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GLOBAL DYNAMICS OF A GENERAL BRUCELLOSIS MODEL WITH DISCRETE DELAY

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Abstract For the prevention and control of brucellosis, it is important to investigate the mechanism of brucellosis transmission. Based on the characteristics of the spread of brucellosis, a susceptible-exposed-infectious-brucella (SEIB) delay dynamic model is proposed with the general incidence, elimination rate and shedding rate of pathogen. Under biologically motivated assumptions, it shows the uniqueness of the endemic equilibrium, and investigates the global asymptotically stability of the disease-free equilibrium and the endemic equilibrium. The results suggest that the global stability of equilibria depends entirely on the basic reproduction number R_0 and time delay is harmless for the stability of equilibria. Finally, some specific examples and numerical simulations are used to illustrate the utilization of research results and reveal the biological significance of hypothesis (H_7), which implies that the dynamics of brucellosis transmission depend largely on the development of the prevention and control strategies.

Keywords Brucellosis, indirect transmission, discrete delay, global stability, Lyapunov function.

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1. Introduction

Brucellosis, is one of the worlds major infectious bacterial disease, can be transmitted to other animals (such as sheep, cattle, pig) with exposure to infected animals or via ingestion of pathogens in the environment. Although brucellosis is well controlled in some developed countries, such as bovine brucellosis in Australia, it is still one of the common clinical diseases in the world [23]. Particularly, brucellosis not only brings serious economic losses, but also represents a significant public health burden on developing countries and continues receiving worldwide attention.

Statistical methods have been widely applied to the quantitative study of brucellosis transmission, the research results on the American Yellowstone National Park and the Middle East countries are worthy of attention (see [9, 17, 28, 31]). Some dynamic models have been proposed to study the complex dynamics of brucellosis transmission [2,11,22,25,27,30]. In particular, many models have been used

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to predict the spread of brucellosis and assess brucellosis prevention measures, for example, Zinsstag et al. [32] studied a dynamic model of animal (sheep and cattle)-to-human brucellosis transmission in terms of the characteristics and the data of Mongolia. Roy et al. [24] proposed an approach of network control to model and optimally control brucellosis. However, most of these studies focused on analyzing the spread of brucellosis with the direct transmission (contact transmission). In recent years, some researchers proposed mathematical models with indirect transmission for brucellosis epidemic in animals and the transmission from sheep to humans. Alnseba et al. [1] proposed an SIC dynamic model for brucellosis transmission in ovine through direct and indirect ways. Li et al. [21] established a deterministic model to investigate the transmission dynamics of brucellosis in Hinggan League of Inner Mongolia of China. Hou et al. [12] studied a dynamic model of sheep-to-human brucellosis with indirect transmission in terms of the characteristics and the data of Inner Mongolia of China. Recently, based on common characteristics of brucellosis and tuberculosis transmission, Hou et al. [13] formulated a general dynamic model with indirect transmission, and the global stability results of equilibria are obtained. Indirect transmission mode has been used to investigate brucellosis transmission in these literatures, but details of the transmission cycle of many animal brucellosis remain unclear, taking bovine brucellosis as an example, it is not sure whether animals have an infectivity in the latent period. On the other hand, the latent period is expressed in terms of an extra class which is defined as E. Its relevance in context of epidemiology may cause some doubts, this approach implies the assumption of the exponentially distributed time delay. In reality, it often appears that an assumption of a constant delay is more reasonable, which leads to a delay model.

Epidemic models with time delays have been extensively studied, and the stability analysis of the models is one of the main contents. The global stability of some delayed epidemic models are analyzed by means of an iteration technique and Lyapunov functional technique, such as the models by Xu and Ma, Huang et al., Enatsu et al., Fang et al., Li et al., Lai and Zou [8,10,14,16,18,29]. In recent years, the global stability of the endemic equilibrium for multi-group models with time delays has been investigated with a graph-theoretical approach to the method of global Lyapunov functions [5, 7, 19, 20, 26]. However, indirect transmission mode is not reflected in these studies, and there is no research by now studying the global dynamics of brucellosis transmission models with indirect transmission and time delay. In this paper, we propose a general susceptible-exposed-infectious-brucella (SEIB) dynamic model with time delay and indirect transmission for the spread of brucellosis. Under biologically motivated assumptions, using Lyapunov functional technique, we show that the global dynamics is completely determined by R_0: if $R_0 \leq 1$, the disease-free equilibrium is globally asymptotically stable, and the disease dies out; if $R_0 > 1$, the disease persists and a unique endemic equilibrium is globally asymptotically stable.

This work is structured as follows. In the next Section, we first formulate our model with discrete delay, and show the uniqueness of the endemic equilibrium. In Section 3, the global stability of equilibria of system is established. In Section 4, some examples and numerical simulations are given. A brief summary is given in Section 5.

2. The model and equilibria

Based on the mechanisms of brucellosis transmission, animal population is classified into three compartments: the susceptible compartment $S(t)$, the exposed compartment $E(t)$ and the infectious compartment $I(t)$. On the other hand, infectious animal can shed brucella into the environment through abortion or animal secretions, which can survive for several weeks, or even months in the feces or contaminated environment under suitable conditions. Brucella can be *harvested* by susceptible individuals that become infected individuals depending on the ingested dose. Therefore, an infected animal generates infection in two ways: the direct and indirect modes of transmission. Let $B(t)$ denote pathogens in the environment. According to the interpretation of introduction, we ignore the infection of exposed animal and assume the latent period span is τ, then the transfer rate from the exposed class into the infected class is given by $e^{-\mu\tau}n(S(t-\tau)(f(I(t-\tau))+g(B(t-\tau)))$. Therefore, we obtain the following compartmental model:

$$\begin{aligned}
\frac{dS}{dt} &= A - n(S)(f(I) + g(B)) - \mu S,\\
\frac{dE}{dt} &= n(S)(f(I) + g(B)) - \mu E - e^{-\mu\tau}n(S(t-\tau))(f(I(t-\tau)) + g(B(t-\tau))),\\
\frac{dI}{dt} &= e^{-\mu\tau}n(S(t-\tau))(f(I(t-\tau)) + g(B(t-\tau))) - \varphi(I),\\
\frac{dB}{dt} &= h(I) - \theta(B).
\end{aligned} \tag{2.1}$$

Here, A is the recruitment rate of the animal population, and μ is natural elimination rate. $n(S)$ is a contact function. The elimination rate of the infected animals, including the disease induced death rate, is denoted by $\varphi(I)$. We define $h(I)$ as the pathogen shedding rate of infectious animals. $\theta(B)$ represents the disinfection rate and decaying rate of pathogen in the environment. $\tau \geq 0$ represents a time delay describing the latent period of the disease, the term $e^{-\mu\tau}n(S(t-\tau)(f(I(t-\tau)) + g(B(t-\tau)))$ represents the individuals surviving in the incubation period and becoming infective at time t. The initial conditions for system (2.1) take the following form:

$$\begin{aligned}
&S(x) = \phi_1(x), E(x) = \phi_2(x), I(x) = \phi_3(x), B(x) = \phi_4(x),\\
&\phi_i(x) \geq 0, x \in [-\tau, 0], \phi_i(0) > 0, \phi_i \in C^+, i = 1, 2, 3, 4.
\end{aligned} \tag{2.2}$$

Here, C denotes the Banach space $C([-\tau, 0], \Re)$ of continuous functions mapping the interval $[-\tau, 0]$ into $\Re$ equipped with the sup-norm $\|\phi\| = \sup_{x\in[-\tau,0]} |\phi(x)|$ for $\phi \in C$. The nonnegative cone of C is defined as $C^+ = C([-\tau, 0], \Re^+)$.

For continuity of the initial conditions, we need to further require

$$E(0) = \int_{-\tau}^{0} n(\phi_1(x))(f(\phi_3(x)) + g(\phi_4(x)))e^{\mu x}dx. \tag{2.3}$$

The mechanism of animal brucellosis transmission is identical, but the incidence rate, elimination rate and decaying rate of pathogen is dependent on animal breeding environment and resources, and the specific forms of these functions are unclear. To make biological sense for our model, we assume the functions n, f, g, φ, h and θ are sufficiently smooth, and satisfy the following hypotheses:

(H_1) $n(0) = 0$, and $n(S) > 0, n'(S) > 0$ for $S > 0$.
(H_2) $f(0) = g(0) = 0$, and $f(I), g(B) > 0$ for $I, B > 0$.
(H_3) $f'(I) \geq 0,\ \ g'(B) \geq 0$ for $B, I \geq 0$.
(H_4) $h(0) = 0$, $h(I) > 0, h'(I) > 0$ for $I > 0$.
(H_5) $\varphi(0) = 0$, and $\varphi'(I) > 0$ for $I \geq 0$; there exists constant $\mu_1 > 0$ such that $\varphi(I) \geq \mu_1 I$.
(H_6) $\theta(0) = 0$, and $\theta'(B) > 0$ for $B \geq 0$.

Based on biological considerations, we are interested in solutions that are nonnegative and bounded. In fact, adding the first three equations of (2.1) yields that

$$\begin{aligned}(S + E + I)' =& A - \mu(S + E) - \varphi(I)\\ \leq& A - \mu(S + E) - \mu_1 I\\ \leq& A - \mu_0(S + E + I),\end{aligned}$$

where $\mu_0 = \min\{\mu, \mu_1\}$, then it follows that

$$\lim_{t\to+\infty} \sup(S + E + I) \leq \frac{A}{\mu_0}, \qquad \lim_{t\to+\infty} \sup B \leq \theta^{-1}(h(\frac{A}{\mu_0})).$$

Therefore, the set

$$\Omega = \{(S, E, I, B) \in R_4^+ : \|S + E + I\| \leq \frac{A}{\mu_0}, \|B\| \leq \theta^{-1}(h(\frac{A}{\mu_0}))\}$$

is the positively invariant set for system (2.1).

The assumption (H_1) represents a common contact function, such as $\frac{S^q}{1+MS^q}$ with $q > 0$ and $M \geq 0$. The assumption (H_2) indicates that incidence rate is greater than or equal to 0. The two inequalities in assumption (H_3) implies that increased infection and pathogens in the environment lead to higher incidence rate. The assumption (H_4) states that the pathogen concentration increases with the growing number of the infectious individuals. The assumption (H_5) implies that the more the infected animals are, the more infected animals to be eliminated will be. The assumption (H_6) shows that the disinfection and decaying rate of pathogen is monotonically increasing.

Since $n(0) = \varphi(0) = h(0) = \theta(0) = 0$, it is easy to see that the system (2.1) admits a unique disease-free equilibrium $P_0 = (S_0, 0, 0, 0)$. We define the basic reproduction number R_0 of our model by

$$R_0 = \frac{e^{-\mu\tau} n(S_0) f_I(0)}{\varphi_I(0)} + \frac{e^{-\mu\tau} n(S_0) g_B(0) h_I(0)}{\varphi_I(0)\theta_B(0)}.$$

In order to analyze the uniqueness of the endemic equilibrium, and prove the global asymptotic stability of the equilibria, some additional conditions are imposed on the functional coefficients. Suppose the followings:
(H_7) $\frac{f}{\varphi}, \frac{g}{\theta}$ and $\frac{h}{\varphi}$ are nonincreasing on $(0, +\infty)$.

The endemic equilibrium $P_*(S^*, E^*, I^*, B^*)$ of system (2.1) is determined by equations:

$$\begin{aligned}&A - \mu S^* = n(S^*)(f(I^*) + g(B^*)),\\ &\mu E^* = (1 - e^{-\mu\tau}) n(S^*)(f(I^*) + g(B^*)),\\ &e^{-\mu\tau} n(S^*)(f(I^*) + g(B^*)) = \varphi(I^*),\\ &h(I^*) = \theta(B^*).\end{aligned}$$

It is equivalent to solving the following equation:

$$\begin{aligned} &A-\mu S^*=n(S^*)(f(I^*)+g(B^*)),\\ &n(S^*)(f(I^*)+g(B^*))=e^{\mu\tau}\varphi(I^*),\\ &h(I^*)=\theta(B^*). \end{aligned} \tag{2.4}$$

From the last equation in (2.4), we can obtain

$$B^*=\theta^{-1}(h(I^*))\triangleq H(I^*). \tag{2.5}$$

Substituting (2.5) into the first two equations in (2.4), we get

$$\begin{aligned} &m(S^*)\triangleq A-\mu S^*=n(S^*)(f(I^*)+g(H(I^*))),\\ &\Phi(I^*)\triangleq e^{\mu\tau}\varphi(I^*)=n(S^*)(f(I^*)+g(H(I^*))). \end{aligned}$$

Let us define

$$\begin{aligned} &F_1(S,I)\triangleq m(S)-n(S)(f(I)+g(H(I))),\\ &F_2(S,I)\triangleq n(S)(f(I)+g(H(I)))-\Phi(I). \end{aligned}$$

Since $F_1(S,I)$ is strictly decreasing for $S>0$ and $F_1(0,I)\cdot F_1(S_0,I)<0$ for $I>0$, the equation $F_1(S,I)=0$ can be uniquely solved with S as a function of I for all I. That is to say, there is a function $S=\phi_1(I)$ which satisfies

$$\frac{m(\phi_1(I))}{n(\phi_1(I))}=f(I)+g(H(I))\triangleq G(I).$$

Since $\frac{m}{n}$ is strictly decreasing and G is strictly increasing, it follows that ϕ_1 is strictly decreasing. Note that deriving from (2.4) and (2.5), $\lim_{I\to\frac{A}{\mu_0}}\phi_1(I)=0$.

We also note that $F_2(S,I)$ is strictly increasing for $S>0$ and $F_2(0,I)<0$ for all I, while it is not necessarily true that $F_2(S_0,I)>0$. So the same approach would not be used to solve the equation $F_2(S,I)=0$. Since we are searching for a unique endemic equilibrium and for a uniquely corresponding I^*, we only need the local solvability of the equation $F_2(S,I)=0$ on a certain condition.

We assume for the moment that the equation $F_2(S,I)=0$ may also be uniquely solved with S as a function of I (locally for I). That is, there is a function $S=\phi_2(I)$ which satisfies

$$n(\phi_2(I))=\frac{\Phi(I)}{G(I)}.$$

Since $\frac{f}{\varphi}$, $\frac{g}{\theta}$ and $\frac{h}{\varphi}$ are nonincreasing, so we obtain

$$\begin{aligned} (\frac{g(H(I))}{\varphi(I)})'=&\frac{g_B(B)\frac{1}{\theta_B(B)}h_I(I)\varphi(I)-\varphi_I(I)g(B)}{\varphi^2(I)}\\ =&\frac{g_B(B)h_I(I)\varphi(I)-\theta_B(B)\varphi_I(I)g(B)}{\theta_B(B)\varphi^2(I)}\\ \leq&0, \end{aligned}$$

where

$$\frac{h_I(I)\varphi(I)}{\varphi_I(I)} - \theta(B) = \frac{h_I(I)\varphi(I) - \varphi_I(I)h(I)}{\varphi_I(I)} \leq 0,$$

which is equivalent to $\frac{h_I(I)\varphi(I)}{\varphi_I(I)} \leq \theta(B)$. Therefore, the function $\frac{\Phi(I)}{G(I)}$ is increasing on $(0,\infty)$, and the function n is strictly increasing, then ϕ_2 is also increasing.

Since ϕ_1 is strictly decreasing, ϕ_2 is increasing and $\lim_{I\to\frac{A}{\mu_0}} \phi_1(I) = 0$, the curves defined by $S = \phi_1(I)$ and $S = \phi_2(I)$ have a common point (S^*, I^*) with $S^* > 0, I^* > 0$ on condition that if and only if $\phi_1(0) > \phi_2(0)$ or $n(\phi_1(0)) > n(\phi_2(0))$. Since $\phi_1(0) = S_0$ and $n(\phi_2(0)) = \lim_{I\to 0} \frac{\Phi(I)}{G(I)}$, the existence condition is $n(S_0) > \lim_{I\to 0} \frac{\Phi(I)}{G(I)}$. Using L'Hospital rule and the basic reproduction number of the system (2.1), this condition can be rewritten as $R_0 > 1$.

We have shown that if the equation $F_2(S, I) = 0$ is solvable with S as a function of I, then the necessary and sufficient condition for the existence of positive (S^*, I^*) is that $R_0 > 1$. In this case, we have

$$F_2(S, I) = \Phi(I)(\frac{n(S)G(I)}{\Phi(I)} - 1)$$

and $F_2(S_0, I)$ is positive for I in a vicinity of 0 if $R_0 > 1$. It follows that the equation $F_2(S, I)$ is solvable with S as a function of I (locally for I), that is, we have shown that the existence of positive (S^*, I^*) is equivalent to the valid condition $R_0 > 1$. So system (2.1) have a unique positive solutions $P_* = (S^*, E^*, I^*, B^*)$.

According to the above discussion, we have the following results:

Theorem 2.1. *Assume that conditions $(H_1) - (H_7)$ hold. Then there is a unique positive endemic equilibrium $P_* = (S^*, E^*, I^*, B^*)$ of system (2.1) if and only if $R_0 > 1$.*

Remark. We note that conditions (H_7) (combined with $R_0 > 1$) are sufficient for the existence of the endemic equilibrium rather than necessary. For instance, if one assumes that the removal rate $\varphi(I)$ of the infected animals is influenced by the resource which is used to monitor and cull infected animals, such as $\varphi(I) = \mu I + \frac{cI}{a+I}$ with constants $\mu, c, a > 0$, c represents the maximal supply of resources for monitoring and culling per unit time and a is half-saturation constant, measuring the efficiency of the resource supply in the sense. The disease-free equilibrium may coexist with multiple positive endemic equilibria when $R_0 < 1$.

3. Stability of equilibria

In this section, we study the global stability of disease-free equilibrium and the endemic equilibrium of system (2.1). It is important for us to understand the extinction and persistence of animal brucellosis.

3.1. Stability of the disease-free equilibrium

In this subsection, by constructing a Lyapunov function, we establish the global asymptotic stability of the disease-free equilibrium of system (2.1). Noting that the

variable $E(t)$ does not appear in the first, the third and the fourth equations of system (2.1), we first consider the following subsystem:

$$\begin{aligned}
&\frac{dS}{dt} = A - n(S)(f(I) + g(B)) - \mu S,\\
&\frac{dI}{dt} = e^{-\mu\tau} n(S(t-\tau))(f(I(t-\tau)) + g(B(t-\tau))) - \varphi(I),\\
&\frac{dB}{dt} = h(I) - \theta(B).
\end{aligned} \tag{3.1}$$

Lemma 3.1. *Assume that conditions $(H_1) - (H_7)$ are satisfied. If $R_0 \le 1$, the disease-free equilibrium $E_0 = (S_0, 0, 0)$ of system (3.1) is globally asymptotically stable.*

Proof. Since the function $\frac{f}{\varphi}$, $\frac{g}{\theta}$ and $\frac{h}{\varphi}$ are nonincreasing, we have

$$\begin{aligned}
&\frac{n(S)f(I)}{\varphi(I)e^{\mu\tau}} \le \lim_{I\to 0^+} \frac{n(S_0)f(I)}{\varphi(I)e^{\mu\tau}} = \frac{n(S_0)f_I(0)}{\varphi_I(0)e^{\mu\tau}} \triangleq b_1,\\
&\frac{n(S)g(B)}{\theta(B)e^{\mu\tau}} \le \lim_{B\to 0^+} \frac{n(S_0)g(B)}{\theta(B)e^{\mu\tau}} = \frac{n(S_0)g_B(0)}{\theta_B(0)e^{\mu\tau}} \triangleq b_2,\\
&\frac{h(I)}{\varphi(I)} \le \lim_{I\to 0^+} \frac{h(I)}{\varphi(I)} = \frac{h_I(0)}{\varphi_I(0)}.
\end{aligned}$$

Define

$$J = \begin{pmatrix} 1 & 0 \\ -\frac{h_I(0)}{\varphi_I(0)} & 1 \end{pmatrix}, \qquad (a_1, a_2) = (b_1, b_2)J^{-1}.$$

Thus, $a_1 = R_0 \le 1$, we define the Lyapunov function

$$\begin{aligned}
L =& R_0\Big(\int_{S_0}^{S} \frac{n(x) - n(S_0)}{n(x)}dx + e^{\mu\tau} I\Big) + a_2 e^{\mu\tau} B\\
&+ R_0 \int_{t-\tau}^{t} (n(S(x))f(I(x)) + n(S(x))g(B(x)))dx.
\end{aligned}$$

Then the derivative of L along positive solutions of system (3.1) is

$$\begin{aligned}
\frac{dL}{dt} =& -\mu R_0(S_0 - S)\Big(\frac{n(S_0)}{n(S)} - 1\Big)\\
&+ R_0\Big(\frac{n(S_0)f(I)}{\varphi(I)e^{\mu\tau}}, \frac{n(S_0)g(B)}{\theta(B)e^{\mu\tau}}\Big)(\varphi(I)e^{\mu\tau}, \theta(B)e^{\mu\tau})^\tau\\
&- (R_0, a_2)\begin{pmatrix} 1 & 0 \\ -\frac{h(I)}{\varphi(I)} & 1 \end{pmatrix}(\varphi(I)e^{\mu\tau}, \theta(B)e^{\mu\tau})^\tau\\
\le& R_0\Big(\frac{n(S_0)f_I(0)}{\varphi_I(0)e^{\mu\tau}}, \frac{n(S_0)g_B(0)}{\theta_B(0)e^{\mu\tau}}\Big)(\varphi(I)e^{\mu\tau}, \theta(B)e^{\mu\tau})^\tau\\
&- (R_0, a_2)\begin{pmatrix} 1 & 0 \\ -\frac{h_I(0)}{\varphi_I(0)} & 1 \end{pmatrix}(\varphi(I)e^{\mu\tau}, \theta(B)e^{\mu\tau})^\tau\\
=& (R_0 - 1)(b_1, b_2)(\varphi(I)e^{\mu\tau}, \theta(B)e^{\mu\tau})^\tau\\
\le& 0.
\end{aligned}$$

Therefore, the equality $\frac{dL}{dt} = 0$ holds if and only if $S = S_0$ and either $R_0 = 1$ or $I = 0$. Since E_0 is the only invariant set of system (3.1) in $\{(S, I, B) : \frac{dL}{dt} = 0\}$, the disease-free equilibrium E_0 is globally asymptotically stable by LaSalle's Invariance Principle. □

Theorem 3.1. *Assume that conditions $(H_1) - (H_7)$ are satisfied. If $R_0 \leq 1$, the disease-free equilibrium $P_0 = (S_0, 0, 0, 0)$ of system (2.1) is globally asymptotically stable.*

3.2. Stability of the endemic equilibrium

In this subsection, we analyze the stability of the endemic equilibrium. Similar to the above discussion, we first investigate the global asymptotic stability of system (3.1).

Lemma 3.2. *Assume that conditions $(H_1) - (H_7)$ are satisfied. If $R_0 > 1$, the endemic equilibrium $E_* = (S^*, I^*, B^*)$ of system (3.1) is globally asymptotically stable.*

Proof. Define

$$L_1 = \int_{S^*}^{S} \frac{n(x) - n(S^*)}{n(x)} dx + e^{\mu\tau} \int_{I^*}^{I} \frac{\varphi(x) - \varphi(I^*)}{\varphi(x)} dx.$$

Finding the time derivative of L_1 along the positive solutions of system (3.1) gives

$$\begin{aligned}
\frac{dL_1}{dt} =& (1 - \frac{n(S^*)}{n(S)})\frac{dS}{dt} + e^{\mu\tau}(1 - \frac{\varphi(I^*)}{\varphi(I)})\frac{dI}{dt} \\
=& (1 - \frac{n(S^*)}{n(S)})(n(S^*)(f(I^*) + g(B^*)) - n(S)(f(I) + g(B)) - \mu(S - S^*)) \\
&+ (1 - \frac{\varphi(I^*)}{\varphi(I)})(n(S(t-\tau))(f(I(t-\tau)) + g(B(t-\tau))) - \varphi(I)e^{\mu\tau}) \\
=& -\mu(S - S^*)(1 - \frac{n(S^*)}{n(S)}) - e^{\mu\tau}\varphi(I) + e^{\mu\tau}\varphi(I^*) \\
&- n(S)(f(I) + g(B)) + n(S^*)(f(I) + g(B)) \\
&- \frac{n(S^*)}{n(S)} n(S^*)(f(I^*) + g(B^*)) + n(S^*)(f(I^*) + g(B^*)) \\
&+ n(S(t-\tau))(f(I(t-\tau)) + g(B(t-\tau))) \\
&- \frac{\varphi(I^*)}{\varphi(I)} n(S(t-\tau))(f(I(t-\tau)) + g(B(t-\tau))) \\
=& -\mu(S - S^*)(1 - \frac{n(S^*)}{n(S)}) - n(S)(f(I) + g(B)) \\
&+ n(S(t-\tau))(f(I(t-\tau)) + g(B(t-\tau))) \\
&- \frac{\varphi(I^*)}{\varphi(I)} n(S(t-\tau))(f(I(t-\tau)) + g(B(t-\tau))) \\
&+ n(S^*)f(I^*)(2 + \frac{f(I)}{f(I^*)} - \frac{n(S^*)}{n(S)} - \frac{\varphi(I)}{\varphi(I^*)} - \frac{n(S)f(I)\varphi(I^*)}{n(S^*)f(I^*)\varphi(I)}) \\
&+ n(S^*)g(B^*)(2 + \frac{g(B)}{g(B^*)} - \frac{n(S^*)}{n(S)} - \frac{\varphi(I)}{\varphi(I^*)} - \frac{n(S)g(B)\varphi(I^*)}{n(S^*)g(B^*)\varphi(I)})
\end{aligned}$$

$$+\frac{\varphi(I^*)}{\varphi(I)}n(S)(f(I)+g(B)).$$

Define

$$\begin{aligned}L_2 =&n(S^*)f(I^*)\int_{t-\tau}^{t}(\frac{n(S(x))f(I(x))}{n(S^*)f(I^*)}-1-\ln\frac{n(S(x))f(I(x))}{n(S^*)f(I^*)})dx\\&+n(S^*)g(B^*)\int_{t-\tau}^{t}(\frac{n(S(x))g(B(x))}{n(S^*)g(B^*)}-1-\ln\frac{n(S(x))g(B(x))}{n(S^*)g(B^*)})dx.\end{aligned}$$

A direct calculation shows that

$$\begin{aligned}\frac{dL_2}{dt} =&n(S)(f(I)+g(B))-n(S(t-\tau))(f(I(t-\tau))\\&+g(B(t-\tau)))+n(S^*)f(I^*)\ln\frac{n(S(t-\tau))f(I(t-\tau))}{n(S)f(I)}\\&+n(S^*)g(B^*)\ln\frac{n(S(t-\tau))g(B(t-\tau))}{n(S)g(B)}.\end{aligned}$$

Define

$$L_3=\frac{n(S^*)g(B^*)}{h(I^*)}\int_{B^*}^{B}\frac{\theta(x)-\theta(B^*)}{\theta(x)}dx.$$

By simple calculation, we obtain

$$\frac{dL_3}{dt}=(1-\frac{\theta(B^*)}{\theta(B)})\frac{dB}{dt}=n(S^*)g(B^*)(\frac{h(I)}{h(I^*)}-\frac{\theta(B)}{\theta(B^*)}-\frac{h(I)\theta(B^*)}{h(I^*)\theta(B)}+1).$$

For system (3.1), we consider the following Lyapunov function:

$$L=L_1+L_2+L_3.$$

Calculating the derivative of L along positive solutions of system(3.1), it follows that

$$\begin{aligned}\frac{dL}{dt} =&\frac{dL_1}{dt}+\frac{dL_2}{dt}+\frac{dL_3}{dt}\\=&-\mu(S-S^*)(1-\frac{n(S^*)}{n(S)})-\frac{\varphi(I^*)}{\varphi(I)}n(S(t-\tau))(f(I(t-\tau))+g(B(t-\tau)))\\&+n(S^*)f(I^*)(2+\frac{f(I)}{f(I^*)}-\frac{n(S^*)}{n(S)}-\frac{\varphi(I)}{\varphi(I^*)}-\frac{n(S)f(I)\varphi(I^*)}{n(S^*)f(I^*)\varphi(I)})\\&+n(S^*)g(B^*)(2+\frac{g(B)}{g(B^*)}-\frac{n(S^*)}{n(S)}-\frac{\varphi(I)}{\varphi(I^*)}-\frac{n(S)g(B)\varphi(I^*)}{n(S^*)g(B^*)\varphi(I)})\\&+n(S^*)g(B^*)(\frac{h(I)}{h(I^*)}-\frac{\theta(B)}{\theta(B^*)}-\frac{h(I)\theta(B^*)}{h(I^*)\theta(B)}+1)\\&+n(S^*)f(I^*)\ln\frac{n(S(t-\tau))f(I(t-\tau))}{n(S)f(I)}\\&+n(S^*)g(B^*)\ln\frac{n(S(t-\tau))g(B(t-\tau))}{n(S)g(B)}+\frac{\varphi(I^*)}{\varphi(I)}n(S)(f(I)+g(B)).\end{aligned}\tag{3.2}$$

We consider the function $M(x) = 1 - x + \ln x$, which is nonpositive for $x > 0$ and $M(x) = 0$ if and only if $x = 1$. Eq. (3.2) is equivalent to

$$\begin{aligned}\frac{dL}{dt} =& -\mu(S - S^*)(1 - \frac{n(S^*)}{n(S)}) \\ &+ n(S^*)f(I^*)(\frac{f(I)}{f(I^*)} - 1)(1 - \frac{f(I^*)\varphi(I)}{f(I)\varphi(I^*)}) \\ &+ n(S^*)f(I^*)(M(\frac{f(I^*)\varphi(I)}{f(I)\varphi(I^*)}) + M(\frac{n(S^*)}{n(S)})) \\ &+ n(S^*)g(B^*)(\frac{g(B)}{g(B^*)} - 1)(1 - \frac{g(B^*)\theta(B)}{g(B)\theta(B^*)}) \\ &+ n(S^*)g(B^*)(\frac{h(I)}{h(I^*)} - 1)(1 - \frac{h(I^*)\varphi(I)}{h(I)\varphi(I^*)}) \\ &+ n(S^*)g(B^*)(M(\frac{n(S^*)}{n(S)}) + M(\frac{h(I)\theta(B^*)}{h(I^*)\theta(B)})) \\ &+ n(S^*)g(B^*)(M(\frac{h(I^*)\varphi(I)}{h(I)\varphi(I^*)}) + M(\frac{g(B^*)\theta(B)}{g(B)\theta(B^*)})) \\ &+ n(S^*)f(I^*)M(\frac{\varphi(I^*)n(S(t-\tau))f(I(t-\tau))}{n(S^*)f(I^*)\varphi(I)}) \\ &+ n(S^*)g(B^*)M(\frac{\varphi(I^*)n(S(t-\tau))g(B(t-\tau))}{n(S^*)g(B^*)\varphi(I)}). \end{aligned} \tag{3.3}$$

By assumption (A_7), we have the following results:

$$\begin{aligned}&(\frac{f(I)}{f(I^*)} - 1)(1 - \frac{f(I^*)\varphi(I)}{f(I)\varphi(I^*)}) \\ =&\frac{\varphi(I)}{f(I)f(I^*)}(f(I) - f(I^*))(\frac{f(I)}{\varphi(I)} - \frac{f(I^*)}{\varphi(I^*)}) \\ \le& 0, \\ &(\frac{g(B)}{g(B^*)} - 1)(1 - \frac{g(B^*)\theta(B)}{g(B)\theta(B^*)}) \le 0\end{aligned}$$

and

$$(\frac{h(I)}{h(I^*)} - 1)(1 - \frac{h(I^*)\varphi(I)}{h(I)\varphi(I^*)}) \le 0. \tag{3.4}$$

It follows from (3.3) and (3.4) that

$$\frac{dL}{dt} = \frac{dL_1}{dt} + \frac{dL_2}{dt} + \frac{dL_3}{dt} \le 0.$$

The equality $\frac{dL}{dt} = 0$ implies that $\frac{n(S^*)}{n(S)} = 1, \frac{f(I)}{f(I^*)} = 1$ and $\frac{g(B)}{g(B^*)} = 1$. That is, the equality $\frac{dL}{dt} = 0$ holds only for $S = S^*, I = I^*, B = B^*$, which means that E_* is the maximum invariant set of system (3.1) in the set $\{\frac{dL}{dt} = 0\}$, and then the endemic equilibrium E_* is globally asymptotically stable. □

Theorem 3.2. *Assume that conditions $(H_1) - (H_7)$ are satisfied. If $R_0 > 1$, the endemic equilibrium $P_* = (S^*, E^*, I^*, B^*)$ of system (2.1) is globally asymptotically stable.*

Proof. It follows from the second equation of system (2.1) that

$$E(t) = \int_{t-\tau}^{t} n(S(x))(f(I(x)) + g(B(x)))e^{-\mu(t-x)}dx. \tag{3.5}$$

From Lemma 3.2 and Eq.(3.5), we get

$$\begin{aligned}\lim_{t\to+\infty} E(t) =& \lim_{t\to+\infty} \int_{t-\tau}^{t} n(S(x))(f(I(x)) + g(B(x)))e^{-\mu(t-x)}dx \\ =& \lim_{t\to+\infty} \frac{\int_{t-\tau}^{t} n(S(x))(f(I(x)) + g(B(x)))e^{\mu x}dx}{e^{\mu t}} \\ =& \lim_{t\to+\infty} \frac{1}{\mu} n(S)(f(I) + g(B))(1 - e^{-\mu\tau}) \\ =& E^*.\end{aligned}$$

Therefore, if $R_0 > 1$, P_* of system (2.1) is globally asymptotically stable. □

4. Several specific examples and numerical simulation

To illustrate the usefulness of the results, we consider the following the nonlinear system:

$$\begin{aligned}\frac{dS}{dt} =& A - Sf(I) - Sg(B) - \mu S, \\ \frac{dE}{dt} =& Sf(I) + Sg(B) - \mu E - e^{-\mu\tau}S(t-\tau)(f(I(t-\tau)) + g(B(t-\tau))), \\ \frac{dI}{dt} =& e^{-\mu\tau}S(t-\tau)(f(I(t-\tau)) + g(B(t-\tau))) - (c+\mu)I, \\ \frac{dB}{dt} =& kI^q - dB,\end{aligned} \tag{4.1}$$

where A, μ, τ, k, d and $c > 0$, $0 < q \leq 1$, $n(S) = S$, $\varphi(I) = (c+\mu)I$, $h(I) = kI^q$, $\theta(B) = dB$, and the functions $g(B)$ and $f(I)$ are strictly monotonously increasing. (A_7) can be satisfied by the following nonlinear incidence functions:

$$\frac{X_i^p}{1 + T_i X_i^p}, \qquad i = 1, 2,$$

where $X_1 = I, X_2 = B$, $0 < p \leq 1, T_i \geq 0$.

If $g(B) = \frac{\lambda B}{1+TB}$ or $\eta(1-e^{-\alpha B})$ and $f(I) = k\ln(1+\frac{\lambda I}{k})$ with constants $\lambda, \eta, k, \alpha > 0$, $T \geq 0$ [3, 4, 6, 15], the assumption (H_7) holds. In these cases, if $R_0 \leq 1$, the disease-free equilibrium is globally asymptotically stable, and system (4.1) has a unique endemic equilibrium, which is also globally asymptotically stable if $R_0 > 1$.

For $\varphi(I) = \mu I + \frac{cI}{a+I}$, $f(I) = \beta I, g(B) = \lambda B$ and $q = 1$. It is easy to see that system (4.1) has a disease-free equilibrium $(\frac{A}{\mu}, 0, 0, 0)$. We drive the basic reproduction number by

$$R_0^{11} = \frac{Aae^{-\mu\tau}(d\beta + k\lambda)}{d\mu(a\mu + c)}.$$

To determine the endemic equilibrium, we solve nonlinear equations given by

$$\begin{aligned} &A = \beta SI + \lambda SB + \mu S, \\ &e^{-\mu\tau} S(\beta I + \lambda B) = \mu I + \frac{cI}{a+I}, \\ &kI = dB. \end{aligned} \tag{4.2}$$

So we have

$$R_2 I^2 + (R_1 - R_0^{11})I + a(1 - R_0^{11}) = 0,$$

where $R_2 = \frac{a(d\beta+\lambda k)}{d(a\mu+c)}$, $R_1 = a(\frac{d\beta+\lambda K}{d\mu} + \frac{\mu}{a\mu+c})$, $\Delta = (R_1 - R_0^{11})^2 - 4aR_2(1 - R_0^{11})$. Therefore, system (4.1) has two endemic equilibria when $R_1 < R_0^{11} < 1$ and $\Delta > 0$, and there is a unique endemic equilibrium when $R_0^{11} > 1$. The above analysis suggests that system (2.1) may go through backward bifurcation if the assumption (H_7) is not satisfied, which implies that the disease-free equilibrium of system (4.1) is not globally asymptotically stable. Biologically speaking, even if R_0 is reduced and kept under unity, disease can not be ultimately eliminated.

To better understand the results, we make $n(S) = S$, $f(I) = \beta I$, $g(B) = \lambda B$, $h(I) = kI$ and $\theta(B) = dB$, then system (2.1) can be rewritten as

$$\begin{aligned} \frac{dS}{dt} =& A - \beta SI - \lambda SB - \mu S, \\ \frac{dE}{dt} =& \beta SI + \lambda SB - \mu E - e^{-\mu\tau} S(t-\tau)(\beta I(t-\tau) + \lambda B(t-\tau)), \\ \frac{dI}{dt} =& e^{-\mu\tau} S(t-\tau)(\beta I(t-\tau) + \lambda B(t-\tau)) - \varphi(I), \\ \frac{dB}{dt} =& kI - dB. \end{aligned} \tag{4.3}$$

Considering the following parameter values and initial values:

$$A = 210, \beta = 0.025, \lambda = 0.005, \mu = 0.1, k = 2, d = 4$$

and

$$S(0) = 200, E(0) = 10, I(0) = 30, B(0) = 100.$$

When $\varphi(I) = (\mu + c)I$, it is easy to see that the endemic equilibrium of system (4.3) is globally asymptotically stable and the persistent scale of the disease is reduced with the increase of time delay τ from Fig.1(a). For $\varphi(I) = \mu I + \frac{cI}{a+I}$, system (4.3) presents periodic oscillation behavior from Fig.1(b), which shows that the endemic equilibrium of system (4.3) is not globally asymptotically stable, and implies that system (4.3) experiences bifurcation.

5. Conclusions

In this paper, we formulated a general SEIB dynamic model for animal brucellosis transmission with the general incidence, shedding rate of pathogen, removal rate and a time delay to describe the fixed latency period of animal brucellosis. Under the biologically motivated assumptions, the disease-free equilibrium of system (2.1) shows globally asymptotically stable if $R_0 \leq 1$, which means that the extinction of infectious diseases is independent of initial sizes of the populations and the

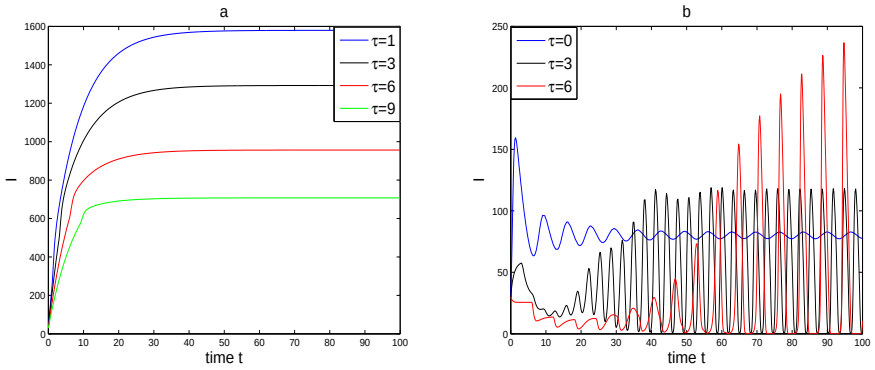

Figure 1. Fixed all other parameters except time delay τ. (a) Simulation of the number of infected individuals on variable τ (1, 3, 6 and 9) with $c = 0.02$. (b) Simulation of the number of infected individuals on variable τ (0, 3 and 6) with $c = 240$ and $a = 20$.

disease will be eliminated; and if $R_0 > 1$, system (2.1) admits a unique endemic equilibrium which is also globally asymptotically stable, implying that the disease always remains endemic and persists at a unique endemic equilibrium, no matter how small the size of the initial infection is. These results suggest that time delay is harmless for the stability of equilibria of system (2.1). Furthermore, if $\frac{f}{\varphi}$, $\frac{g}{\theta}$ and $\frac{h}{\varphi}$ are increasing, system (2.1) may have other dynamical features such as cycle oscillations according to the examples in Section 4. In other words, the persistent level of the disease is very low in a certain time period, but it does not imply that the disease will die out. In addition, as is shown in Fig.1(b), the impact of time delay on the bifurcation of system (2.1) is still unclear. Therefore, the development of the prevention and control strategies has significant effects on the spread of brucellosis, but our knowledge of the dynamics of brucellosis transmission remains incomplete. We leave other dynamical properties for further research.

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