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STUDY OF THE BRUCELLOSIS TRANSMISSION WITH MULTI-STAGE

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Abstract. In this paper, based on characteristics of brucellosis infection in some regions in China, a multi-stage dynamic model is proposed for sheep brucellosis transmission. The birth rate is related to the adult and vaccinated sheep. More realistically, the immigration from other place is also considered. Firstly, the basic reproduction number R_0 is determined and the dynamical properties of the model is discussed. It is concluded that the unique endemic equilibrium exists when $R_0 > 1$. By constructing suitable Lyapunov function, the global stability of the endemic equilibrium is verified. By carrying out sensitivity analysis of the basic reproduction number in term of the parameters, it is concluded that increasing the sheep vaccination rate and elimination rate of infected sheep is important for the control brucellosis.

Keywords: brucellosis; multi-stage; basic reproduction number; asymptotic stability; global stability.

2010 AMS Subject Classification: 34D20,34D23.

1. Introduction

Brucellosis, is an acute and chronic infectious disease caused by Brucella that is mainly infected with livestock. The World Health Organization has classified it as a Category B animal

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disease, and China has classified it as a Category II animal disease [1]. Brucellosis can occur throughout the year. It can live about 4 months in soil and water, survive in meat, dairy product about 2 months and die out immediately when boiled. Generally, disinfectants are used to kill the pathogen within a few hours. In natural conditions, animals susceptible to Brucella are widely distributed. Wild animals are hosts of Brucella and mainly infect cattle, sheep, and pigs. The disease also can be transmitted to human being from the infected animals or the infected environment.

In China, brucellosis exists in most areas, especially in the north. In the 1990s, the epidemic of brucellosis was mainly concentrated in the five major pastoral areas, Inner Mongolia, Xinjiang, Qinghai, Ningxia and Tibet. Using the mathematical models to the research on the prevention and control of the epidemic spread has important significance [2]. The transmission of many diseases is related to its different stage structure. For example, diseases such as measles and chickenpox are more common in the early childhood stages, but for brucellosis and in terms of typhoid fever, it appears more often in the adult stage[3]. Because the population shows different characteristics at different stages, it is a great theoretical and practical significance to study the dynamics of infectious diseases with stage structure.

There are many studies about brucellosis transmission models. Recently, G.Q. Sun considered a type of disease model with birth items [4], X.J. Wang studied a type of brucellosis model with nonlinear contact rate [5], B. Hao, Mi R.M. Zhang discussed an human and sheep co-infection model and reached some conclusions[6], M.T. Li discussed a four-dimensional, staged brucellosis model [7]. A class of brucellosis infection model with direct exposure to latencies and immunization is discussed in[8]. Based on these works, we will consider a stage structured, six-dimensional model with birth rate and with indirect environmental infection term.

Firstly, we will introduce the dynamical model, give out the basic reproduction number R_0 and the disease free equilibrium in Section 2. We will analyze the stability of the disease free equilibrium in Section 3. The existence and global stability of endemic equilibrium is discussed in Section 4. Some numerical simulations will be used to verify our analytical results in Section 5. Finally, we will conclude the paper with some discussion in Section 6.

2. Dynamic Model

Based on the obvious structural characteristics of Brucella, we divided sheep population into susceptible young sheep, susceptible adult sheep, latent sheep, immunized sheep and infected sheep, denoted separately by $S_1(t), S_2(t), E(t), I(t), V(t)$. Taking into account the indirect environmental transmission factors, we use $B(t)$ to denote the Brucella bacteria in the environment at time t, susceptible sheep can be affected by direct contact with the infected sheep or indirect contact with contaminated environment. Notice that susceptible young sheep and susceptible adult sheep has different infection rates(actually the infection rate for susceptible young sheep is smaller than susceptible adult sheep). It is assumed that the birth rate of sheep is only related with the adult and immunized individuals, and culling measures are taken for infected sheep. Then we have the following brucellosis transmission model:

$$\begin{cases} \dfrac{dS_1}{dt} = A + \alpha(S_2+V) - (\mu+m)S_1 - \varepsilon(\beta S_1 I + \beta S_1 E + \beta_1 S_1 B) \\ \dfrac{dS_2}{dt} = mS_1 - \theta S_2 - \mu S_2 + \delta V - (\beta S_2 I + \beta S_2 E + \beta_1 S_2 B) \\ \dfrac{dE}{dt} = \varepsilon(\beta S_1 I + \beta S_1 E + \beta_1 S_1 B) + (\beta S_2 I + \beta S_2 E + \beta_1 S_2 B) - (\mu+\sigma)E \\ \dfrac{dI}{dt} = \sigma E - (\mu+\gamma)I \\ \dfrac{dV}{dt} = \theta S_2 - (\mu+\delta)V \\ \dfrac{dB}{dt} = k(E+I) - (d+n\tau)B \end{cases} \tag{2.1}$$

Consider that all parameters in system(2.1) are nonnegative, and satisfies $\mu > \alpha$. The parameters are described in following table.

Assume that $N(t)$ is the total number of the sheep population, that is $N(t) = S_1(t) + S_2(t) + E(t) + I(t) + V(t)$, then

$$\frac{dN}{dt} = A + \alpha(S_2+V) - \mu N - \gamma I \leq A - (\mu - \alpha)N$$

it follows that

$$\limsup_{t\to\infty} N(t) \leq \frac{A}{\mu-\alpha} \tag{2.2}$$

From the last equation of system (2.1) we can obtain that:

$$\frac{dB}{dt} \leq kN - (d+n\tau)B \leq \frac{kA}{\mu-\alpha} - (d+n\tau)B$$

parameters	comments	unit
A	the input number of young sheep	$year^{-1}$
ε	the ratio coefficient of infection of young sheep	$year^{-1}$
β	the infection rate of latent and infected sheep to susceptible sheep	$year^{-1}$
μ	the natural death rate of sheep	$year^{-1}$
β_1	the infection rate from contaminated environment to susceptible sheep	$year^{-1}$
σ	the transfer rate from exposed to infectious compartment	$year^{-1}$
γ	the disease-related elimination rate	$year^{-1}$
k	brucella shedding rate from exposed and infectious sheep into the environment	$year^{-1}$
d	the natural decaying rate of brucella in environment	$year^{-1}$
n	disinfection times	$time^{-1}$
τ	the efficient disinfection rate	$year^{-1}$
m	transfer rate from young sheep to adult sheep	$year^{-1}$
θ	adult sheep vaccination rate	$year^{-1}$
δ	vaccination loss rate	$year^{-1}$
α	the birth rate of sheep	$year^{-1}$

that is

$$\limsup_{t\to\infty} B(t) \leq \frac{kA}{(\mu-\alpha)(d+n\tau)} \tag{2.3}$$

By equations (2.2) and (2.3), we can conclude that

$$\Gamma = \{(S_1,S_2,E,I,V,B) \mid S_1,S_2,E,I,V,B \geq 0, 0 \leq (S_1+S_2+E+I+V) \leq \frac{A}{\mu-\alpha}, B \leq \frac{kA}{(\mu-\alpha)(d+n\tau)}\}$$

is the positively invariant set respect to system (2.1).

It's evident that the system (2.1) has a disease-free equilibrium $E_0 = (S_1^0, S_2^0, 0, 0, V^0, 0)$, which satisfies :

$$\begin{cases} A+\alpha(S_2+V)-(\mu+m)S_1 = 0 \\ mS_1-\theta S_2-\mu S_2+\delta V = 0 \\ \theta S_2-(\mu+\delta)V = 0 \end{cases} \tag{2.4}$$

Where

$$S_1^0 = \frac{A\mu}{\mu^2+\mu m-\alpha m},$$
$$S_2^0 = \frac{Am(\mu+\delta)}{(\mu^2+\mu m-\alpha m)(\mu+\delta+\theta)}, \tag{2.5}$$
$$V^0 = \frac{Am\theta}{(\mu^2+\mu m-\alpha m)(\mu+\delta+\theta)}$$

Following the method of Van den Driessche and Watmough [9], we have:

$$F = \begin{pmatrix} \varepsilon\beta S_1^0+\beta S_2^0 & \varepsilon\beta S_1^0+\beta S_2^0 & \varepsilon\beta_1 S_1^0+\beta_1 S_2^0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \qquad V = \begin{pmatrix} \mu+\sigma & 0 & 0 \\ -\sigma & \mu+\gamma & 0 \\ -k & -k & d+n\tau \end{pmatrix}$$

the basic reproduction number of system (2.1) is:

$$R_0 = \rho(FV^{-1}) = \frac{\varepsilon\beta S_1^0+\beta S_2^0}{\mu+\sigma} + \frac{\sigma(\varepsilon\beta S_1^0+\beta S_2^0)}{(\mu+\sigma)(\mu+\gamma)} + \frac{k(\mu+\sigma+\gamma)(\varepsilon\beta_1 S_1^0+\beta_1 S_2^0)}{(\mu+\gamma)(\mu+\sigma)(d+n\tau)} \tag{2.6}$$

Let $M = F - V$, we have:

$$M = \begin{pmatrix} \varepsilon\beta S_1^0+\beta S_2^0-(\mu+\sigma) & \varepsilon\beta S_1^0+\beta S_2^0 & \varepsilon\beta_1 S_1^0+\beta_1 S_2^0 \\ \sigma & -(\mu+\gamma) & 0 \\ k & k & -(d+n\tau) \end{pmatrix}$$

Define $s(M) = max\{Re\lambda : \lambda$ is an eigenvalue of $M\}$, $s(M)$ is a simple eigenvalue of M with a positive eigenvector , by the Theorem 2 in [9], we have

$$R_0 > 1 \Leftrightarrow s(M) > 0, R_0 < 1 \Leftrightarrow s(M) < 0$$

3. The stability of disease-free equilibrium

Theorem 3.1.

The disease-free equilibrium E_0 of system (2.1) is local stability when $R_0 < 1$.

Proof.

It's obvious that the hypothesis (A1-A4) of Theorem 2 in [9] is satisfied. Next, to verify (A5), we only need prove that all the eigenvalues of :

$$J\mid_{E_0}=\begin{pmatrix} M & 0 \\ J_3 & J_4 \end{pmatrix}$$

have negative real parts, where $J_3 = -F$.

$$J_4 = \begin{pmatrix} -(\mu+m) & \alpha & \alpha \\ m & -(\mu+\theta) & \delta \\ 0 & \theta & -(\mu+\delta) \end{pmatrix}$$

Next we calculate the eigenvalues of J_4, the characteristic equation is:

$$p(\lambda) = \lambda^3 + b_1\lambda^2 + b_2\lambda + b_3 = 0$$

in which

$$\begin{aligned} b_1 &= 3\mu+\theta+m+\delta \\ b_2 &= \mu(\mu+\theta+\delta)+(\mu+m)(2\mu+\theta+\delta)-m\alpha \\ b_3 &= \mu(\mu+m)(\mu+\theta+\delta)-m\alpha(\mu+\theta+\delta) \end{aligned}$$

It's obvious that $b_1 > 0$, $b_2 > 0$, $b_3 > 0$, and

$$\begin{aligned} b_1b_2-b_3 &= (3\mu+\theta+\delta+m)[(\mu+\theta+\delta)(2\mu+m)+\mu(\mu+m)-m\alpha] \\ &- (\mu+\theta+\delta)(\mu^2+m\mu-m\alpha) \\ &> (3\mu+\theta+\delta+m)(\mu+\theta+\delta)(2\mu+m)-(\mu+\theta+\delta)(\mu^2+m\mu) \\ &+ (\mu+\theta+\delta)m\alpha \\ &> 0 \end{aligned}$$

Using the Routh-Hurwitz criteria, we can conclude that all the eigenvalues of J_4 have negative real parts. Therefore, if $R_0 < 1$, then $s(M) < 0$ and $s(J\mid_{E_0}) < 0$. This means the disease-free equilibrium E_0 of system (2.1) is locally stable. This completes the proof.

Theorem 3.2.

The disease-free equilibrium E_0 of system (2.1) is globally asymptotically stable when $R_0 < 1$.

Proof.

Constructing a Lyapunov function as follows:

$$\begin{aligned} L_1(t) &= S_1(t)-S_1^0-S_1^0\ln\frac{S_1(t)}{S_1^0}+S_2(t)-S_2^0-S_2^0\ln\frac{S_2(t)}{S_2^0}+V(t)-V^0-V^0\ln\frac{V(t)}{V^0}+E \\ &+ \frac{(d+n\tau)[\mu+\sigma-(\varepsilon\beta S_1^0+\beta S_2^0)]-k(\varepsilon\beta_1 S_1^0+\beta_1 S_2^0)}{\sigma(d+n\tau)}I+\frac{\varepsilon\beta_1 S_1^0+\beta_1 S_2^0}{d+n\tau}B \end{aligned}$$

From the definition of R_0, it is easy to see that

$$\frac{(\mu+\sigma)(d+n\tau)-(d+n\tau)(\varepsilon\beta S_1^0+\beta S_2^0)-k(\varepsilon\beta_1 S_1^0+\beta_1 S_2^0)}{\sigma(d+n\tau)}>0$$

holds when $R_0<1$. Calculating the derivative of $L_1(t)$, we have

$$\begin{aligned} \frac{dL_1(t)}{dt} &= (1-\frac{S_1^0}{S_1})[A+\alpha(S_2+V)-\varepsilon(\beta S_1 I+\beta S_1 E+\beta_1 S_1 B)-\frac{A+\alpha(S_2^0+V^0)}{S_1^0}S_1] \\ &+ (1-\frac{S_2^0}{S_2})[mS_1+\delta V-(\beta S_2 I+\beta S_2 E+\beta_1 S_2 B)-\frac{mS_1^0+\delta V^0}{S_2^0}S_2] \\ &+ (1-\frac{V^0}{V})[\theta S_2-\frac{\theta S_2^0}{V^0}V] \\ &+ \varepsilon(\beta S_1 I+\beta S_1 E+\beta_1 S_1 B)+(\beta S_2 I+\beta S_2 E+\beta_1 S_2 B)-(\mu+\sigma)E \\ &+ \frac{(\mu+\sigma)(d+n\tau)-(d+n\tau)(\varepsilon\beta S_1^0+\beta S_2^0)-k(\varepsilon\beta_1 S_1^0+\beta_1 S_2^0)}{\sigma(d+n\tau)}[\sigma E-(\mu+\gamma)I] \\ &+ \frac{\varepsilon\beta_1 S_1^0+\beta_1 S_2^0}{d+n\tau}[k(E+I)-(d+n\tau)B] \end{aligned}$$

Notice that

$$A=\mu S_1^0+\mu V^0+\mu S_2^0-\alpha(S_2^0+V^0),\quad mS_1^0=\mu V^0+\mu S_2^0,\quad \theta S_2^0=(\mu+\delta)V^0,$$

then

$$\begin{aligned} \frac{dL_1(t)}{dt} &= \mu S_1^0(2-\frac{S_1^0}{S_1}-\frac{S_1}{S_1^0})+(\mu V^0-\alpha V^0)(4-\frac{S_1^0}{S_1}-\frac{S_2^0 S_1}{S_1^0 S_2}-\frac{V}{V^0}-\frac{S_2 V^0}{S_2^0 V}) \\ &+ (\mu S_2^0-\alpha S_2^0)(3-\frac{S_1^0}{S_1}-\frac{S_2}{S_2^0}-\frac{S_2^0 S_1}{S_1^0 S_2})+\delta V^0(2-\frac{S_2^0 V}{S_2 V^0}-\frac{S_2 V^0}{S_2^0 V}) \\ &+ \alpha S_2^0(2-\frac{S_2^0 S_1}{S_1^0 S_2}-\frac{S_1^0 S_2}{S_2^0 S_1})+\alpha V^0(3-\frac{S_2 V^0}{S_2^0 V}-\frac{S_1^0 V}{S_1 V^0}-\frac{S_2^0 S_1}{S_1^0 S_2}) \\ &+ \frac{(\mu+\sigma)(\mu+\gamma)}{\sigma}I(R_0-1) \end{aligned}$$

Therefore, when $R_0 < 1$, we have $\frac{dL_1}{dt} \leq 0$, and the equation $\frac{dL_1(t)}{dt} = 0$ holds if and only if $S_1 = S_1^0, S_2 = S_2^0, E = 0, I = 0, V = V^0, B = 0$. Thus the disease-free equilibrium E_0 is globally asymptotic stable in Γ by LaSalle's Invariance Principle[10]. This completes the proof.

4. The existence and global stability of endemic equilibrium

The possible endemic equilibrium $E^*(S_1^*, S_2^*, E^*, I^*, V^*, B^*)$ of system (2.1) derived by the following equations:

$$\begin{cases} A + \alpha(S_2 + V) - (\mu + m)S_1 + \varepsilon(\beta S_1 I + \beta S_1 E + \beta_1 S_1 B) = 0 \\ mS_1 - \theta S_2 - \mu S_2 + \delta V - (\beta S_2 I + \beta S_2 E + \beta_1 S_2 B) = 0 \\ \varepsilon(\beta S_1 I + \beta S_1 E + \beta_1 S_1 B) + (\beta S_2 I + \beta S_2 E + \beta_1 S_2 B) - (\mu + \sigma)E = 0 \\ \sigma E - (\mu + \gamma)I = 0 \\ \theta S_2 - (\mu + \delta)V = 0 \\ k(E + I) - (d + n\tau)B = 0 \end{cases} \tag{4.1}$$

then we have

$$E = \frac{(\mu + \gamma)I}{\sigma}, V = \frac{\theta S_2}{(\mu + \delta)}, B = \frac{kI(\mu + \gamma + \sigma)}{\sigma(d + n\tau)} \tag{4.2}$$

Let $H = \beta + \beta\frac{\mu+\gamma}{\sigma} + \beta_1\frac{k(\mu+\gamma+\sigma)}{\sigma(d+n\tau)}$. From the first and second equations in (4.1), we get

$$S_1 = \frac{A[(\mu + \delta)(IH + \theta + \mu) - \delta\theta]}{(IH\varepsilon + \mu + m)[(\mu + \delta)(IH + \theta + \mu) - \delta\theta] - \alpha m(\mu + \delta + \theta)} \tag{4.3}$$

From the second and fifth equations in (4.1), we obtain

$$S_2 = \frac{mS_1 - \mu V}{\mu + \beta I + \beta E + \beta_1 B}$$

By (4.2),(4.3) we can obtain

$$S_2 = \frac{Am(\mu + \delta)}{(IH\varepsilon + \mu + m)[(\mu + \delta)(IH + \theta + \mu) - \delta\theta] - \alpha m(\mu + \delta + \theta)} \triangleq F_1(I)$$

From the third equation in (4.1), we have

$$S_2 = \frac{E(\mu + \sigma)}{\beta I + \beta E + \beta_1 B} - \varepsilon S_1 \tag{4.4}$$

Substituting (4.2) and (4.3) into (4.4), we get

$$S_2 = \frac{(\mu+\gamma)(\mu+\sigma)}{\sigma H} - \frac{A\varepsilon[(\mu+\delta)(IH+\theta+\mu)-\delta\theta]}{(IH\varepsilon+\mu+m)[(\mu+\delta)(IH+\theta+\mu)-\delta\theta]-\alpha m(\mu+\delta+\theta)} \triangleq F_2(I)$$

Then $\limsup_{I\to\infty} F_1(I) = 0$ and

$$F_1^{'}(I) = \frac{-mA(\mu+\delta)[H(\mu+\delta)(IH\varepsilon+\mu+m)+IH^2\varepsilon(\mu+\delta)+H\varepsilon\mu(\mu+\delta+\theta)]}{[(IH\varepsilon+\mu+m)[(\mu+\delta)(IH+\theta+\mu)-\delta\theta]-\alpha m(\mu+\delta+\theta)]^2}$$

We can see that $F_1^{'}(I) < 0$, for all $I \in \Gamma$, so $F_1(I)$ is monotonically decreasing in Γ.

Using the same method, we can conclude that $F_2(I)$ is monotonically increasing in Γ. Noticing that

$$F_1(0) = \frac{Am(\mu+\delta)}{(\mu+m)\mu(\mu+\delta+\theta)-\alpha m(\mu+\delta+\theta)} > 0$$

and

$$F_2(0) = \frac{(\mu+\gamma)(\mu+\sigma)}{\sigma H} - \frac{A\varepsilon\mu}{\mu^2+m\mu-\alpha m}$$

Then

$$\begin{aligned}
&F_1(0) - F_2(0)\\
=&\frac{Am(\mu+\delta)\sigma H + A\varepsilon\sigma H\mu(\mu+\delta+\theta) - [\mu(\mu+m)-\alpha m](\mu+\delta+\theta)(\mu+\gamma)(\mu+\sigma)}{\sigma H(\mu+\delta+\theta)[\mu(\mu+m)-\alpha m]}\\
=&\frac{1}{\sigma H}[\frac{Am(\mu+\delta)\sigma H}{[\mu(m+\mu)-\alpha m](\mu+\delta+\theta)} + \frac{A\varepsilon\sigma H\mu(\mu+\delta+\theta)}{[\mu(m+\mu)-\alpha m](\mu+\delta+\theta)} - (\mu+\gamma)(\mu+\sigma)]
\end{aligned} \tag{4.5}$$

Substituting $H = \beta + \beta\frac{\mu+\gamma}{\sigma} + \beta_1\frac{k(\mu+\gamma+\sigma)}{\sigma(d+n\tau)}$ into (4.5), we have:

$$\begin{aligned}
&\frac{Am(\mu+\delta)\sigma H}{[\mu(m+\mu)-\alpha m](\mu+\delta+\theta)} + \frac{A\varepsilon\sigma H\mu(\mu+\delta+\theta)}{[\mu(m+\mu)-\alpha m](\mu+\delta+\theta)} - (\mu+\gamma)(\mu+\sigma)\\
=&\frac{Am(\mu+\delta)}{[\mu(m+\mu)-\alpha m](\mu+\delta+\theta)}[\beta\sigma+\beta(\mu+\gamma)+\frac{\beta_1 k(\mu+\gamma+\sigma)}{d+n\tau}]\\
+&\frac{A\varepsilon\mu(\mu+\delta+\theta)}{[\mu(m+\mu)-\alpha m](\mu+\delta+\theta)}[\beta\sigma+\beta(\mu+\gamma)+\frac{\beta_1 k(\mu+\gamma+\sigma)}{d+n\tau}] - (\mu+\gamma)(\mu+\sigma)
\end{aligned}$$

Noticing (2.5)(2.6), when $R_0 > 1$, there is:

$$\begin{aligned}
&\frac{Am(\mu+\delta)}{[\mu(m+\mu)-\alpha m](\mu+\delta+\theta)}[\beta\sigma+\beta(\mu+\gamma)+\frac{\beta_1 k(\mu+\gamma+\sigma)}{d+n\tau}]\\
+&\frac{A\varepsilon\mu(\mu+\delta+\theta)}{[\mu(m+\mu)-\alpha m](\mu+\delta+\theta)}[\beta\sigma+\beta(\mu+\gamma)+\frac{\beta_1 k(\mu+\gamma+\sigma)}{d+n\tau}]\\
>&(\mu+\gamma)(\mu+\sigma)
\end{aligned}$$

So, while $R_0 > 1$ we have $F_1(0) - F_2(0) > 0$. Let $I_m = \frac{A}{\mu-\alpha}$, by similar calculation, we also have $F_2(I_m) - F_1(I_m) > 0$. Therefore, system (2.1) has a unique positive equilibrium E^* when $R_0 > 1$.

Theorem 4.1.

If $R_0 > 1$, then the endemic equilibrium $E^* = (S_1^*, S_2^*, E^*, I^*, V^*, B^*)$ of system (2.1) is globally asymptotic stable.

Proof.

Define a Lyapunov function as follows:

$$\begin{aligned} L_2 &= S_1(t) - S_1^* - S_1^* \ln \frac{S_1(t)}{S_1^*} + S_2(t) - S_2^* - S_2^* \ln \frac{S_2(t)}{S_2^*} + V(t) - V^* - V^* \ln \frac{V(t)}{V^*} \\ &+ E(t) - E^* - E^* \ln \frac{E(t)}{E^*} + \frac{\varepsilon\beta_1 S_1^* B^* + \beta_1 S_2^* B^*}{kE^* + kI^*}[B(t) - B^* - B^* \ln \frac{B(t)}{B^*}] \\ &+ (\frac{\varepsilon\beta S_1^* I^* + \beta S_2^* I^*}{\sigma E^*} + \frac{kI^*(\varepsilon\beta_1 S_1^* B^* + \beta_1 S_2^* B^*)}{\sigma E^*(kE^* + kI^*)})[I(t) - I^* - I^* \ln \frac{I(t)}{I^*}] \end{aligned}$$

Calculating the derivative of this function along with the solution of system (2.1), we have

$$\begin{aligned} \frac{dL_2(t)}{dt} &= (1 - \frac{S_1^*}{S_1})[A + \alpha(S_2 + V) - \varepsilon(\beta S_1 I + \beta S_1 E + \beta_1 S_1 B) \\ &- (1 - \frac{S_1^*}{S_1})\frac{A + \alpha(S_2^* + V^*) - \varepsilon(\beta S_1^* I^* + \beta S_1^* E^* + \beta_1 S_1^* B^*)}{S_1^*} S_1] \\ &+ (1 - \frac{S_2^*}{S_2})[mS_1 + \delta V - (\beta S_2 I + \beta S_2 E + \beta_1 S_2 B)] + (1 - \frac{V^*}{V})[\theta S_2 - \frac{\theta S_2^*}{V^*} V] \\ &- (1 - \frac{S_2^*}{S_2})[\frac{mS_1^* + \delta V^* - (\beta S_2^* I^* + \beta S_2^* E^* + \beta_1 S_2^* B^*)}{S_2^*} S_2] \\ &+ (1 - \frac{E^*}{E})[\varepsilon(\beta S_1 I + \beta S_1 E + \beta_1 S_1 B) + \beta S_2 I + \beta S_2 E + \beta_1 S_2 B] \\ &- (1 - \frac{E^*}{E})[\frac{\varepsilon(\beta S_1^* I^* + \beta S_1^* E^* + \beta_1 S_1^* B^*) + \beta S_2^* I^* + \beta S_2^* E^* + \beta_1 S_2^* B^*}{E^*} E] \\ &+ (\varepsilon\beta S_1^* I^* + \beta S_2^* I^*)(1 - \frac{I^*}{I})(\frac{E}{E^*} - \frac{I}{I^*}) + \frac{kI^*(\varepsilon\beta_1 S_1^* B^* + \beta_1 S_2^* B^*)}{kE^* + kI^*}(1 - \frac{I^*}{I})(\frac{E}{E^*} - \frac{I}{I^*}) \\ &+ \frac{\varepsilon\beta_1 S_1^* B^* + \beta_1 S_2^* B^*}{kE^* + kI^*} kE^*(1 - \frac{B^*}{B})(\frac{E}{E^*} - \frac{B}{B^*}) + \frac{\varepsilon\beta_1 S_1^* B^* + \beta_1 S_2^* B^*}{kE^* + kI^*} kI^*(1 - \frac{B^*}{B})(\frac{I}{I^*} - \frac{B}{B^*}) \end{aligned}$$

Noticing that

$$\theta S_2^* = (\mu + \delta)V^*, mS_1^* = \mu(S_2^* + V^*) + \beta S_2^* I^* + \beta S_2^* E^* + \beta_1 S_2^* B^*$$

$$A = \mu(S_1^* + S_2^* + V^*) - \alpha(S_2^* + V^*) + \varepsilon(\beta S_1^* I^* + \beta S_1^* E^* + \beta_1 S_1^* B^*) + \beta S_2^* I^* + \beta S_2^* E^* + \beta_1 S_2^* B^*$$

Then

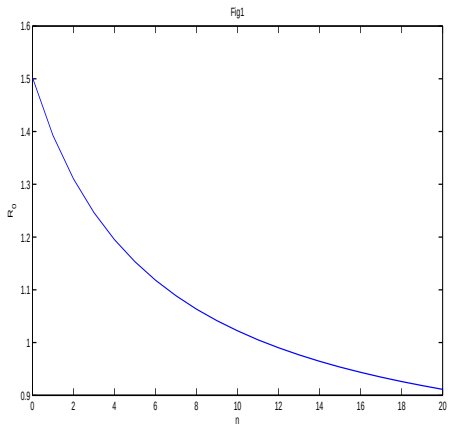
$$
\begin{aligned}
\frac{dL_2(t)}{dt} &= \mu S_1^*(2-\frac{S_1^*}{S_1}-\frac{S_1}{S_1^*})+\mu V^*(4-\frac{S_1^*}{S_1}-\frac{S_2^*S_1}{S_1^*S_2}-\frac{V}{V^*}-\frac{S_2V^*}{S_2^*V})\\
&+ \mu S_2^*(3-\frac{S_1^*}{S_1}-\frac{S_2}{S_2^*}-\frac{S_2^*S_1}{S_1^*S_2})+\delta V^*(2-\frac{S_2^*V}{S_2V^*}-\frac{S_2V^*}{S_2^*V})\\
&- \alpha S_2^*(1-\frac{S_1^*}{S_1}-\frac{S_2}{S_2^*}+\frac{S_2S_1^*}{S_1S_2^*})-\alpha V^*(1-\frac{S_1^*}{S_1}-\frac{V}{V^*}+\frac{VS_1^*}{S_1V^*})\\
&+ \varepsilon\beta S_1^*I^*(3-\frac{S_1^*}{S_1}-\frac{I^*E}{IE^*}-\frac{E^*S_1I}{ES_1^*I^*})+\varepsilon\beta S_1^*E^*(2-\frac{S_1^*}{S_1}-\frac{S_1}{S_1^*})\\
&+ \varepsilon\beta_1 S_1^*B^*(2-\frac{S_1^*}{S_1}-\frac{E}{E^*}+\frac{B}{B^*}-\frac{E^*S_1B}{ES_1^*B^*})+\beta S_2^*I^*(4-\frac{S_1^*}{S_1}-\frac{I^*E}{IE^*}-\frac{S_1S_2^*}{S_2S_1^*}-\frac{E^*S_2I}{ES_2^*I^*})\\
&+ \beta S_2^*E^*(3-\frac{S_1^*}{S_1}-\frac{S_1S_2^*}{S_2S_1^*}-\frac{S_2}{S_2^*})+\beta_1 S_2^*B^*(3-\frac{S_1^*}{S_1}-\frac{S_1S_2^*}{S_2S_1^*}-\frac{E}{E^*}+\frac{B}{B^*}-\frac{E^*S_2B}{ES_2^*B^*})\\
&+ \frac{kI^*\varepsilon\beta_1S_1^*B^*}{kE^*+kI^*}(2+\frac{E}{E^*}-\frac{B}{B^*}-\frac{I^*E}{IE^*}-\frac{B^*I}{BI^*})+\frac{kI^*\beta_1S_2^*B^*}{kE^*+kI^*}(2+\frac{E}{E^*}-\frac{B}{B^*}-\frac{I^*E}{IE^*}-\frac{B^*I}{BI^*})\\
&+ \frac{kE^*\varepsilon\beta_1S_1^*B^*}{kE^*+kI^*}(\frac{E}{E^*}-\frac{B}{B^*}-\frac{B^*E}{BE^*}+1)+\frac{kE^*\beta_1S_2^*B^*}{kE^*+kI^*}(\frac{E}{E^*}-\frac{B}{B^*}-\frac{B^*E}{BE^*}+1)\\
&= \mu S_1^*(2-\frac{S_1^*}{S_1}-\frac{S_1}{S_1^*})+(\mu V^*-\alpha V^*)(4-\frac{S_1^*}{S_1}-\frac{S_2^*S_1}{S_1^*S_2}-\frac{V}{V^*}-\frac{S_2V^*}{S_2^*V})\\
&+ (\mu S_2^*-\alpha S_2^*)(3-\frac{S_1^*}{S_1}-\frac{S_2}{S_2^*}-\frac{S_2^*S_1}{S_1^*S_2})+\delta V^*(2-\frac{S_2^*V}{S_2V^*}-\frac{S_2V^*}{S_2^*V})\\
&+ \alpha S_2^*(2-\frac{S_2^*S_1}{S_1^*S_2}-\frac{S_1^*S_2}{S_2^*S_1})+\alpha V^*(3-\frac{S_2^*S_1}{S_1^*S_2}-\frac{S_1^*V}{V^*S_1}-\frac{S_2V^*}{S_2^*V})\\
&+ \varepsilon\beta S_1^*I^*(3-\frac{S_1^*}{S_1}-\frac{I^*E}{IE^*}-\frac{E^*S_1I}{ES_1^*I^*})+\frac{kE^*\beta_1S_2^*B^*}{kE^*+kI^*}(4-\frac{S_1^*}{S_1}-\frac{S_1S_2^*}{S_2S_1^*}-\frac{B^*E}{BE^*}-\frac{E^*S_2B}{ES_2^*B^*})\\
&+ \varepsilon\beta S_1^*E^*(2-\frac{S_1^*}{S_1}-\frac{S_1}{S_1^*})+\beta S_2^*I^*(4-\frac{S_1^*}{S_1}-\frac{I^*E}{IE^*}-\frac{S_1S_2^*}{S_2S_1^*}-\frac{E^*S_2I}{ES_2^*I^*})\\
&+ \beta S_2^*E^*(3-\frac{S_1^*}{S_1}-\frac{S_1S_2^*}{S_2S_1^*}-\frac{S_2}{S_2^*})+\frac{kI^*\varepsilon\beta_1S_1^*B^*}{kE^*+kI^*}(4-\frac{S_1^*}{S_1}-\frac{I^*E}{IE^*}-\frac{B^*I}{BI^*}-\frac{E^*S_1B}{ES_1^*B^*})\\
&+ \frac{kI^*\beta_1S_2^*B^*}{kE^*+kI^*}(5-\frac{S_1^*}{S_1}-\frac{S_1S_2^*}{S_2S_1^*}-\frac{I^*E}{IE^*}-\frac{B^*I}{BI^*}-\frac{E^*S_2B}{ES_2^*B^*})\\
&+ \frac{kE^*\varepsilon\beta_1S_1^*B^*}{kE^*+kI^*}(3-\frac{S_1^*}{S_1}-\frac{B^*E}{BE^*}\frac{E^*S_1B}{ES_1^*B^*})\\
&\leq 0
\end{aligned}
$$

The equation $\frac{dL(t)}{dt}=0$ holds if and only if $S_1=S_1^*, S_2=S_2^*, E=E^*, I=I^*, V=V^*, B=B^*$. Thus the endemic equilibrium E^* is globally asymptotic stable in Γ by LaSalle's Invariance Principle. This completes the proof.

5. Numerical simulations

In this section we will give some numerical simulations to support our results. Some parameters came from the real data and others are fitted.

Firstly, using MATLAB, we will take some sensitivity analysis of the basic reproduction number, that is to see that how is the parameters will influence it. Taking $\mu = 0.25, \alpha = 0.015, \gamma = 0.15, \sigma = 1, d = 3.6, \tau = 0.6, \varepsilon = 0.4, \beta = 0.000038, k = 16, \beta_1 = 0.0000135, m = 1.06, \theta = 2.8, \delta = 0.4$, and the parameter n (disinfection times) is varied, we have Fig 1, seeing that the basic reproduction number decreases with the increase of n. Let $n = 3$ and other parameters remain the same, changing θ, we also can have the Fig 2, shows that increasing with θ, the basic reproduction number is decreasing.



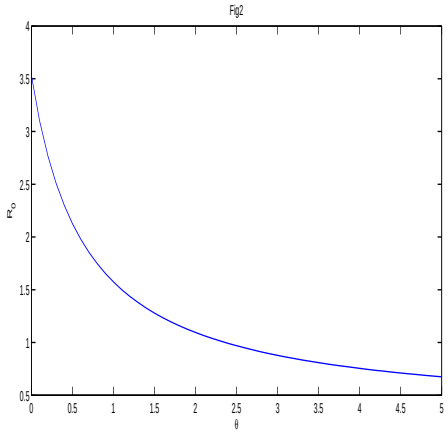
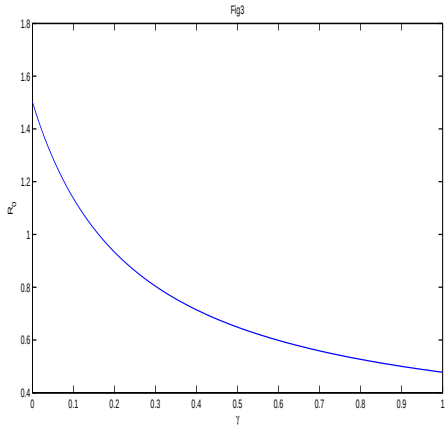
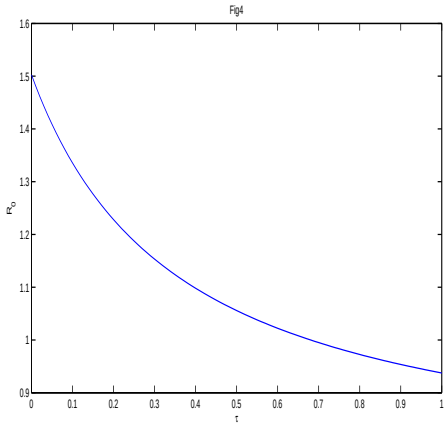
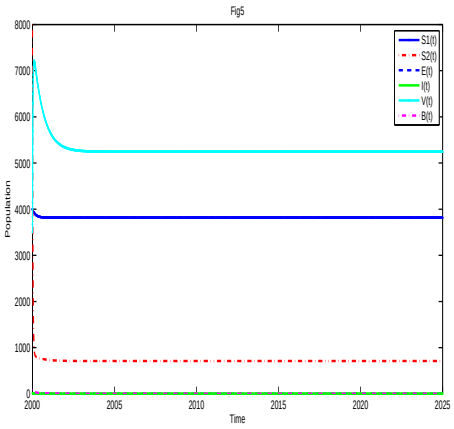


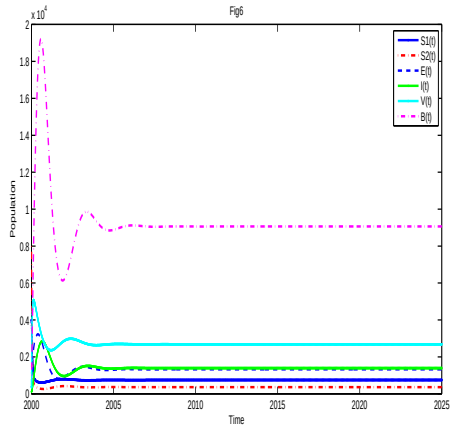
Fig 3 and Fig 4 is to show the influence of changing values of γ and τ on the basic reproduction number. It is seen that increasing disinfection times and the adult sheep vaccination rates are more efficient to reduce the basic reproduction number. That is to say, to reduce the brucellosis we can increase the vaccination rates and disinfection times. It is also useful to choose more efficient disinfection products and the increasing the elimination rate of infected sheep. Taking $A = 3000, \mu = 0.25, \alpha = 0.015, \gamma = 0.7, \sigma = 1, d = 3.6, n = 2, \tau = 0.6, \varepsilon = 0.4, \beta = 0.000038, k = 16, \beta_1 = 0.0000135, m = 1.06, \theta = 2.8, \delta = 0.4$, then, $R_0 = 0.37 < 1$. Taking the initial values as $S_1(0) = 4000, S_2(0) = 5000, E(0) = 7, I(0) = 14, V(0) = 3500, B(0) = 100$, we obtain Fig 5, it shows that the solutions tends to the disease-free equilibrium point, so the disease will die out. Changing $\gamma = 0.15, \theta = 1, n = 2$, and the other parameters remains the





same, then the basic reproduction number $R_0 = 1.157325 > 1$. Taking the same initial values given above, we have Fig 6, which shows the global stability of the endemic equilibrium point.





6. Conclusion and discussion

Brucellosis is one of the major public health problems in the world, which has caused a lot of economic and health problems. Based on the characteristics of brucellosis infection in some areas in China, this paper constructed a brucellosis model with multi-stage, the contaminated environment and immunized individuals. We obtained the basic reproduction number R_0 , disease-free equilibrium and endemic equilibrium. By constructing suitable Lyapunov functions, we proved the global asymptotic stability of the disease free equilibrium and endemic equilibrium. Finally, we performed a sensitivity analysis of R_0 and conducted numerical simulations to prove the corresponding conclusion. From the numerical analysis, we can get that

increasing the times of disinfection, enhancing immunity or increasing the slaughter rate of infected individuals, will have a great impact on the control of the disease.From Fig 6, the brucellosis will sustain when $R_0 > 1$.

Conflict of Interests

The authors declare that there is no conflict of interests.

Acknowledgments

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