Dynamics of a SEIVQ Epidemic Model for Brucellosis and the Analysis of Control Measures

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Abstract. In this work, we construct and analyze a brucellosis mathematical model. In this model, the population is divided into susceptible, immunization, latent, infected subclasses. Susceptible individuals can contract the disease in two ways: i) direct mode caused by contact with infected individuals; ii) indirect mode related to the presence of virulent organisms in the environment. We derive the basic reproductive number and analyze the global asymptotic behavior of the model. We also perform some numerical simulations and make sensitivity analysis of control parameters. Finally, we discuss the applicability of the model and the resurgence of the disease.

Keywords: Brucellosis; Epidemiological model; Basic reproduction number; Global stability.

1. Introduction

Brucellosis is a zoonotic infectious diseases caused by Brucella and it is widespread all over the world. At present, annual rate of the world is over 500,000 new patients with brucellosis. What is more incidence in some countries and regions reached one out of 10,000 [1]. Although brucellosis mortality is very low, people infected with strong disability, as well as lead to contamination of livestock abortion and meat, milk and other products. During the 200 countries and regions in the world, there are more than 170 places where exist human and livestock brucellosis. World Health Organization (WHO) classified brucellosis as class B infectious diseases [2].Test data from around the world in recent years, show that Brucellosis outbreak is worsening. Therefore, do not take effective control measures, not only will cause great pain to patients, while economic losses are enormous. The United States during 1934 to 1997 the cost to eradicate brucellosis issued for $3.5 billion, while in 1952 only one year because of bovine brucellosis leads to decreased milk production and miscarriages suffered losses amounted to $40 billion [3].

Brucellosis infection route for the digestive tract, respiratory tract, mucous membranes, conjunctiva and skin, particularly damaged skin. Brucellosis can also be spread by polluted air. Brucellosis after polluting the air, with the respiratory tract into the nasal cavity, nasopharynx, trachea and form the focus in the alveolar place; or enter the bloodstream, causing systemic infection [4]. Due to the high morbidity and rapid atomization characteristics, Suis Brucella, Abortus Brucella, Melitensis Brucella are listed as a potential biological weapon by the Centers for Disease Control and Prevention (CDC). Human brucellosis, primarily by direct contact with sick animals, eating diseased animal products and live in a polluted environment. There were no reports of horizontal transmission from patient to person [5]. Therefore, we focus on infection between animals.

Several mathematical models have been proposed to study brucellosis [6, 7, 8]. Using singular perturbation theory was established including susceptible classes, abortion has been contagious, infected people, vaccinees categories four types of dynamic model of Abortus brucellosis [6]. In 2010, Bedr. Chahrazed and Pierre analyze the model of ovine brucellosis incorporating direct and indirect transmission [7]. In 2005 Zinsstag established the Mongolia's livestock and human brucellosis transmission dynamic model including the interspecies transmission of cattle and sheep, as well as the spread of animal and human [8]. On the control measures, also there were several mathematical models have been proposed. In 2006, Shim ET analysis of the rotavirus vaccine control measures [9]. Towers and Feng, Qiu and Feng studied different control strategies of influenza vaccine [10, 11]. In

2011, Linhua Zhou and Meng Fan proposed an SIR epidemic model with limited medical resources revisited [12]. Through improvement of the previous models, we establish a containing several control measures, including direct and indirect transmission model. Moreover, the model universal, can adapt to a variety of situations.

The paper is organized as follows. In section 2, we present the model. In section 3, we analyze the stability of the model. In section 4, we present the sensitive analysis of the control parameters and some numerical simulations. In section 5, we will discuss the results obtained in sections 3 and 4. Moreover, we will discuss the universality of the model and give some proposals.

2. The Model

In this section, a Brucellosis SQEIV model with immunization, direct transmission and indirect transmission is introduced. The population is partitioned into four compartments: Susceptible compartment(S), in which individuals are not infected by Brucellosis; Immunization compartments (Q), in which individuals who have been immunized; Latent compartments (E), in which individuals are infected but not sick. Moreover we introduced environment compartments (V), where the bacterial survive. The transfer among compartments is schematically depicted in Fig 1.

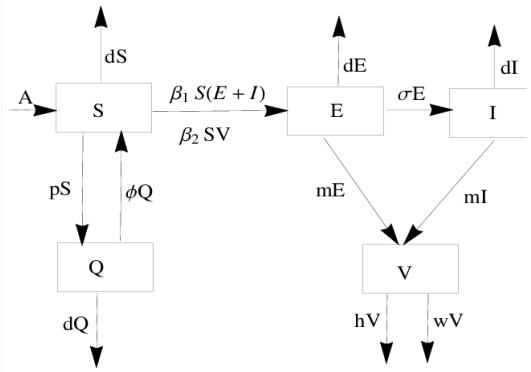

Fig. 1 The transfer diagram for the model

The transfer diagram leads to the following system of ordinary differential equations:

$$\begin{cases} \dfrac{dS}{dt} = A - \beta_1 S(E+I) - \beta_2 SV - dS - pS + \phi Q \\ \dfrac{dE}{dt} = \beta_1 S(E+I) + \beta_2 SV - dE - \sigma E \\ \dfrac{dI}{dt} = \sigma E - cI - dI \\ \dfrac{dV}{dt} = m(E+I) - wV - hV \\ \dfrac{dQ}{dt} = pS - \phi Q - dQ \end{cases} \tag{1}$$

Here, A is the input rate of the population; d is the removal rate of the population(including the natural death rate, the sale rate and the slaughter rate); β_1 is the transmission coefficient between infected individuals(including the latent) and susceptible individuals; β_2 is the bacteria infection rate for susceptible individuals; p is the effective immunization rate of susceptible individuals; $1/\phi$ is the effective protection of the vaccines; σ is the rate coefficient at which an individual leaves the latent class and becomes infectious; c is the rejection rate due to illness; m is the infected individuals release rate of the bacteria; w is the natural death rate of the bacteria; h is the effective disinfection rate.

3. System analysis

3.1 The basic reproduction number.

In this section we first calculate the disease-free equilibrium of system (1). Obviously, system (1) always has the disease-free equilibrium $E^0 = (S^0, Q^0, 0, 0, 0)$, where $S^0 = A(d+\phi)/d(d+p+\phi)$,

$Q^0 = Ap/d(d+p+\phi)$. In the following, the basic reproduction number of system (1) will be obtained by the next generation matrix method formulated in [13]. According to Theorem 2 in [13], the basic reproduction number of system(1) is

$$R_0 = \frac{\beta_1 A(d+\phi)(w+h)(d+c+\sigma)+\beta_2 Am(d+c+\sigma)(d+\phi)}{d(d+\sigma)(d+c)(w+h)(d+p+\phi)}$$

The epidemiological interpretation of the basic reproduction number, R_0 is the expected number of secondary cases produced, in a completely susceptible population, by a typical infectious individual.

System stability analysis.

Direct calculation shows that, when $R_0 > 1$, system (1) also has a unique endemic equilibrium P*(S*,Q*,E*,I*,V*),where

$$S^* = \frac{(c+d)(h+w)(d+\sigma)}{\beta_1(h+w)(d+c+\sigma)+\beta_2 m(c+d+\sigma)}$$

$$Q^* = \frac{p(c+d)(h+w)(d+\sigma)}{\beta_1(h+w)(d+c+\sigma)(d+\phi)+\beta_2 m(c+d+\sigma)(d+\phi)}$$

$$E^* = \frac{d(c+d)(h+w)(d+p+\phi)(R_0-1)}{\beta_1(h+w)(d+c+\sigma)(d+\phi)+\beta_2 m(c+d+\sigma)(d+\phi)}$$

$$I^* = \frac{d\sigma(h+w)(d+p+\phi)(R_0-1)}{\beta_1(h+w)(d+c+\sigma)(d+\phi)+\beta_2 m(c+d+\sigma)(d+\phi)}$$

$$V^* = \frac{md(d+\sigma)(d+p+\phi)(d+c)(w+h)(R_0-1)}{\beta_1(h+w)(d+\phi)+\beta_2 m(d+\phi)}$$

Then, For the stability of system(1), we have the following results.

Theorem 1. For system (1), when $R_0 \le 1$,the disease-free equilibrium E_0 is globally stable.

Proof. Define Liapunov function,

$$L = (S - S^0 - S^0 \log\frac{S}{S^0}) + (Q - Q^0 - Q^0 \log\frac{Q}{Q^0}) + E + \frac{\beta_2 A(d+\phi)}{d(d+p+\phi)(w+h)}V + \frac{\beta_1 A + d(d+\sigma)}{d(d+c+\sigma)}I$$

then the total differential of the L

$$\frac{dL}{dt} = (S-S^0)\frac{S'}{S} + (Q-Q^0)\frac{Q'}{Q} + E' + \frac{\beta_2 A(d+\phi)}{d(d+p+\phi)(w+h)}V' + \frac{\beta_1 A + d(d+\sigma)}{d(d+c+\sigma)}I'$$

$$= A(S-S^0)(\frac{1}{S}-\frac{1}{S^0}) + p(Q-Q^0)(\frac{S}{Q}-\frac{S^0}{Q^0}) + \phi(S-S^0)(\frac{Q}{S}-\frac{Q^0}{S^0})$$

$$+ \frac{(d+c)(d+\sigma)}{d(d+c+\sigma)}(R_0-1)(E+I)$$

Since $A = pS^0 - \phi Q^0 + dS^0$, $dQ^0 = pS^0 - \phi Q^0$ then

$$\frac{dL}{dt} = \frac{(d+c)(d+\sigma)}{d(d+c+\sigma)}(R_0-1)(E+I) + dS^0(2-\frac{S}{S^0}-\frac{S^0}{S}) + dQ^0(3-\frac{S^0}{S}-\frac{Q}{Q^0}-\frac{SQ^0}{S^0Q})$$

$$+ \phi Q^0(2-\frac{SQ^0}{S^0Q}-\frac{S^0Q}{SQ^0})$$

It is obvious that $\frac{dL}{dt} < 0$, if $R_0 \le 1$, $\frac{dL}{dt} = 0$ if and only if $E = I = 0$, $S = S^0$, $Q = Q^0$, Therefore, it follows from LaSalle Invariance Principle[14] that E0 is globally stable if $R_0 \le 1$.

Theorem 2. For system (1), the endemic equilibrium P^* is globally stable if $R_0 > 1$.

Proof. Let $s = \frac{S}{S^*}$, $q = \frac{Q}{Q^*}$, $e = \frac{E}{E^*}$, $i = \frac{I}{I^*}$, $v = \frac{V}{V^*}$, then

Define Liapunov function,

$$L = S^*(s-1-\log s) + E^*(e-1-\log e) + \frac{\beta_1(w+h)S^* + m\beta_2 S^*}{(d+c)(w+h)} I^*(i-1-\log i) +$$
$$+ \frac{\beta_2 S^*}{w+h} V^*(v-1-\log v) + \frac{\phi}{d+\phi} Q^*(q-1-\log q)$$

then the total differential of the L

$$\frac{dL}{dt} = (2A + \beta_1 S^* I^* + \beta_2 S^* V^* + \frac{m\beta_2 S^* I^*}{w+h}) - dS^* s - A\frac{1}{s} - \beta_1 S^* I^* \frac{si}{e} - \beta_2 S^* V^* \frac{sv}{e}$$
$$- \beta_1 S^* I^* \frac{e}{i} - \frac{m\beta_2 S^* I^*}{w+h}\frac{e}{i} - \frac{m\beta_2 S^* E^*}{w+h}\frac{i}{v} + \phi Q^*(q - s - \frac{q}{s} + 1) + pS^*(s - q - \frac{s}{q} + 1)$$
$$= dS^*(2 - s - \frac{1}{s}) + \beta_1 S^* I^*(3 - \frac{1}{s} - \frac{si}{e} - \frac{e}{i}) + \frac{m\beta_2 S^* E^*}{w+h}(3 - \frac{1}{s} - \frac{sv}{e} - \frac{e}{v})$$
$$+ \frac{m\beta_2 S^* I^*}{w+h}(4 - \frac{1}{s} - \frac{sv}{e} - \frac{e}{i} - \frac{i}{v}) + \phi S^*(2 - \frac{q}{s} - \frac{s}{q})$$

It is obvious that $\frac{dL}{dt} < 0$ and $\frac{dL}{dt} = 0$ if and only if $s = e = i = v = q = 1$. Therefore, it follows from LaSalle Invariance Principle [14] that P^* is globally stable if $R_0 > 1$.

4. Sensitive analysis and Numerical simulations

4.1 Sensitive analysis

We start this section by summarizing the parameters of the model and their values taken from the literature (where possible). These values are used for the numerical simulations of the model in Fig 2, 3, 4, 5 and 6. The remaining parameters are fixed in order to investigate several scenarios.

Table 1 Model parameters

parameter	description	value
A	Input rate	50000
d	Removal rate	0.2
β_1	Transmission coefficient between animal	$1.2*10^{-7}$
β_2	Environmental transmission coefficient	$5.5*10^{-6}$
σ	Incubation period prevalence	3
c	Slaughter rate due to illness	0.6
m	Bacteria release	68.6
w	Natural death rate of the bacteria	6
h	Effective disinfection rate	26
p	Immunization rate	0.85
$1/\phi$	Immune duration	3

In table 1, the value of parameters is on dairy cattle. According to common sense, dairy cattle's milk production time is last 5 years, so the average value of the removal rate d is 0.2[15]. Bovine brucellosis incubation period is generally 81-120 days, in this model, we selected an incubation period of 120 days, so $1/\sigma$ is $1/3$ year [16]. Brucellosis in different environment, survival time was different, and survived longer in a damp environment, survive in the soil for about 2 months. Therefore the natural extinction rate of bacteria w is 6[17]. According to the survey, farms disinfected once a week, there are 52 weeks a year, year disinfection efficiency remains at 0.5, so the value of h is 26. Scope of immunization rates are [0, 0.85], here the value p is 0.85. Immune duration $1/\phi$ is 3 years [18]. The value of A is assumption. Other parameters can be obtained by fitting [20].

From Theorem 1 and 2, the basic reproduction numbers of the model is the threshold determining that brucellosis whether dies out eventually or persists in population. To understand the difference between single parameter, we show the relationship among the basic reproduction number R_0 and single parameter (A,c,h,p). Figure 2 shows the relationship, in the figure p, A, c, h impact on the basic reproduction number R_0. The $c-R_0$ curve , $h-R_0$, $p-R_0$ curve are concave curves, while A and R_0 is linearly related. What is more, in the figure, we found that single parameter c, h, p cannot make the basic reproductive number $R_0<1$, Of course the disease will not be extinct. Parameter A can make the $R_0<1$, when A < 29341. In Figure 3, 4, 5, 6, we show the different value of parameter (A, p, c, h), it implies that A reflects the population size and the influence is significant. With the downsizing of the population, the disease to be controlled or even disappears gradually; Although the disease can be controlled to some extent, since the population flow, vaccine's role is not especially evident; Enhance the elimination rate of sick animals can effectively control the disease, but all killing cannot completely eliminate disease;

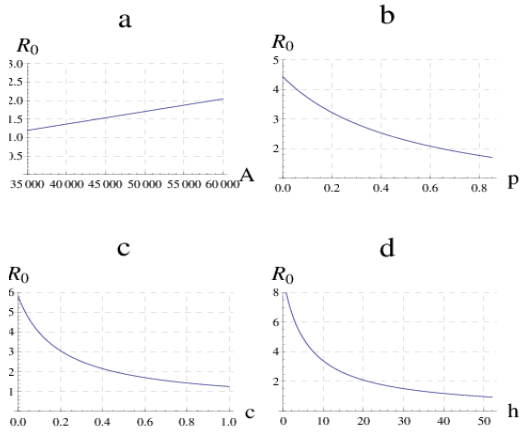

Fig. 2 The relationship among R_0 and single parameter

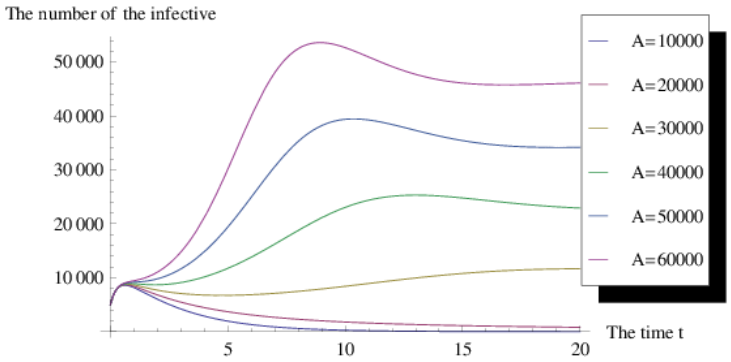

Fig. 3 Sensitivity analysis of parameters A. The value of parameters in Table 1

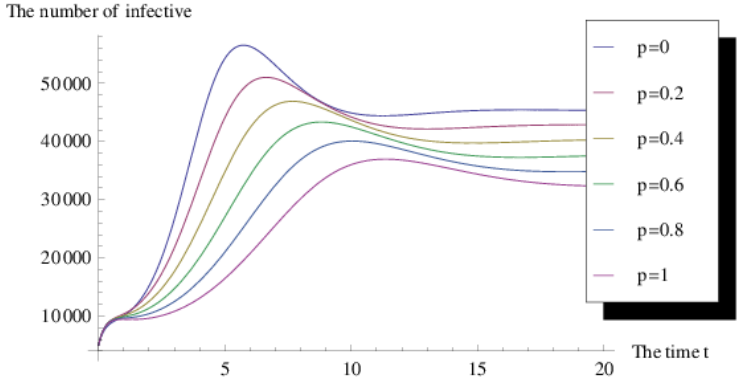

Fig. 4 Sensitivity analysis of parameters p. The value of parameters in Table 1

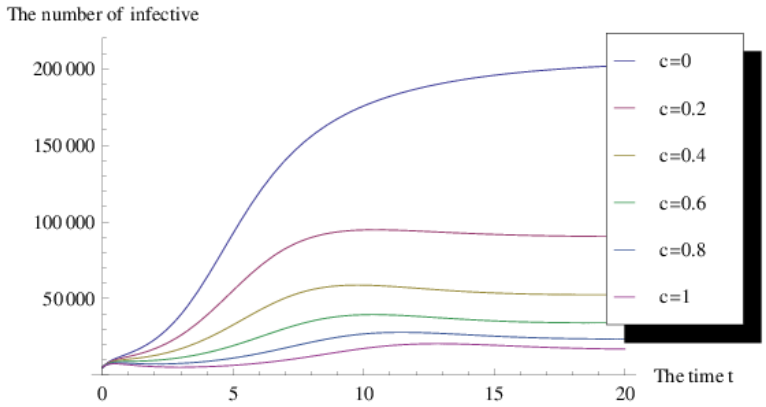

Fig. 5 Sensitivity analysis of parameters c. The value of parameters in Table 1

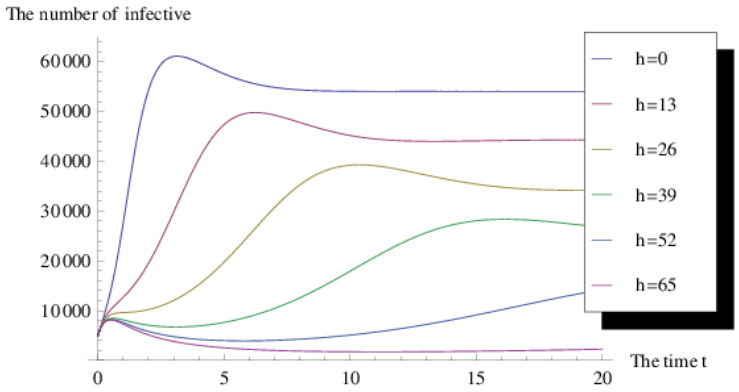

Fig. 6 Sensitivity analysis of parameters h. The value of parameters in Table 1

4.2 Numerical simulations

In this section, we will provide some numerical examples. In Fig 7, we fix A = 20000, other parameters are in Table 1, we observe that the disease-free equilibrium E0 is globally stable and the disease goes to extinct. We can calculate in these conditions the the basic reproduction numbers $R_0 = 0.977043$, according to the above described and the Theorem 1, we also define the disease-free equilibrium E_0 is globally stable and the disease goes to extinct. In Fig 8, all the parameters are in Table 1, direct calculation shows that the basic reproduction numbers $R_0 = 2.44261$, we can observe that the system has a unique endemic equilibrium P^*, moreover, P^* is globally stable, and the disease is endemic. This is consistent with the description of the article and Theorem 2.

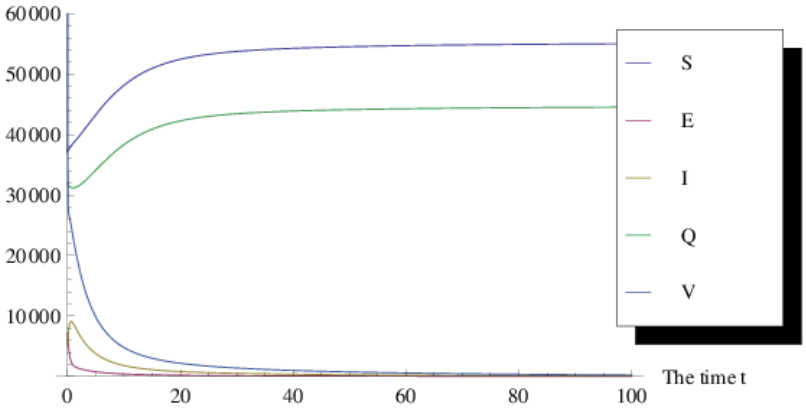

Fig. 7 The globally stable of E_0

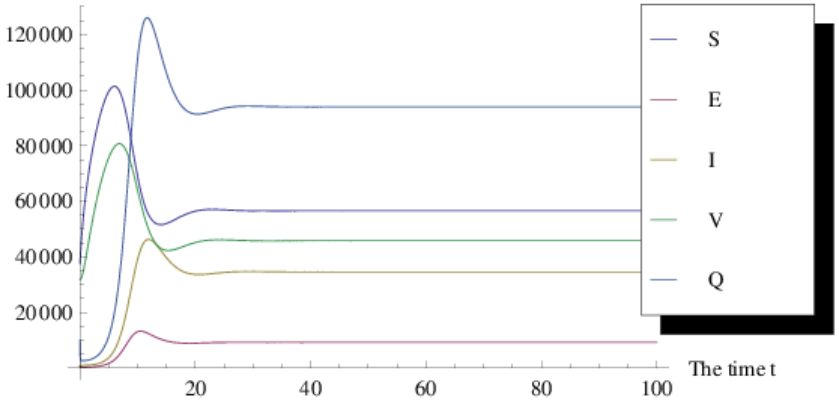

Fig. 8 The globally stable of P^*

5. Conclusion

In this article, we have formulated a containing several control measures, including direct and indirect transmission model. Moreover, we were able to describe the global dynamic of the model. In particular we obtained the basic reproductive number

$$R_0 = \frac{\beta_1 S^0}{d+c} + \frac{\sigma\beta_1 S^0}{(d+c)(d+\sigma)} + \frac{\beta_2 S_0 m(d+c+\sigma)}{(d+c)(d+\sigma)(w+h)}$$

In the above formula, the contribution of the direct transmission is $\frac{\beta_1 S^0}{d+c} + \frac{\sigma\beta_1 S^0}{(d+c)(d+\sigma)}$, the contribution of the indirect transmission is $\frac{\beta_2 S_0 m(d+c+\sigma)}{(d+c)(d+\sigma)(w+h)}$, and the contribution of the Latent individuals is $\frac{\sigma\beta_1 S^0}{(d+c)(d+\sigma)}$ [7]. In our model, quarantine is not control measure, due to Brucellosis is an asymptomatic disease and for security not necessary to isolate the animals[19].In practice, Brucellosis situation in different countries and regions are not the same. However, in our model, the values of different parameters can be used to simulate different situations. For example, in some developing countries, due to limited funding, limited funding medical resources and some historical or religious reasons, the vaccination rates are low, even without vaccination, so in these areas require through control scale, sterilization and increasing the elimination rate of illness to control the epidemic and in some countries, because of the large demand, it is necessary to maintain a certain scale. Of course, there are other situations, we can according to the actual situation transform parameters.

In addition, it is necessary to describe the slaughter rate due to illness(c). In Fig 2-c and Fig 5, we can found that even if c=1 the disease will persist. This illustrates that kill all sick animals, the disease would remain and to some extent, explained single method cannot eliminate brucellosis. In some countries, this is one of the reason for the resurgence of this disease, so various measures must be taken to eliminate this disease.

To conclude this article, we would like to mention some possibilities for further investigations in the context of brucellosis. In this work, our aim is to reduce brucellosis as much as possible and did not take into account the optimization of economy and control measures. Another important aspect is Brucellosis can broadcast to other species and the Brucella can also cross-species infection. These questions will be further investigated in some future works.

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