

## **BOVINE NEOSPOROSIS: FROM BIOLOGY TO CONTROL IN DAIRY AND BEEF HERDS**

### **NEOSPOROSE BOVINA: DA BIOLOGIA AO CONTROLE EM REBANHOS LEITEIROS E DE CORTE**

### **NEOSPOROSIS BOVINA: DE LA BIOLOGÍA AL CONTROL EN HATOS LECHEROS Y DE CARNE**



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#### **ABSTRACT**

Bovine neosporosis, caused by *Neospora caninum*, is an important etiology of reproductive losses in dairy and beef herds, with significant economic impact. This literature review summarizes evidence on the parasite's biology, transmission routes, epidemiology, clinical manifestations, diagnosis, and control strategies in cattle. Transmission occurs primarily vertically, which maintains the agent in the herd, and horizontally from canines, the definitive hosts that disseminate oocysts into the environment. Sporadic or outbreak-related abortions—most frequent from the second to seventh month of gestation—are the main clinical manifestation. Serological methods (IFA, ELISA) are useful for population screening and risk assessment, while confirmation of abortions depends on the combination of histopathology, immunohistochemistry, and/or molecular detection. There is no field-proven curative treatment; Thus, control is based on biosecurity (restriction of dog access and appropriate management of placentas and fetal remains), reproductive measures (judicious use of embryo transfer, culling or non-breeding of females with compatible reproductive histories), and environmental risk management. Gaps persist in vaccine efficacy, mitigation of transplacental transmission, and standardization of cost-effective diagnostic algorithms. It

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is concluded that integrated and contextual approaches, combining surveillance, reproductive management, and biosecurity, are essential to reduce the disease burden.

**Keywords:** *Neospora caninum*. Bovine Abortion. Vertical Transmission. Diagnosis. Biosecurity. Health Control.

## RESUMO

A neosporose bovina, causada por *Neospora caninum*, é importante etiologia de perdas reprodutivas em rebanhos leiteiros e de corte, com impacto econômico significativo. Esta revisão de literatura sintetiza evidências sobre biologia do parasito, vias de transmissão, epidemiologia, manifestações clínicas, diagnóstico e estratégias de controle em bovinos. A transmissão ocorre principalmente por via vertical, responsável pela manutenção do agente no rebanho, e por via horizontal a partir de canídeos, hospedeiros definitivos que disseminam oocistos no ambiente. Abortos esporádicos ou em surtos—mais frequentes do segundo ao sétimo mês de gestação—constituem a principal expressão clínica. Métodos sorológicos (IFI, ELISA) são úteis para triagem populacional e investigação de risco, enquanto a confirmação em eventos abortivos depende da associação entre histopatologia, imuno-histoquímica e/ou detecção molecular. Não há tratamento curativo comprovado em campo; assim, o controle baseia-se em biosseguridade (restrição de acesso de cães e manejo adequado de placentas e restos fetais), medidas reprodutivas (uso criterioso de transferência de embriões, descarte ou não reprodução de fêmeas com histórico reprodutivo compatível) e gestão do risco ambiental. Persistem lacunas quanto à eficácia de vacinas, à mitigação da transmissão transplacentária e à padronização de algoritmos diagnósticos custo-efetivos. Conclui-se que abordagens integradas e contextuais, combinando vigilância, manejo reprodutivo e biosseguridade, são essenciais para reduzir a carga da doença.

**Palavras-chave:** *Neospora caninum*. Aborto Bovino. Transmissão Vertical. Diagnóstico. Biosseguridade. Controle Sanitário.

## RESUMEN

La neosporosis bovina, causada por *Neospora caninum*, es una etiología importante de pérdidas reproductivas en hatos lecheros y de carne, con un impacto económico significativo. Esta revisión bibliográfica resume la evidencia sobre la biología del parásito, las vías de transmisión, la epidemiología, las manifestaciones clínicas, el diagnóstico y las estrategias de control en el ganado. La transmisión se produce principalmente por vía vertical, lo que mantiene al agente en el hato, y por vía horizontal desde los caninos, huéspedes definitivos que diseminan los oocistos al ambiente. Los abortos esporádicos o similares a brotes, más frecuentes entre el segundo y el séptimo mes de gestación, son la principal manifestación clínica. Los métodos serológicos (IFA, ELISA) son útiles para el cribado poblacional y la evaluación de riesgos, mientras que la confirmación de los abortos depende de la combinación de histopatología, inmunohistoquímica y/o detección molecular. No existe un tratamiento curativo probado en campo. Por lo tanto, el control se basa en la bioseguridad (restricción del acceso de perros y manejo adecuado de placentas y restos fetales), medidas reproductivas (uso prudente de la transferencia de embriones, sacrificio o no reproducción de hembras con antecedentes reproductivos compatibles) y gestión de riesgos ambientales. Persisten deficiencias en la eficacia de las vacunas, la mitigación de la transmisión transplacentaria y la estandarización de algoritmos de diagnóstico rentables. Se concluye que los enfoques integrados y contextuales, que combinan vigilancia, manejo reproductivo y bioseguridad, son esenciales para reducir la carga de la enfermedad.



**Palabras clave:** *Neospora caninum*. Aborto Bovino. Transmisión Vertical. Diagnóstico. Bioseguridad. Control Sanitario.



## 1 INTRODUCTION

Neosporosis, caused by the obligate intracellular protozoan *Neospora caninum*, is recognized as one of the main causes of abortion in cattle in several countries, including Brazil, generating significant economic losses for dairy and beef cattle (DUBEY; SCHARES; ORTEGA-MORA, 2007; ROCHA et al., 2015). Since its initial description in the 1980s, the disease has received increasing attention due to its wide distribution, high seroprevalence and complexity in control, associated with the agent's ability to remain in herds by vertical and horizontal transmission (AMARAL et al., 2012; GOODSWEH; KENNEDY; ELLIS, 2013).

The heteroxenon biological cycle of *N. caninum* involves definitive hosts — mainly dogs (*Canis lupus familiaris*) — and several intermediate hosts, such as cattle, sheep, goats, horses and wild animals (TEIXEIRA et al., 2010; REICHEL et al., 2020). Infection can result in varied clinical manifestations, but miscarriage, especially in the second trimester of pregnancy, is the most common and impactful sign for production (GOTTSTEIN et al., 2020).

Epidemiological studies indicate that factors such as age, reproductive management, presence of dogs in the environment and contact with wild animals influence the spread of the protozoan (OLIVEIRA et al., 2010; SOUSA et al., 2012). Transplacental transmission is considered the main route of disease maintenance in herds, while the ingestion of sporulated oocysts present in the environment represents the predominant route of horizontal infection (DUBEY et al., 2017).

In view of the health and economic impact of neosporosis, an in-depth understanding of its etiology, biological cycle, epidemiology, pathogenesis, and prevention measures is essential to support effective control strategies. This review aims to compile and critically analyze the available knowledge about *Neospora caninum* in cattle, highlighting the main scientific advances, risk factors and gaps in the literature.

## 2 LITERATURE REVIEW

### *Neospora caninum* (N. caninum)

Etiology Neosporosis is considered the main cause of abortions in cattle, totaling large economic losses on the properties. It is an obligate intracellular parasite *Neospora caninum* of the phylum Apicomplexa, class Sporozoa, order Eucoccidiorida, suborder Eimeriiformes, family Sarcocystidae, subfamily Toxoplasmatinae (ROCHA et al, 2015). This disease was first described in 1984 in Norway, but the agent was confused with *Toxoplasma gondii* and the diagnosis given was deadly encephalopathy in dogs. This



occurred as a result of the biological and structural similarities of both. However, despite belonging to the same family, they are antigenically different, putting an end to the controversies from 1988 onwards (CHECHIN, 2013). The first definitive recognized host of this disease was the dog, but in some cases it has been found that it can also assume the role of intermediate host. However, studies have shown that coyotes, gray wolves and dingoes also have the possibility of being definitive hosts, as they have been observed to be animals capable of eliminating oocysts through feces. The intermediate hosts discovered were: ruminants, wild rats, horses, foxes and deer, among others (TEIXEIRA et al, 2010).

## 2.1 BIOLOGICAL CYCLE AND HOSTS

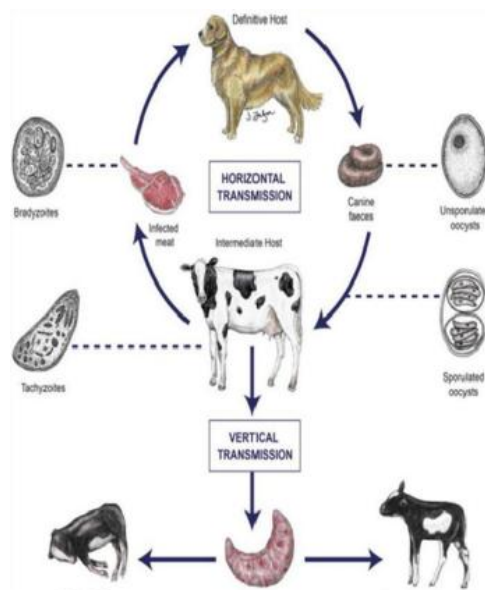
Infection by *Neospora caninum* occurs through the ingestion of these oocysts, and this protozoan presents itself with several known infective forms, namely: Tachyzoites, oocysts and tissue cysts containing bradyzoites, these can be transmitted in different ways. Its life cycle is heteroxene with sexual reproduction in the definitive host, and asexual reproduction occurs in the intermediate hosts. The oocysts finish their development in the definitive hosts, and these eliminate them through the feces, contaminating food, water and pastures (SOUSA et al, 2012). The definitive host becomes infected after ingesting the cysts with bradyzoites present in infected tissues, and after about five days will eliminate non-sporulated oocysts in the feces. These oocysts in the environment can then sporulate within 72 hours, depending on environmental conditions. These oocysts are made up of a thick wall that allows the sporocysts to survive even in unfavorable environmental conditions for a long period of time (PIAGENTINI et al, 2012).

Intermediate hosts, on the other hand, become infected through the ingestion of infected tissues with the presence of bradyzoites or ingestion of food and water contaminated with oocysts, as well as fluids with tachyzoites (horizontal transmission). When they reach the stomach of this host, they will rupture by mechanical action, and in the intestine will be released the infecting sporozoites that penetrate various tissues, and by asexual reproduction will originate mobile tachyzoites (OLIVEIRA et al, 2010). In this phase, they will multiply rapidly and spread the infection, damaging cells, causing lysis of the host cell and release of tachyzoites that are free to infect a variety of tissues and cell types. This event favors the dissemination and establishment of parasitemia. To complete the life cycle, it is then necessary that the bradyzoites be ingested by the definitive host (ROCHA et al, 2015). In this way, the contamination of intermediate hosts

denotes a vertical or transplacental route that causes fetal infection and can generate abortion, as well as by horizontal transmission (PEREIRA, 2018). The vertical route is one of the main casuistries for the spread of neosporosis among cattle, especially by younger cows, and is interconnected with the maintenance of the disease in the herd and also dissemination. The intense occurrence of a latent infection during pregnancy can increase the risk of miscarriage (MOURA et al, 2012).

**Figure 1**

*Heteroxenon life cycle of *Nesopora caninum**



Source: ROCHA, et al 2015.

**Epidemiology and risk factors** It is of paramount importance to know the risk factors of *N. caninum* in order to establish control measures against the disease and improve the sanitary management of cattle herds. Thus, it is found that the age of the animal is a factor to be considered, because with age/and/or number of births the risk of contracting the infection is greater (AMARAL et al, 2012) The presence of dogs among the herd increases the possibility of horizontal transmission, as they eliminate oocysts when they defecate and contaminate pastures, water and food. This occurrence is more intense in younger dogs that are able to eliminate a greater amount of oocysts (OLIVEIRA et al, 2010). According to Silva et al (2012), the access of wild animals to the herd also revealed a significant association with the occurrence of the disease. It is also necessary to monitor the reproductivity of cows, as cows with a history of reproductive disorders were associated with seropositivity for neosporosis, with abortion being the most frequent symptom. Thus, the occurrence of anestrus, repetition of heat, may mean a relationship with the prevalence of neosporosis (PIAGENTINI et al, 2012). According





to Amaral et al (2012), there is greater persistence of the disease in herds with a greater number of animals and depending on aptitude, with a greater risk for dairy herds, which can be associated with differentiated management (OLIVEIRA et al, 2010). There are also controversies about a lactogenic transmission of milk containing tachyzoites, which is also considered a risk factor. Some authors report that the presence of other diseases can lead to immunosuppression and favor infection (CHECHIN, 2013).

## 2.2 PATHOGENESIS

It was found that in calves of mothers born seropositive for neospora, there is the presence of pre-colostral antibodies, leading to the conclusion that there is transmission of the protozoan to later generations (PEREIRA, 2018). The bovine fetus is vulnerable to *N. caninum*, because in the initial third of gestation it cannot recognize the pathogen, and immunity develops according to the period of pregnancy. Thus, this fetal recognition is inefficient in the 5th and 6th months, resulting in the period with the highest occurrence of miscarriages (SOUSA et al, 2012). At the beginning of pregnancy, the risk of miscarriage is higher, as there is low production of progesterone and Th2, which is responsible for humoral immunity, but the risk of transmission is low (TEIXEIRA et al, 2010). On the other hand, if the infection occurs in the third trimester of pregnancy, the risk of miscarriage is lower, but placental transmission is lower.

is higher, suggesting congenital transmission, as it is a stage in which progesterone and Th2 are already higher (AMARAL et al, 2012). By presenting an efficient immune response, the tachyzoites will transform into bradyzoites and form tissue cysts that attach mainly to central nervous tissue, but in this way the animal does not present clinical symptoms. However, when there is a possible drop in immunity, bradyzoites or tachyzoites can be differentiated, culminating in activation or reactivation of the latent infection. There are factors that make this scenario more worrying, such as: changes in the hormones of the pregnant female, failure to recognize the fetus so as not to have rejection, and the existence of mycotoxins in the animals' food (ROCHA et al, 2015). In the case of bulls, it is possible for transmission via semen to occur, although the chances are lower. This category sporadically excretes deoxyribonucleic acid (DNA) of the neoprosis agent in semen, complementing some studies that have shown impaired embryonic development in cows impregnated with semen from bulls infected with tachyzoites (CHECHIN, 2013). The protozoan, when entering the uterine cells, multiplies, resulting in local destruction in fetal and maternal tissues, resulting in an intense inflammatory response. Destruction then spreads to the chorio-allantois among



the cotyledons. At the same time, *N. caninum* can invade other tissues, with a predilection for the central nervous system, where it has a predilection for the periphery of blood vessels (PIAGENTINI et al 2012).

### 2.3 CLINICAL SIGNS

One of the main clinical manifestations in infected cattle is abortion that occurs between the third and eighth month of gestation. It is capable of causing fetal death at the beginning of pregnancy, resulting in embryo resorption and return to heat. Most abortions occur in the second trimester of pregnancy (PEREIRA, 2018). The fetus can die in the womb, be reabsorbed, mummify, autolyze, die soon after birth (stillbirth), be born alive with clinical signs with proprioceptive deficit to complete paralysis, or be born clinically normal but chronically infected (GOTTSTEIN et al., 2005). Macroscopically, in aborted fetuses, there is autolysis with accumulation of serosanguineous fluid in the body cavities. White multifocal areas in the skeletal and cardiac muscles are rarely observed, as well as hemorrhagic foci in the lungs (BARROS et al, 2010).

### 2.4 DIAGNOSIS

The diagnosis should be made by associating the history, in order to evidence the etiological agent such as the immunohistochemistry technique that enables the visualization of cysts and tachyzoites (PIAGENTINI et al 2012), in addition to serological tests using indirect immunofluorescence tests (IFA) or ELISA (PEREIRA, 2018).

### 2.5 DIFFERENTIAL DIAGNOSIS

According to EMBRAPA 2012, the differential diagnosis for abortion should include bovine diarrhea virus (BVD), infectious bovine rhinotracheitis (IBR), leptospirosis and brucellosis.

### 2.6 ECONOMIC LOSSES

Neosporosis is a disease that affects cattle and has a great economic impact, as it is considered one of the main causes of reproductive disorders in cattle (SARTOR et al, 2005). Through some economic losses related to neosporosis is abortion, and the low rate of enjoyment that represent an economic loss of 27.3% of the total revenue at the time the calf is sold, with a loss of R\$66,372.39 for a production system with 1,000 heifers (BARROS et al, 2010).





## 2.7 CONTROL AND PREVENTION

Neosporosis control should be done through means aimed at interrupting the transmission cycle of the agent. Animals that tested positive in the herd should be slaughtered later, in order to prevent the entry of new infected animals into the herd, which can reduce vertical transmission (TEIXEIRA et al, 2010). As for horizontal transmission, a control should be carried out in the population of definitive hosts (DUBEY et al., 2007). *N. caninum* has no effective treatment, however scientists are studying ways to block transplacental transmission through drugs such as toltrazuril that are being tested in mice (GOTTSTEIN et al., 2005).

Some other precautions that can be taken are: performing embryo transfer, avoiding interactions with existing dogs on the property, in order to prevent fecal infection of water, pasture shed (feed and silo).

## 3 CONCLUSION

Bovine neosporosis represents a persistent challenge for livestock due to its high prevalence, potential to cause significant reproductive losses, and absence of effective treatment. *Neospora caninum* demonstrates a great capacity for adaptation and maintenance in herds, mainly through vertical transmission, which makes it difficult to eradicate (DUBEY et al., 2007; GOTTSTEIN et al., 2020).

The analysis of the literature indicates that integrated management, including the identification and selective disposal of seropositive animals, the control of the access of dogs and wild animals to breeding areas, and safe reproductive practices, such as embryo transfer, are the main tools available to reduce the spread of the agent (REICHEL et al., 2020; DUBEY et al., 2017).

Despite advances in diagnostic techniques, such as the use of ELISA and PCR, there are still gaps in the development of effective vaccines and safe therapeutic protocols. Investments in research that elucidate immunological mechanisms of protection, host-pathogen interactions, and environmental factors associated with infection are crucial for new prevention approaches.

Therefore, mitigating the impacts of neosporosis requires multidisciplinary strategies that combine biosecurity measures, rational reproductive management, and continuous epidemiological surveillance. The strengthening of public policies and health education programs is also essential to increase the awareness of producers and professionals, contributing to the sustainable control of this important disease in cattle farming.



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