to occupational exposure, as these patients had prior contact with sheep. These cases were treated through incision, drainage of suppurative lymphadenitis, and the use of antibiotics. However, the increased use of a caseous lymphadenitis vaccine for sheep in Australia has resulted in a decrease in this zoonosis.

According to Brazilian legislation (Brazil, 2020), the carcasses of animals with caseous lymphadenitis lesions in lymph nodes across different regions, with or without impairment of the animal's general condition, must be condemned. Only carcasses from animals with discrete, calcified lymph node lesions may be approved for consumption, provided that the drainage area of the affected lymph nodes is removed and condemned.

***C. pseudotuberculosis* in the reproductive organs of goats**

Khuder et al. (2012) were pioneers in reporting the effects of caseous lymphadenitis on reproductive hormone concentrations and histopathological changes in reproductive organs, correlating the presence of the bacterium in the bodies of experimentally inoculated rats with changes in testosterone concentrations and, to a lesser extent, in serum progesterone (P4) levels. These effects were attributed to tissue damage observed in the ovaries, which may lead to blockage of the hypothalamic-pituitary-gonadal axis.

Latif et al. (2016), Othman et al. (2016), and Abdullah et al. (2020) observed the pathological effects of *C. pseudotuberculosis* on the reproductive tract of goats after inoculation of the agent. The results showed histological alterations in the uterus, ovaries, uterine horns, cervix, and vagina, leading to cellular degeneration and blood vessel congestion in these organs, among other changes that demonstrate the severe pathogenicity of the bacterium.

Othman et al. (2014) and Abdullah et al. (2020) found a significant increase in estrogen levels in the blood of animals subjected to experimental inoculation with C. pseudotuberculosis, indicating that the bacterium has the capacity to increase the secretion of this hormone locally or via the hypothalamic-pituitary-gonadal complex.

Regarding progesterone, Abdullah et al. (2020) reported a gradual decrease in blood progesterone levels in females following experimental inoculation with C. pseudotuberculosis. Levels decreased as the infection duration increased, suggesting a possible relationship between the chronicity of the disease and the reduction in progesterone secretion.

The inoculation of *C. pseudotuberculosis* in rats resulted in tissue damage in reproductive tract organs, possibly associated with hormonal changes, as such damage would affect the hormonal feedback necessary for the regular functioning of the hypothalamic-pituitary-gonadal axis (Khuder et al., 2012). In a study on the pathogenic effects of bacterial diseases affecting the mammalian reproductive tract, Sheldon et al. (2009) concluded that, in animals affected by these diseases, progesterone levels post-ovulation were lower compared to those of healthy animals.

CONCLUSÃO

Caseous lymphadenitis (CL), caused by *C. pseudotuberculosis,* represents a significant challenge for goat farming in Northeastern Brazil, as well as in other regions with high concentrations of goats. This chronic, infectious, and contagious disease severely compromises herd health and results in substantial economic losses due to decreased meat, milk, and wool production, as well as negatively impacting the animals' reproductive efficiency.

Studies reveal that CL can induce hormonal and pathological changes in the reproductive organs of goats, leading to issues such as infertility and reduced reproductive efficiency. The presence of the pathogen in reproductive organs is associated with alterations in estrogen and progesterone levels, compromising the estrous cycle and fertility in females. This economic impact is considerable, affecting herd productivity and product quality, which necessitates effective control and management strategies.

The implementation of prophylactic measures, including biosecurity practices, sanitary surveillance, and pharmacological control, is essential to minimize the impacts of CL. In addition, the adoption of proper management strategies and educating producers about the risks and control methods are crucial to improving herd health and the profitability of goat farming.

REFERENCES

Abdullah JFF, Odhah MN, Abba Y, Garba B, Mahmood Z, Hambali IU, et al. Responses of female reproductive hormones and histopathology in the reproductive organs and associated lymph nodes of Boer does challenged with Corynebacterium pseudotuberculosis and its immunogenic corynomycolic acid extract. Microb Pathog. 2020;139:103965.

Alves FSF, Pinheiro RR, Pires PC. Linfadenite caseosa: patogenia, diagnóstico, controle. Sobral: EMBRAPA-CNPC; 1997. Documento 27.

Arashiro EKN, Viana JHM, Fonseca JF, Camargo LSA, Fernandes CAC, Brandão FZ. Luteal dynamics in goats: morphological and endocrine features. Rev Bras Zootec. 2010;39(9):1958-67.

Arseneault J, Girard C, Dubreuil P, Daignault D, René J, Boisclair GJ, et al. Prevalence of and carcass condemnation from maedi-visna, paratuberculosis and caseous lymphadenitis in culled sheep from Quebec, Canada. Prev Vet Med. 2003;59:67-81.

Baird GJ, Fontaine MC. Corynebacterium pseudotuberculosis and its role in ovine caseous lymphadenitis. J Comp Pathol. 2007;137(4):179-210.

Bastos CR, Blagitz MG, Souza FN, Batista CF, Stricagnolo CAR, Azevedo MR, et al. Viabilidade celular, fagocitose e espraiamento de fagócitos mononucleares, e liberação de peróxido de hidrogênio por leucócitos de glândulas mamárias sadias e infectadas. Pesq Vet Bras. 2012;32:850-4.

Belchior ES. Actualización sobre linfadenitis caseosa: El agente etiológico y la enfermedad. Vet Argent. 2006;23(224):258-78.

Bezerra AC, Pandorfi H, Gama RM, Carvalho FFR, Guiseiline C. Desenvolvimento de um modelo de rastreabilidade para caprinos e ovinos de corte. Rev Eng Agrícola. 2017;37(5):782-90.

Bogdan J, Newlands-Monteith C, Ellis J. Nitric oxide production following in vitro stimulation of ovine pulmonary alveolar macrophages. Vet Immunol Immunopathol. 1997;56:299-310.

Brasil. Decreto nº 10.468, de 18 de agosto de 2020. Altera o Decreto nº 9.013, de 29 de março de 2017, que dispõe sobre o Regulamento da inspeção industrial e sanitária de produtos de origem animal - RIISPOA.

Camargo EV, Barboza CS, Krewer C, Vargas APC, Cecim M, Leal ML. Isolamento de Corynebacterium pseudotuberculosis no sêmen de um carneiro na região central do Rio Grande do Sul. Arq Inst Biol. 2010;77(1):139-42.

De Sá MCA, Rocha Filho JTR, Rosa DS, De Sá SA, Freire DP, Alcantara ME, et al. Linfadenite caseosa em caprinos e ovinos: Revisão. PUBVET. 2018;12:133.

Delgado JA, Fitz-Rodríguez G, Duarte G, Véliz FG, Carrillo E, Flores JA, et al. Management of photoperiod to control caprine reproduction in the subtropics. Reprod Fertil Dev. 2004;16:471-8.

Dorella FA, Pacheco LGC, Oliveira SC, Miyoshi A, Azevedo V. Corynebacterium pseudotuberculosis: microbiology, biochemical properties, pathogenesis and molecular studies of virulence. Vet Res. 2006;37(2):201-18.

Duno AD, Zárraga J, Chirino-Zárraga CI, Portillo LL. Caracterización epidemiológica da linfadenite caseosa em caprinos rebanhos na Península Paraguana, Venezuela. Rev Med Vet. 2016;31:19-26.

Faccioli-Martins PY, Alves FSF, Pinheiro RR. Linfadenite caseosa: perspectivas no diagnóstico, tratamento e controle. Embrapa Caprinos e Ovinos-Documentos (INFOTECA-E). 2014. p. 69.

FAO. FAOSTAT Productive on live animals. 2019 [Internet]. Available from: http://www.fao.org/faostat/en/?#data/QA/visualize. Accessed 14 Jan 2020.

Farias AEM, Alves JRA, Alves FSF, Pinheiro RR, Faccioli-Martins PY, Lima AMC, et al. Soroprevalência da infecção por Corynebacterium pseudotuberculosis em caprinos no Nordeste brasileiro utilizando a técnica de imunoabsorção enzimática (ELISA – indireto). Pesq Vet Bras. 2018;38:1344-50.

aprinos e Ovinos-Artigo em periódico indexado (ALICE). 2019.

Grosso FV, Tinkler S, Sola M, Miller M, Gan Heng H. Radiographic and computed tomographic appearance of caseous lymphadenitis in a goat. Vet Radiol Ultrasound. 2020;61(1):104-9.

Guedes MT, Souza BC, Sousa TJ, Loureiro D, Moura-Costa LF, Azevedo V, et al. Infecção por Corynebacterium pseudotuberculosis em equinos: aspectos microbiológicos, clínicos e preventivos. Pesq Vet Bras. 2015;35(8):701-8.

Guimarães AS, Carmo FB, Pauletti RB, Seyffert N, Ribeiro D, Lage AP, et al. Caseous lymphadenitis: epidemiology, diagnosis, and control. The II OAB Journal. 2011;2:33-43.

Hafez B, Hafez ESE. Reprodução animal. São Paulo: Manole; 2004.

IBGE. Censo Agropecuário 2017. Disponível em: https://censos.ibge.gov.br/agro/2017/templates/censo_agro/resultadosagro/pecuaria.html?localidade=0&tema=75662. Acesso em 10 fev 2020.

Khuder Z, Osman AY, Jesse FF, Haron AW, Saharee AA, Sabri J, et al. Sex hormone profiles and cellular changes of reproductive organs of mice experimentally infected with C. pseudotuberculosis and its exotoxin phospholipase D (PLD). IOSR J Agric Vet Sci. 2012;1(3):24-9.

Latif NAA, Abba Y, Jesse FFA, Chung ELT, Zamri-Saad M, Saharee AA, et al. Histopathological assessment of chronic Corynebacterium pseudotuberculosis infection in the reproductive tract and iliac lymph node of Katjang does. Comp Clin Pathol. 2016;26(1):147-54.

Mahmood ZK, Jin ZAM, Jesse FF, Saharee Sabri J, Yusoff R, Haron AW. Relationship between the Corynebacterium pseudotuberculosis, phospholipase D inoculation and the fertility characteristics of crossbred Boer bucks. Livest Sci. 2016;191:12-21.

Meyer R, Carminati R, Cerqueira RB, Vale V, Viegas S, Martinez T, Nascimento I, Schaer R, Silva JAH, Ribeiro M, et al. Avaliação da resposta imune humoral em caprinos inoculados com uma vacina viva atenuada liofilizada contra Corynebacterium pseudotuberculosis. Rev Ciênc Méd Biol. 2002;1(1):42-8.

Nóbrega KF. Linfadenite caseosa: revisão e considerações sobre a utilização de vacinas no Brasil. Patos: Universidade Federal de Campina Grande; 2010.

Nogueira Filho A, Yamamoto A, Figueiredo Júnior CA. Panorama atual da caprino-ovinocultura nordestina. Informe Rural ETENE. 2008;2(10).

O'Reilly KM, Green LE, Malone FE, Medley GF. Parameter estimation and simulations of a mathematical model of Corynebacterium pseudotuberculosis transmission in sheep. Prev Vet Med. 2008;83(3-4):242-59.

Othman AM, Jesse FFA, Adamu L, Abba Y, Adza Rina MN, Saharee AA, et al. Changes in serum progesterone and estrogen concentrations in non-pregnant Boer does following experimental infection with Corynebacterium pseudotuberculosis. J Vet Adv. 2014;4(5):524-8.

Othman AML, Abba Y, Jesse FFA, Iliyasu YM, Saharee AA, Haron AW, et al. Reproductive pathological changes associated with experimental subchronic Corynebacterium pseudotuberculosis infection in non-pregnant Boer does. J Pathog. 2016;2016.

Pedrosa KYF, Barreto JR, Costa ES. Aspectos epidemiológicos e sanitários das criações de caprinos na zona noroeste do Rio Grande do Norte. Caatinga. 2003;16:17-21.

Peel MM, Palmer GG, Stacpoole AM, Kerr TG. Human Lymphadenitis Due to Corynebacterium pseudotuberculosis: Report of Ten Cases from Australia and Review. Clin Infect Dis. 1997;24:185-91.

Pépin M, Paton MW. Caseous lymphadenitis in sheep and goats. In: Lefevre PC, Blancou J, Chermette R, Uilenberg G, editors. Infectious and parasitic diseases of livestock. Paris: Lavoisier; 2011. p. 1153-65.

Pinheiro RR, Ximenes LJF, Pinheiro AA, Teixeira MFS. Lentivírus de pequenos ruminantes: diagnóstico, prevenção e vacinas. In: Embrapa Caprinos e Ovinos-Capítulo em livro científico (ALICE). 2009. p. 24.

Pugh DG. Clínica de ovinos e caprinos. São Paulo: Roca; 2005. p. 228-9.

Radostits OM, Gay CC, Blood DC, Hinchcliff KW. Clínica veterinária: Um tratado de doenças de bovinos, ovinos, suínos, caprinos e equinos. 9th ed. Rio de Janeiro: Guanabara Koogan; 2000. p. 874-87.

Ribeiro D, Dorella FA, Pacheco LGC, Seyffert N, Castro TLP, Portela RWD, et al. Subclinical Diagnosis of Caseous Lymphadenitis Based on ELISA in Sheep from Brazil. J Bacteriol Parasitol. 2013;4(3).

Ribeiro SDA. Caprinocultura: Criação Racional de Caprinos. São Paulo: Nobel; 1997.

Santana-Jorge KTO, Santos TM, Tartaglia NR, Aguiar EL, Souza RFS, Mariutti RJ, et al. Putative virulence factors of Corynebacterium pseudotuberculosis FRC41: vaccine potential and protein expression. Microb Cell Fact. 2016;15(1):83.

Santarosa BP, Dantas GN, Amorim RL, Chiacchio SB, Oliveira F, Amorim RM, et al. Meningoencefalite supurativa por Corynebacterium pseudotuberculosis em cabra com linfadenite caseosa: Relato de caso. Vet Zootec. 2014;37:537-42.

Smith MF, McIntushi EW, Smith GW. Mechanism associated with corpus luteum development. J Anim Sci. 1994;72:1857-72.

Solanet JJ, Malena R, Estein SM, Belchior SE, Paolicchi. Desarrollo de una prueba de ELISA para detectar anticuerpos en carneros vacunados o infectados con Corynebacterium pseudotuberculosis. Rev Argent Microbiol. 2011;43(1):9-17.

Souza FM, Carvalho AQ, Garino Jr F, Riet-Correa F. Linfadenite caseosa em ovinos deslanados abatidos em um frigorífico da Paraíba. Pesq Vet Bras. 2011;31(3):224-30.

Souza Neto J. Características gerais da caprinocultura leiteira no estado de Pernambuco. Sobral: EMBRAPA – CNPC; 1987. Boletim n. 4.

Williamson LH. Caseous lymphadenitis in small ruminants. Vet Clin North Am Food Anim Pract. 2001;17:359-71.