UNIVERSIDAD TECNOLÓGICA METROPOLITANA del Estado de Chile
UTEM
https://revistammsb.utem.cl | revista.mmsb@utem.cl
ISSN-L: 2735-6817 | ISSN (online): 2735-6817

REVISTA MMSB
Revista de Modelamiento Matemático de Sistemas Biológicos
Vol.4(2024), pp.1–10, e24R01
https://doi.org/10.58560/rmmsb.v04.e.024.01

Mathematical modelling of *Neospora caninum* infection in dairy cattle and domestic dogs

Modelado matemático de la infección por *Neospora caninum* en ganado lechero y perros domésticos.

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Recepción: 2023-10-26 | Aceptación: 2024-05-01 | Publicación: 2024-09-30

Recommended Citation: Bergero, P. *et al.* (2024). *'Mathematical modelling of* Neospora caninum *infection in dairy cattle and domestic dogs'*. Rev. model. mat. sist. biol. Vol.4, e24R01, doi:10.58560/rmmsb.v04.e.024.01

Support: This work was supported by the CONICET and the UNLP.

ABSTRACT

Bovine neosporosis is a global disease caused by the protozoan parasite *Neospora caninum*. It is a major contributor to abortions in both dairy and beef cattle, resulting in significant economic losses annually. Domestic dogs and certain species of wild carnivores serve as definitive hosts, shedding oocysts into the environment through feces. Two primary transmission mechanisms have been identified: horizontal transmission, occurring through the ingestion of raw or undercooked meat containing cysts or water contaminated with oocysts, and vertical or transplacental transmission, where tachyzoites pass to the fetus. In cattle, the disease exhibits two epidemiological manifestations: endemic and epidemic abortions, known as *abortion storms*. Dynamic models of infectious diseases have proven valuable for studying dynamic effects and evaluating various control strategies. In this study, we present a compartmental model for neosporosis in both dairy cattle and the domestic dog population. The cattle disease submodel categorizes the population based on the infection mechanism (congenital or acquired through ingestion) to more accurately describe the two epidemiological patterns of the disease. The dog disease submodel represents disease transmission in this host, including infected cattle as a source of infection. A third submodel accounts for environmental contamination with oocysts, acting as a source of infection for cattle. Our goal was to provide a more realistic description of transmission in dairy farms by considering the complete life cycle of *N. caninum*.

Keywords:

Neosporosis, Mathematical Epidemiology

RESUMEN

La neosporosis bovina es una enfermedad global, cuyo agente etiológico es el parásito protozoario *Neospora caninum*. Es la principal causa de abortos en ganado lechero y de carne, generando pérdidas económicas significativas cada año. Los perros domésticos y ciertas especies de carnívoros silvestres actúan como hospedadores definitivos, eliminando ooquistes en el ambiente a través de las heces. Se han identificado dos mecanismos principales de transmisión: la transmisión horizontal, producida por la ingestión de carnes crudas o mal cocidas con la presencia de quistes o agua contaminada con ooquistes, y la transmisión vertical o transplacentaria por el pasaje de taquizoítos al feto. En los bovinos, la enfermedad presenta dos tipos de manifestaciones epidemiológicas: abortos endémicos y epidémicos, conocidos como "tormentas de abortos". Los modelos dinámicos de enfermedades infecciosas han demostrado ser un abordaje valioso, permitiendo estudiar efectos dinámicos y la evaluación de diversas estrategias de control. En este estudio, presentamos un modelo compartimental de la neosporosis tanto para el ganado lechero como para la población de perros domésticos. El submodelo de la enfermedad en el ganado clasifica la población según el mecanismo de infección (congénito o adquirido mediante la alimentación), con el fin de describir de manera más precisa los dos patrones epidemiológicos de la enfermedad. El submodelo de la enfermedad en los perros representa la transmisión de la enfermedad en este hospedador, incluyendo a su vez al ganado infectado como fuente de infección. Un tercer submodelo representa la contaminación del entorno con ooquistes, que actúan como fuente de infección para el ganado. Nuestro objetivo fue proporcionar una descripción más realista de la transmisión en el ganado lechero al considerar el ciclo de vida completo de *N. caninum*.

Palabras Claves:

Neosporosis bobina, Epidemiología Matemática

2020 AMS Mathematics Subject Classification: Primary: 92B05; Secondary: 92D30

INTRODUCTION

Neosporosis is a disease with great impact in cattle. The infection with the protozoan *Neospora caninum* in dairy herds is responsible of reproductive failure: abortions, that occur mostly in the second and last trimester of gestation, birth of clinically normal but congenitally infected calves and less frequently observed neuromuscular damage in newborn calves. (Dubey *et al.*, 2007) The economic losses in dairy herds include fetal loss, laboratory diagnosis, reduced milk yield and replacement of the aborted culled cow(Moore *et al.*, 2013) Reproductive failures exhibit two patterns: endemic and epidemic abortions. The epidemic abortions, also called abortion storms, were early described by Wouda et al, who reported abortion storms in 50 related *N. caninum* infection that ranged from 6 to 65 days.(Wouda *et al.*, 1999) Horizontal transmission in cattle and dogs occur due to oocyst-contaminated feed/water.(Trees *et al.*, 2002) Regarding vertical transmission, the gestational pattern of susceptibility and the consequences of neosporosis in cattle are complex. Experiments suggest that transplacental transmission is rare when non-infected cows consume oocysts in the first trimester of gestation, while it is highly efficient when oocysts are consumed in the third trimester. Between 70 and 160 days of gestation, transplacental infection occurs in a proportion of pregnancies, leading to abortion approximately 6 weeks later.(Gondim and McAllister, 2022)

The presence of canids in dairy and beef herd has been proposed as a risk factor for the disease.McAllister *et al.* (2000) The oral transmission of *N. caninum* between dogs and cattle was demonstrated by feeding dogs with tissues from *N. caninum*-infected calves. The experiment showed that as few as 300 oocysts were sufficient to successfully infect the calves, and the tissues from these calves induced patent infections in dogs. Furthermore, oocysts from one of these dogs were administered to another calf, and the tissues from this calf subsequently induced a third dog to shed oocysts. This study confirmed the bidirectional transmission of *N. caninum* between dogs and cattle through oral ingestion.(Gondim *et al.*, 2002) It was also hypothesized that smaller farms may facilitate greater accessibility for farm dogs to bovine carcasses, aborted fetuses, placenta, and uterine discharge in comparison to larger farms.(Fort *et al.*, 2015) In fact, increasing rates of prevalence of *N. caninum* antibodies in older dogs living in dairy farms suggest postnatal exposure of this parasite.(Basso *et al.*, 2001) The study of Basso et al also revealed that seropositivity was higher in dogs from dairy (48%) and beef (54.2%) farms than in dogs from urban areas (26.2%). Fort identified an association between the introduction of new dogs to the dairy farm and seropositivity in cows in La Pampa, Argentina.(Fort, 2017) He found lower seroprevalence for cows from establishments with low dog entry rates, and higher when the entry rates were higher. However, there is not much research regarding the effect of the presence of seropositive dogs in dairy farms on the incidence of neosporosis. In a study conducted by Moore et al., the epidemiology of *N. caninum* in beef and dairy herds in the Humid Pampas region of Argentina was investigated.(Moore *et al.*, 2002) Among the 17 beef farms and 52 dairy farms included in the study, the seroprevalence of *N. caninum* in beef and dairy cattle was assessed, revealing significant differences based on the proportion of seropositive dogs. Specifically, the seroprevalence of *N. caninum* in dairy cattle was found to be significantly higher ($P < 0.05$) in farms with more than 50% of seropositive dogs). Recently, Pereyra et al studied the seroprevalence of *N. caninum* in cattle from 16 dairy farms (51.6% of the total farms in the province) located in the Valle de Lerma, (Salta, Argentina) during the period 2016-2018, and the risk factors associated with the transmission of this parasite in this region. They found that dogs were present in 62.5% of the farms, with a seropositivity value of approximately 72% ± 20%. Although the study does not allow for a clear association between the presence of infected dogs and intra-herd seroprevalence, a trend was detected that could indicate a positive correlation between both variables.

MATHEMATICAL MODELLING OF NEOSPOROSIS

To date, only a few mathematical models of bovine neosporosis have been developed. The seminal modeling study performed by French et al. (1999) considered two epidemiological classes: susceptible (S) and infected (I) cows, and three sources of infection: vertical transmission, horizontal transmission dependent on herd infection prevalence, and horizontal transmission from outside the herd. Vertical transmission refered to the transfer of infection via the transplacental route. Horizontal transmission from within the herd included the transmission through pooled colostrum or milk from infected cattle while horizontal transmission from outside the herd was caused by oocyst-contaminated feed.(French *et al.*, 1999)

With this Susceptible-Infected (SI) model, French et al. demonstrated that control measures such as culling or selective breeding can significantly reduce the prevalence of neosporosis. However, they stated that complete elimination of the infection was not possible when horizontal transmission was present. Häsler et al. (2006) further refined the SI deterministic model by incorporating the effect of aging. They divided the susceptible (S) and infected (I) populations into six age groups to investigate the impact of test-based culling, medication, vaccination, and selective breeding on the dynamics of the disease.(Häsler *et al.*, 2006) Recently, Liu et al. (2020 and 2021) conducted an evaluation of potential control measures for neosporosis using an age-structured SI model with three age groups. They explored the conditions that are needed in order to eliminate the disease. In their study, susceptible and infected individuals were vaccinated, providing protection against infection. Additionally, they assumed that the vaccine could reduce both the abortion rate and congenital transmission.(Liu *et al.*, 2020) (Liu *et al.*, 2021) In another study, Liu and Wing-Cheong Lo (2022) proposed a dynamic SI model with vaccination for production-

limiting diseases in cattle, such as neosporosis and Johne's disease.(Liu and Lo, 2022) The aim was to assess various control strategies and specifically examine the impact of immunization on the susceptible and infected populations.

To date, all these SI models do not consider the differences between cows that have acquired the disease through vertical transmission and cows that have been infected by ingesting the parasite. They treat the infected population as a single class without distinguishing between infections originating from oocyst ingestion and those resulting from transplacental transmission. However, it has been reported that cows infected through vertical transmission have a lower abortion rate (McAllister *et al.*, 2000) .

Previous SI models also represented the transmission from outside the herd using a single mechanism for the force of infection, assuming a constant per-capita force of infection that is independent of the herd's neosporosis prevalence. However, at least two distinct mechanisms can be identified: continuous transmission from an independent cycle of infection in another host (mostly domestic and feral dogs), leading to oocyst contamination in grass and water, and the occasional ingestion of fodder contaminated with feces from definitive hosts.(Dubey *et al.*, 2007)

To account for these differences, we have developed a model that is composed by three submodels. On the one hand, our submodel for cattle is a modified version of the model proposed by French et al. This submodel is able to distinguish between the dynamics of the disease in two different infected populations: cattle infected via ingestion of contaminated feed or water, and cattle infected via vertical transmission (considering both exogeonous and endogenous transplacental transmission). This differentiation allows us to capture the two patterns of the disease: endemic and epidemic abortions. However, regarding the overall infected cattle, our submodel reduces to the model proposed by French et al. This implies that it exhibits the same behavior and identical equilibrium value that in reference (Clancy and French, 2001). Notice that both the original modeling by French et al (French *et al.*, 1999) and the one presented in this work are suitable for large herd sizes, exceeding 100 individuals. However, for smaller herds, a stochastic formulation, as discussed in (Clancy and French, 2001), proves to be more appropriate.

On the other hand, we have developed a submodel for the infection in dogs, following the formulation used by other authors for infectious diseases in domestic animals (Lélu *et al.*, 2010)(Marinović *et al.*, 2020). This submodel explicitly incorporates the transmission of the disease within the domestic dog population and the dynamics of oocysts in the environment. Through this submodel, which characterizes the force of infection in cows resulting from oocyst ingestion, we can assess the potential impact of controlling the dog population as a management strategy for herds.

A third submodel focuses on the dynamics of oocysts in the environment, encompassing aspects such as their shedding and loss of infectivity.

THE MODEL

Our model establishes a dose-response relationship between infection prevalence in dogs and infection prevalence in cattle. Both submodels are connected through a single constant parameter ω. The third submodel introduces oocysts into the environment based on the infectious dogs populations and regulates their degradation.

SUBMODEL 1: N. CANINUM IN COWS

In this work, we simulate a single herd of cows with a fixed population, which means that the rate of new cows entering the herd (through replacement and acquisition) varies over time. The mortality rate takes into account both abortion and culling. The age structure of the herd is not considered in this study. The proposed formulation enables differentiation between congenitally acquired infection (V_{T_V}) and horizontal transmission (V_{T_H}).

In this submodel, we consider different mechanisms of infection on cows:

- Vertical transmission from cows to calves: *N. caninum* exhibits highly efficient transplacental transmission in cattle, with the probability of vertical transmission ϕ reaching levels as high as 95%. The fraction of susceptible cows is then incremented by

$$(1-\phi)(\rho_{T_H} V_{T_H} + \rho_{T_V} V_{T_V})$$

- Horizontal transmission, that may originate from three different sources:

i) External horizontal force of infection that occurs due to the occasional ingestion of oocysts present in the environment (water or food), which is the main mode of infection in cattle after birth. This contribution originates from the introduction of feral dogs or from an external source of contaminated livestock feed. This external horizontal transmission mechanism is modelled through a constant per-capita force of infection, with parameters τ as proposed by French:

$$\tau V_S$$

ii) Horizontal force of infection due the presence of infected domestic dogs belonging to the dairy herd. This contribution is modelled as a mass action process between susceptible cattle and the oocyst "density", with a parameter ω:

$$\omega(E/E_{MAX})V_S$$

iii) Horizontal transmission dependent on the herd infection prevalence: the rate of new infections would depend on the proportion of infected cows in the herd. An example of this mechanism is lactogenic transmission via pooled colostrum or milk, in which all the neonates are fed with collected colostrum or milk from all the cows.This mechanism is modelled as in (French *et al.*, 1999), as a mass action process with a parameter β:

$$\beta(V_{T_H} + V_{T_V})V_S$$

With these considerations, the equations of submodel 1 are:

$$\frac{dV_S}{dt} = -\beta(V_{T_H} + V_{T_V})V_S - \omega(E/E_{MAX})V_S - \tau V_S +$$
$$(\rho_S - \mu_S)V_S + (1-\phi)(\rho_{T_H}V_{T_H} + \rho_{T_V}V_{T_V})$$
$$\frac{dV_{T_H}}{dt} = \beta(V_{T_H} + V_{T_V})V_S + \omega(E/E_{MAX})V_S + \tau V_S - \mu_{T_H}V_{T_H}$$
$$\frac{dV_{T_V}}{dt} = \phi(\rho_{T_H}V_{T_H} + \rho_{T_V}V_{T_V}) - \mu_{T_V}V_{T_V}$$

Where V_S represents susceptible cattle, V_{T_H} represents cattle that acquired infection by ingestion and V_{T_V} represents cattle that acquired infection via the transplacental route. In the last equation, the term

$$\phi\rho_{T_H}V_{T_H}$$

originates form the scenario of horizontal transmission to a pregnant dam followed by vertical transmission to its fetus (i.e. exogenous transplacental transmission). Meanwhile, the term

$$\phi\rho_{T_V}V_{T_V}$$

represents transmission from a congenitally infected dam to its fetus (i.e. endogenous transplacental transmission). As we impose that the size of the herd do not change, the incorporation rate of non-infected cows ρ_S to the herd satisfies:

$$(\rho_S - \mu_S)V_S + (\rho_{T_H} - \mu_{T_H})V_{T_H}) + (\rho_{T_V} - \mu_{T_V})V_{T_V}) = 0$$

The population with congenitally acquired infection has a lower mortality rate than the population that acquired the infection through oocyst ingestion, this is, μV_{T_V} is lower than μV_{T_H} and both are greater than the mortality of susceptible population, μV_S. Additionally, the birth rate of the V_{T_V} population, ρ_{T_V}, has an intermediate value between that of V_{T_H} population, ρ_{T_H}, and the birth rate correspondent to susceptible population, ρ_S.

Submodels 1 and 2 are connected through the single coupling parameter ω. Sensitivity of submodel 1 to ω is shown in the Appendix.

SUBMODEL 2: N. CANINUM IN DOMESTIC DOGS.

Submodel 2 represents the cycle of *N. caninum* in dogs. This submodel includes three epidemiological classes: susceptible dogs P_S, acutely infected dogs P_A, and chronically infected dogs P_C. The distinction between these last two classes is based on the fact that dogs with acute infection shed more oocysts into the environment compared to chronically infected dogs.

For dogs, the contagion routes are vertical transmission and horizontal transmission from an external source. Vertical route was the early identified in dogs. *N. caninum* is transmitted from the dam to the neonates in a less efficient way than in cattle: as around 80% of pups born to seropositive bitches are uninfected, the probability of vertical transmission ϕ_P is set as 0.2. Regarding horizontal via, it has also

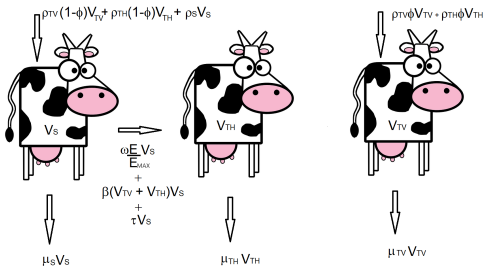

Figure 1: Submodel 1: *N. caninum* in caws. For simplicity, the three terms of the horizontal force of infection are represented by a single arrow.

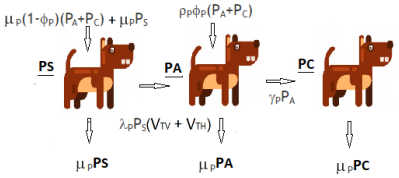

Figure 2: Submodel 2: *N. caninum* in dogs.

been demonstrated that dogs can become infected by ingesting infected tissues, specifically bovine fetal membranes or placentas.(Dubey *et al.*, 2007) This last mechanism is represented as a mass action process, by a force of infection that depends on the fraction of infected cattle with a parameter λ. The parameter μ_P represents both the birth and mortality rates, assuming equal values to maintain a constant population over time.

The equations for the dog submodel are as follows:

$$\frac{dP_S}{dt} = \mu_P(1-\phi_P)(P_A + P_C) - \lambda P_S(V_{T_H} + V_{T_V})$$
$$\frac{dP_A}{dt} = \mu_P\phi_P(P_A + P_C) - P_A(\mu_P + \gamma) + \lambda P_S(V_{T_H} + V_{T_V})$$
$$\frac{dP_C}{dt} = \gamma P_A - \mu_P P_C$$

Sensitivity of submodel 1 to λ is shown in the Appendix.

SUBMODEL 3: THE ENVIRONMENT

Oocysts are introduced into the environment through the feces of infectious dogs. Dogs with acute infection shed more oocysts into the environment compared to chronically infected dogs. In this submodel, dogs in the P_A class contribute to oocyst shedding at a rate of d, while dogs in the P_C class have a shedding rate 100 times lower. Oocysts degrade in the environment at a rate η. Submodel 3 provides a linear relationship between oocysts and the fraction of acute infected

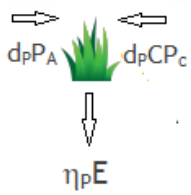

Figure 3: Submodel 3: *N. caninum* in the environment.

dogs. With these consideration, the presence of oocysts in the environment is described by the equation:

$$\frac{dE}{dt} = d(P_A + cP_C) - \eta E$$

Information regarding the biology of oocysts is limited. Oocyst can remain infectious for months, although they gradually degrade over time. The exact point at which they lose their infectivity is not yet determined.(Uzeda *et al.*, 2007) While oocysts typically require 2 to 3 days to sporulate in the environment and become infective, this time is not included in the model due to its negligible duration compared to the overall period of oocyst potential infectivity before degradation. The degradation process is modeled as exponentially decaying with time.

Naturally infected dog can shed a number of *N. caninum* oocysts that ranges from a few to 114,000 per gram of feces.(Dubey *et al.*, 2007) The approach used in similar models is that the probability of infection is proportional to the presence of oocysts. (Arenas *et al.*, 2010)(Turner *et al.*, 2013) However, the explicit representation of contamination by oocyst in the environment via infectious dogs should be interpreted as a homogeneous contamination throughout the entire environment. The maximum value of E, E_{MAX} corresponds to the scenario where the entire dog population is acutely infected. This formulation is sensitive to the fraction of infected dogs but ensures an upper value of 1 for the variable E/E_{MAX}, that acts as a density.

RESULTS

The set of parameters used in the three submodels is listed in Table 1. Figure 4 shows the equilibrium prevalence in cows, obtained with submodel 1 when the system evolves from a disease-free state. Notice that when $\omega(E/E_{MAX}) = 0$ and $\rho_{T_H} = \rho_{T_V}$ then the model can be reduced to the one proposed by French. Considering the overall number of infected cows, the dynamical system has the same equilibrium point that the model proposed by French when λ=0.692 [1/yr]. Additionally, it can be observed that cows infected through horizontal transmission V_{T_H} increase faster and reach the equilibrium value more rapidly than cows infected through vertical transmission V_{T_V}, but they contribute less to the overall prevalence. This fast growth at the beginning of the introduction of the disease in the cattle models the epidemic abortions event, or ´abortion storms´, while the later endemic stage of the disease is due to the high vertical transmission. The equilibrium prevalence of sumbodel 1 corresponds to around 21.7%

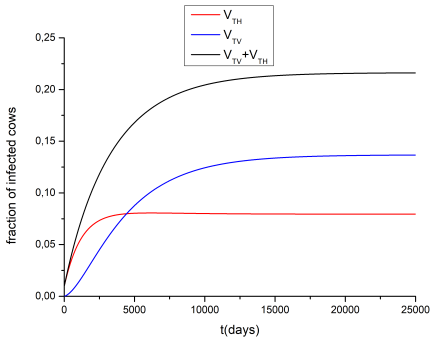

Figure 4: Equilibrium values of submodel 1 introducing the disease when all the horizontal transmission is due to the external contaminated livestock feed (i.e. a herd without domestic dogs). The black line reproduces the dynamics found by French et al.

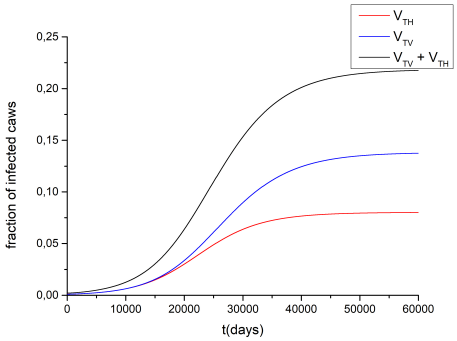

Figure 5: Equilibrium values of submodel 1 introducing the disease when the horizontal transmission is due the presence of domestic dogs (i.e. without external contaminated livestock feed source)

of infected cattle, where 8% correspond to V_{T_V} and 13.7% to V_{T_H}.

Likewise, we explore the sensitivity to the horizontal force of infection β, in submodel 1, as shown in the Appendix.

The coupling parameter ω that connects submodel 1 and 2 establishes the positive association between disease prevalence in cows and prevalence in dogs. The model's sensitivity to this parameter (i.e., the equilibrium total prevalence in dogs and cattle calculated by varying λ for different values of ω) is shown in the Appendix.

The connection between prevalence in dogs and cattle was set in agreement with the available evidence. The parameter ω was fixed to be consistent with the findings presented by Pereyra et al., as shown in Figure 6. The Figure depicts the equilibrium prevalence in dogs and cattle obtained with ω=3.0$[1/yr]$ when λ is varied. Data points reported by Pereyra et al. for dairy farms are also included. Under these condition, the equilibrium prevalence set by French et al corresponds to ω=3.0$[1/yr]$, λ= 0.682, resulting in approximately 21.7% of infected cattle and 38.4% infected dogs. As shown in Figure 6, when seroprevalence in dogs approaches the unity, seroprevalence in cows tends to 41%.

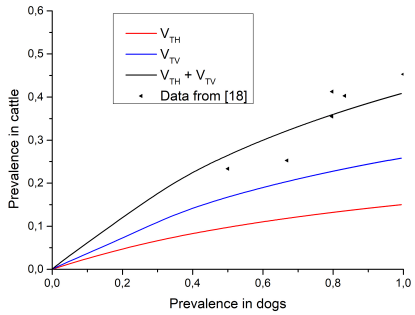

Figure 6: Seroprevalence in dogs and cattle for ω=3.0$[1/yr]$. The dots are seroprevalences reported by Pereyra et al (2021)

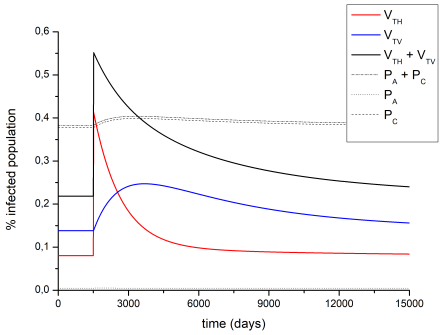

Figure 7: Exogenous food contamination in caws when the external force of infection τ is increased by 20 times for 15 days

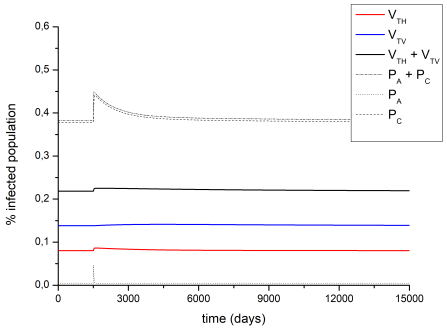

Figure 8: Exogenous food contamination in dogs when the external force of infection λ is increased by 20 times for 15 days

EXOGENOUS CONTAMINATION EVENT

Our model is able describe the effect on both dogs and cattle populations of a contamination event that can occur in cattle or dogs. Following the work of French et al, the introduction of a batch of contaminated livestock feed into the herd can be modeled by setting the parameter τ with a value different from zero during a short time period, as it is shown in Figure 7. As in Figure 4, $V_{T_H}$is responsible for the fast increase in prevalence at the beginning while V_{T_V} grows at a slower rate but sustains the infection over time. As expected, this type of event has a minimal impact on the dog population.

An exceptionally high exogenous food contamination event in dogs (i.e., through the ingestion of contaminated tissues from outside the herd) can be modeled by increasing the external force of infection λ. As depicted in Figure 8, a substantial level of horizontal transmission in dogs leads to a minor increase in infection prevalence in cattle. The external food contamination event affecting domestic dogs results in a significant overall prevalence increase, sustained by vertical transmission.

Table 1: Parameters

Parameter	Value
β	0.025$[1/yr]$ (French *et al.*, 1999)
τ	0.025$[1/yr]$ (French *et al.*, 1999)
ϕ	0.95 (French *et al.*, 1999)
ω	3.0$[1/yr]$
ρ_S	variable (French *et al.*, 1999)
ρ_{T_H}	0.17$[1/yr]$
ρ_{T_V}	0.175$[1/yr]$
μ_S	0.1875$[1/yr]$ (Thurmond and Hietala, 1996)
μ_{T_H}	0.3$[1/yr]$ (French *et al.*, 1999)
μ_{T_V}	0.26$[1/yr]$
μ_p	0.3$[1/yr]$
E_{MAX}	136.36$[oocyst]$
λ	0.682$[1/yr]$
ϕ_p	0.2 (Dubey *et al.*, 2007)
γ_p	1.0/15.0$[1/day]$
d	15000./11.0$[1/day]$
c	0.01
η	10.0 [1/day]

CHANGE IN THE INFECTED DOG POPULATION

Our model can assess the effect of management strategies related to domestic dogs on the prevalence of the disease in cattle. When λ is reduced to zero, meaning that dogs are no longer fed with contaminated tissues, and no additional external source of infection is considered, then the elimination of the diseases in caws becomes possible. The elimination of infected dogs and preventing them from ingesting contaminated tissues proves to be the fastest control strategy for eradicating the disease in cattle (see Figures 9 and 10).

DISCUSSION

Several refinements can be introduced to enhance the realism of our model and better capture the dynamics of the disease in dairy herds and the domestic dog population.

In this study, we asserted that dogs with acute infection shed more oocysts into the environment than chronically infected dogs. However, it is important to note that the chronically infected group could also experience high shedding stages due to factors such as weakened defenses, pregnancy, or re-exposure to the parasite. Although we did not consider this effect, the transition rate from the chronic to the acute class could also be incorporated in the model. As men-

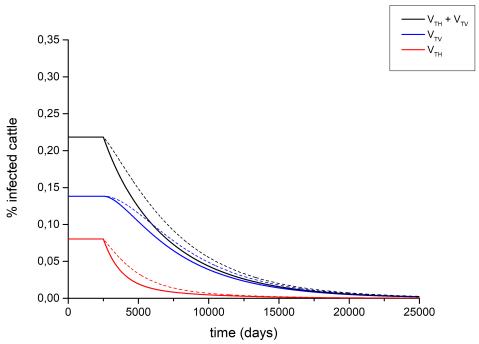

Figure 9: Prevalence in cows when λ and infected dogs are reduced. Solid line: infected dogs and λ are reduced to zero at t=2500 days. Dashed line: only λ is reduced to zero.

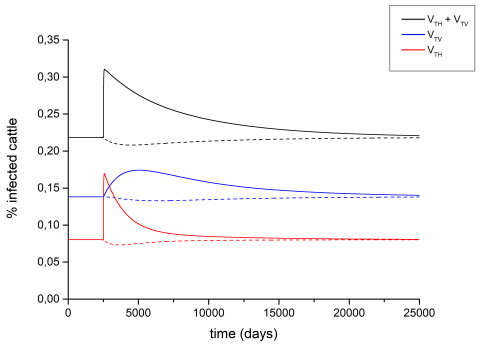

Figure 10: Prevalence in cows due to changes in the prevalence in dogs. Solid line: infected dogs are increased to 100% at t=2500 days. Dashed line: infected dogs are reduced to zero.

tioned earlier, we considered the probability of infection to be proportional to the abundance of oocysts. However, an alternative approach was formulated by Lélu et al., assuming that oocysts are clustered in the environment and infection occurs independently of the dose upon contact with contaminated patches.(Lélu *et al.*, 2010) This approach assigns a fixed probability of infection given contact with contaminated environment. A recent study by Marinovic demonstrated the equivalence of both representations in a toxoplasmosis model with vaccination, particularly at low levels of environmental contamination and for small populations. A similar comparison could be conducted in our model, considering that a more realistic description might lie between the two approaches.Marinović *et al.* (2020)

Incorporating explicit oocyst dynamics that depend on climate variables such as temperature and humidity in future iterations of the model would enable the modeling of environmental effects on oocyst degradation. This would help capture seasonality and variations in prevalence reported in different geographical regions. Finally, some studies suggest that both the management system (intensive or extensive) and the topographic characteristics of the field (elevation, slope) could impact the epidemiology of the disease and could be included in subsequent refinements of the model.

Despite some limitations, the model presented here represents a preliminary attempt to construct a realistic depiction of transmission in dairy farms by considering the complete life cycle of *N. caninum*. The differentiation between populations infected via the two primary transmission mechanisms enables a more accurate description and understanding of the two typical epidemiological patterns of the disease in cattle. The interdependence between the cattle and dog populations facilitates the assessment of the impact of various strategies.

ACKNOWLEDGMENTS

PEB, LMC and JMU are members of the CONICET.

APPENDIX

SENSITIVITY ANALYSIS

We show in Figure 11 the sensitivity of submodel 1 to the parameter that regulates the intraherd force of infection β. Each point on the curve in Figure 9 corresponds to an equilibrium point (always with $V_{T_H} < V_{T_V}$. In the graph, we observe that both V_{T_H} and V_{T_V} increase similarly with β. The sensitivity of the model to the coupling parameter ω was also explored, to select a value in agree with evidence (See Figure 12). Curves showing the dependence of seroprevalence en dogs and cattle with λ were calculated for a set of ω values. Figure 13 shows prevalences in both cattle and dogs populations, obtained by varying the parameter λ for a fixed $\omega = 3.0[1/yr]$.

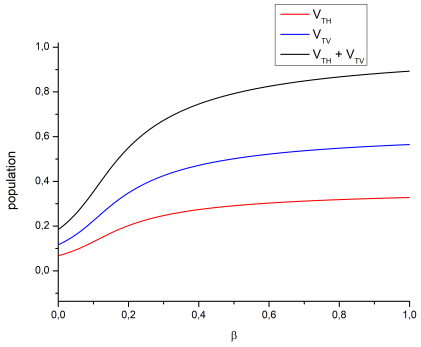

Figure 11: Sensitivity of submodel 1 to the parameter that regulates the intraherd force of infection β

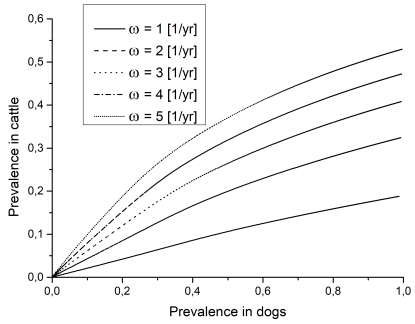

Figure 12: Sensitivity of the model to the coupling parameter ω

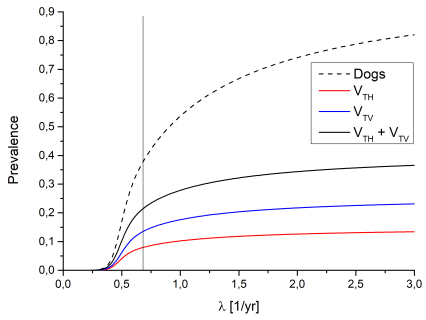

Figure 13: Dependence of seroprevalence in dogs and cattle on λ. The vertical line represents the reference equilibrium stage corresponding to the proposed by French et al

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Recommended Citation: Bergero, P. *et al.* (2024). *'Mathematical modelling of* Neospora caninum *infection in dairy cattle and domestic dogs'*. Rev. model. mat. sist. biol. Vol.4, e24R01, doi:10.58560/rmmsb.v04.e.024.01

Support: This work was supported by the CONICET and the UNLP.