Modeling the Transmission Dynamics of Sheep Brucellosis in Inner Mongolia Autonomous Region, China

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Abstract

Brucellosis is one of the major zoonotic diseases in China, especially in Inner Mongolia where occurs the largest number of human brucellosis cases of Mainland China, which can be attributed to the large number of sheep kept there, since at least 90% of the human brucellosis cases are caused by sheep. Therefore, given the characteristics of the brucellosis infection in Inner Mongolia Autonomous Region, we propose a dynamic model for the sheep-human transmission of brucellosis, involving sheep population, human population and brucella in the environment. We first determine the basic reproduction number $R_0$ and analyze the global stability of the disease-free and endemic equilibrium. Secondly, using the reported human brucellosis data, we carry out numerical simulations and make sensitivity analysis of the basic reproduction number in terms of some parameters. The results show that brucellosis cannot be eradicated even though disinfection rate and vaccination rate of adult sheep are 100%. By investigating and comparing the effect of vaccination, disinfection and eliminating strategies, we find that vaccinating and disinfecting both young and adult sheep are effective strategies to control brucellosis in Inner Mongolia of China.

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1. Introduction

Brucellosis is one of the world’s major zoonoses, which is caused by various species of Brucella [1]. It can be transmitted to other animals and humans with exposure to infected animals or via ingestion of contaminated water and dust, etc [2]. Especially, infections among sheep are highly contagious because of the pathogenicity of B. melitensis and close contact caused by the density of the herd. In animals, brucellosis mainly affects reproduction and fertility, and reduces the survival of newborns [3]. In humans, mortality is negligible, but the illness can last for several years [4]. While brucellosis has been controlled with the disease being eradicated or there being low infecting rate in many industrialized countries, more than 500,000 new cases are reported annually around the world and the disease remains endemic in many areas of the world, including Spain, Latin America, the Middle East, parts of Africa, and Asia [2,5].

Similar to the situation in the above-mentioned areas, brucellosis is also a serious reemerging disease in China. Before 1980s, human brucellosis was quite severe. A total of 4.57 million people were examined from 1952 to 1981 with 385,700 sero-positives and positive rate was 8.43% [6]. During 1980s and early 1990s, vaccination on animals and other prevention strategies were well implemented, animal positive rate was reduced to 0.55% and the brucellosis got controlled well [6]. With the development of animal husbandry, there was a significant increase in the number of animals from 1987 to 2007 in China. Thereinto, the number of sheep increased twice accordingly [7]. However, vaccination rate dropped from 99.71% to 50% or less [8], which led to sheep positive rate to be 1.49% in 2009, and the new cases of human brucellosis reached 37,734, which was 18.6 times larger than that of human brucellosis in 2000 [9]. Now animal brucellosis has been reported in 29 of 32 provinces with some endemic areas remaining. Most of the human brucellosis patients were infected by sheep-type brucella, accounting for 84.5% of the total cases [10]. Brucellosis is a natural focal disease in Inner Mongolia Autonomous Region of China, which is a serious endemic area of Class I [11]. Inner Mongolia keeps the largest number of sheep in Mainland China, accounting for about 18.2% of the total sheep population [12]. However, sheep vaccination rate there is only 31.6% [13] and human brucellosis cases have been ever increasing. In 2007, new cases were reported in 85 of 102 banners/counties and city districts in Inner Mongolia, and there were still 47 banners/counties and city districts where the incidence of human brucellosis was over 1/10,000 [14]. From 1996 to 2010, 78,246 human brucellosis cases were
reported and 90.25% or more of the total cases were caused by sheep-type brucella [15,16], among which 90% of new cases occurred in 2005-2010, accounting for 40% of the total cases of China. Especially in 2010, this proportion reached 47.2% [17]. Inner Mongolia ranks first in China with the number of brucellosis cases.

Several mathematical models have been proposed to research the transmission of brucellosis, such as the models by Al-Talafhah et al., Gonzlez-Guzmn and Naulin, Joly et al., Cross et al., Centrell et al., McGiven, Muma et al. [18-24]. However, these studies did not analyze the impact of brucella in the environment on brucellosis transmission. Recently, J.Zinsstag et al [25] studied a dynamic model of animal (sheep and cattle)-to-human brucellosis transmission in terms of the characteristics and the data of Mongolia. B. Aënseba et al [26] proposed an SIC dynamic model for brucellosis transmission in ovine through direct and indirect ways. Taking the brucellosis transmission in Sub-Saharan Africa as an example, S. Roy et al [27] proposed an approach of network control to model and optimally control zoonoses. It is worthwhile to pay close attention to the research of animal brucellosis transmission in the Yellowstone Area of the United States using mathematical models (see [28-31]). However, there is no research by now studying the influence of the effectiveness of the vaccination and disinfection on brucellosis prevention and brucella spread, and no particular dynamical model investigating the prevalence of brucellosis in humans and animals in China. In this paper, taking into account multiple transmission ways and main source of brucellosis transmission in Inner Mongolia Autonomous Region of China, we propose a susceptible-exposed-infectious-vaccinated-brucella(SEIVB) dynamic model for the sheep-to-human transmission of brucellosis. We firstly determine the basic reproduction number $R_0$ and analyze the global stability of system, and then we carry out some sensitivity analysis of the basic reproduction number $R_0$ on the segmental parameters and discuss the control strategies of brucellosis infection in Inner Mongolia.

The article is structured as follows. In section 2, we present the model and determine the basic reproduction number $R_0$. We analyze the global stability of the disease-free equilibrium and the endemic equilibrium in section 3. In section 4, The model is used to simulate the human brucellosis in Inner Mongolia, and then numerical simulations and sensitivity analysis of the basic reproduction number $R_0$ in terms of various model parameters are carried out. Various control measures and a brief discussion are given in section 5.
2. Dynamic model and basic reproduction number $R_0$

Based on the facts of brucellosis infection in Inner Mongolia, we classify the sheep population into four compartments: the susceptible compartment $S(t)$, the exposed compartment $E(t)$, the infectious compartment $I(t)$, and the vaccinated compartment $V(t)$, and classify the human population into three groups: susceptible $S_h(t)$, acute infections $I_{ah}(t)$, and chronic infections $I_{ch}(t)$. Brucellosis is transmitted in animals through the infection of the respiratory tract, oral mucosa, skin and mucous membranes. On the other hand, exposed and infected sheep can shed brucella into the environment due to abortion or sheep 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 depending on the ingested dose, which is different from direct transmission which assumes that brucella is acquired through an infectious contact with an infected individual. Therefore, an infected or exposed sheep generates infection in two ways: the direct and indirect modes of transmission. We define the average number of brucella that is enough for a host to be infected as an infectious unit. Let $B(t)$ denote the number of infectious unit in the environment. The connections between the four sheep compartments and three human groups are given in Fig. 1, including the number of the infectious unit $B(t)$.

The following are some assumptions and interpretations of our model. (I) In Inner Mongolia, young sheep are not vaccinated or only vaccinated after 6 months of birth or later, so we assume that all young sheep are at the risk of brucellosis in the first year of birth. (II) In Inner Mongolia, S2(B.suis strain 2) vaccine are used to vaccinate sheep and its immunization protection rate is 80% to 93% [32], so some of the vaccinated individuals still can be infected. (III) In general, the exposed individuals have no clinical manifestations, so the exposed sheep with brucella can not be eliminated. (IV) We assume that exposed sheep have the same infectivity as infected sheep. (V) There is no data reporting human-to-human transmission of brucellosis, so we assume that the rate of human-to-human transmission is zero. (VI) From 2005 to 2010, the human population growth rate is very low in Inner Mongolia, and we assume that the human’s birth rate is equal to the natural mortality. In other words, the total population remains constant. Therefore, the dynamic model is described as the following ordinary differential equations:
Fig. 1: Flowchart of sheep brucellosis transmission.

\[
\begin{align*}
\frac{dS}{dt} &= A - \beta S(E + I) - \phi SB - (\mu + \nu)S + \delta V, \\
\frac{dV}{dt} &= \nu S - (\mu + \delta)V - \epsilon \beta V(E + I) - \epsilon \phi VB, \\
\frac{dE}{dt} &= \beta(S + \epsilon V)(E + I) + \phi(S + \epsilon V)B - (\sigma + \mu)E, \\
\frac{dI}{dt} &= \sigma E - (\mu + c)I, \\
\frac{dB}{dt} &= k(E + I) - (d + n\tau)B, \\
\frac{dS_h}{dt} &= -\beta_h S_h(E + I) - \phi_h S_h B + \sigma_h(1 - p)I_{ah}, \\
\frac{dI_{ah}}{dt} &= \beta_h S_h(E + I) + \phi_h S_h B - \sigma_h I_{ah}, \\
\frac{dI_{ch}}{dt} &= \sigma_h p I_{ah}.
\end{align*}
\]

The parameters are described in Table 1.

Because the last three equations are independent of the first five equations, we can only consider the following model:

\[
\begin{align*}
\frac{dS}{dt} &= A - \beta S(E + I) - \phi SB - (\mu + \nu)S + \delta V, \\
\frac{dV}{dt} &= \nu S - (\mu + \delta)V - \epsilon \beta V(E + I) - \epsilon \phi VB, \\
\frac{dE}{dt} &= \beta(S + \epsilon V)(E + I) + \phi(S + \epsilon V)B - (\sigma + \mu)E, \\
\frac{dI}{dt} &= \sigma E - (\mu + c)I, \\
\frac{dB}{dt} &= k(E + I) - (d + n\tau)B.
\end{align*}
\]
Table 1. Parameters and their values (Unit: year$^{-1}$).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Interpretation</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>$A$</td>
<td>11629200</td>
<td>The recruitment rate of the sheep population</td>
<td>[A]</td>
</tr>
<tr>
<td>$\mu$</td>
<td>0.22</td>
<td>Sheep natural elimination rate</td>
<td>[A]</td>
</tr>
<tr>
<td>$c$</td>
<td>0.15</td>
<td>Elimination rate caused by brucellosis</td>
<td>fitting</td>
</tr>
<tr>
<td>$\delta$</td>
<td>0.4</td>
<td>Sheep loss of vaccination rate</td>
<td>[B]</td>
</tr>
<tr>
<td>$\nu$</td>
<td>0.316</td>
<td>Sheep vaccination rate</td>
<td>[14]</td>
</tr>
<tr>
<td>$\beta$</td>
<td>$1.48 \times 10^{-8}$</td>
<td>Sheep-to-sheep transmission rate</td>
<td>fitting</td>
</tr>
<tr>
<td>$\epsilon$</td>
<td>0.18</td>
<td>Invalid vaccination rate</td>
<td>[B]</td>
</tr>
<tr>
<td>$\phi$</td>
<td>$1.7 \times 10^{-10}$</td>
<td>Brucella-to-susceptible sheep transmission rate</td>
<td>fitting</td>
</tr>
<tr>
<td>$\sigma$</td>
<td>1</td>
<td>The rate of clinical outcome of exposed sheep</td>
<td>assumption</td>
</tr>
<tr>
<td>$k$</td>
<td>15</td>
<td>Brucella shedding rate by exposed and infected sheep</td>
<td>fitting</td>
</tr>
<tr>
<td>$d$</td>
<td>3.6</td>
<td>The decaying rate of brucella in the environment</td>
<td>[C]</td>
</tr>
<tr>
<td>$n$</td>
<td>0</td>
<td>Disinfection times</td>
<td>[C]</td>
</tr>
<tr>
<td>$\tau$</td>
<td>0</td>
<td>Effective disinfection rate</td>
<td>[C]</td>
</tr>
<tr>
<td>$\beta_h$</td>
<td>$1.82 \times 10^{-10}$</td>
<td>Transmission rate from sheep to humans</td>
<td>fitting</td>
</tr>
<tr>
<td>$\phi_h$</td>
<td>$1 \times 10^{-11}$</td>
<td>Transmission rate from brucella to humans</td>
<td>fitting</td>
</tr>
<tr>
<td>$\sigma_{hp}$</td>
<td>0.6</td>
<td>Transfer rate from acute infections to chronic infections</td>
<td>assumption</td>
</tr>
<tr>
<td>$\sigma_{h}(1-p)$</td>
<td>0.4</td>
<td>Transfer rate from acute infections to susceptible population</td>
<td>assumption</td>
</tr>
</tbody>
</table>

Notes: [A] In Inner Mongolia, sheep life span is about 4-5 years and the number of sheep remains about $5.286 \times 10^7$ from 2005 to 2010, so we estimate that the average elimination rate of sheep $\mu$ is $\frac{1}{4.5} = 0.22$ and the recruitment rate is $5.286 \times 10^7 \times 0.22 = 11629200$.

[B] In Inner Mongolia, vaccine B.suis strain 2 (S2) has been used to control brucellosis. the valid period of S2 is 2-3 years and it can protect 82% of sheep from brucella [32], so we have $\epsilon = 0.18$ and $\delta = 0.4$.

[C] Brucella’s survival time in manure/dung is one month at $25^\circ C$, one year at $8^\circ C$ and two months in the winter [33, 34]. Based on the climatic conditions in Inner Mongolia, we estimate that $d$ is about 3.6. Given that the farmers rarely disinfect the sheep, or even never do it, then $n$ and $n\tau$ is 0.
From the last two equations in (4), we can obtain

\[ \frac{d(S + V + E + I)}{dt} = A - \mu(S + V + E + I) - cI \leq A - \mu(S + V + E + I), \]

and then it follows that

\[ \limsup_{t \to \infty} (S + V + E + I) \leq \frac{A}{\mu}, \quad \limsup_{t \to \infty} B \leq \frac{kA}{\mu(d + n\tau)}. \]

So the set

\[ \Omega = \{(S, V, E, I, B) \in R^5_+ : S, V, E, I, B \geq 0, S + V + E + I \leq \frac{A}{\mu}, B \leq \frac{kA}{\mu(d + n\tau)} \} \]

is the positively invariant set for model (2). It is easy to see that the model (2) always has a disease-free equilibrium \( P_0 = (S_0, V_0, 0, 0, 0) \), where

\[ S_0 = \frac{A(\mu + \delta)}{\mu(\mu + \delta + \nu)}, \quad V_0 = \frac{A\nu}{\mu(\mu + \delta + \nu)}. \]

According to the next generation matrix formulated in Diekmann et al and van den Driessche and Watmough [35,36], we define the basic reproduction number of model (2) as

\[ R_0 = \frac{((d + n\tau)\beta + k\phi(S_0 + cV_0))}{(d + n\tau)(\mu + \sigma)} + \frac{((d + n\tau)\sigma\beta + k\phi)(S_0 + cV_0)}{(d + n\tau)(\mu + c)(\mu + \sigma)} = R_E + R_{EB} + R_I + R_{IB}, \quad (3) \]

where \( R_E = \frac{\beta(S_0 + cV_0)}{\mu + \sigma}, R_{EB} = \frac{k\phi(S_0 + cV_0)}{(d + n\tau)(\mu + \sigma)}, R_I = \frac{\sigma\beta(S_0 + cV_0)}{(\mu + c)(\mu + \sigma)}, R_{IB} = \frac{k\phi(S_0 + cV_0)}{(d + n\tau)(\mu + c)(\mu + \sigma)}, \) \( R_E \) (\( R_I \)) is the average number of infected individuals by a single exposed (infectious) individual in a fully susceptible population. \( R_{EB} \) (\( R_{IB} \)) is the average number of the infected individuals by the brucella which are excreted into the environment by the exposed (infectious) individual. Therefore, \( R_0 \) denotes the total average number of infections.

The endemic equilibrium \( P^*_E(S^*_E, V^*_E, I^*_E, B^*_E) \) of model (2) is determined by equations:

\[
\begin{align*}
A - \beta S(E + I) - \phi SB - (\mu + \nu)S + \delta V &= 0, \\
\nu S - (\mu + \delta)V - \epsilon \beta V(E + I) - \epsilon \phi V B &= 0, \\
\beta(S + \epsilon V)(E + I) + \phi(S + \epsilon V)B - (\sigma + \mu)E &= 0, \\
\sigma E - (\mu + c)I &= 0, \\
k(E + I) - (d + n\tau)B &= 0.
\end{align*}
\]

From the last two equations in (4), we can obtain

\[ E = \frac{(\mu + c)I}{\sigma}, \quad B = \frac{k(E + I)}{d + n\tau} = \frac{k(\mu + c + \sigma)I}{\sigma(d + n\tau)}. \quad (5) \]
Substituting (5) into the third equation in (4) gives
\[
S + \epsilon V = \frac{(d + n\tau)(\mu + \sigma)(\mu + c)}{\beta + k\phi} = \frac{S_0 + \epsilon V_0}{R_0}.  
\]  
(6)

Substituting (5) into the first two equations in (4) gives
\[
S = \frac{M_0 + M_1 I}{M_2 + M_3 I + M_4 I^2}, \quad V = \frac{\sigma(d + n\tau)\nu(M_0 + M_1 I)}{(M_6 + M_5 I)(M_2 + M_3 I + M_4 I^2)},  
\]  
(7)

where
\[
M_0 = A\sigma^2(d + n\tau)^2(\mu + \delta), \quad M_1 = A\sigma(d + n\tau)(\mu + c + \sigma)(\beta(d + n\tau) + k\phi),  
M_2 = \mu\sigma^2(d + n\tau)^2(\mu + \delta + \nu), \quad M_4 = \epsilon(\mu + c + \sigma)^2(\beta(d + n\tau) + k\phi)^2,  
M_3 = \sigma(d + n\tau)(\mu + c + \sigma)(\beta(d + n\tau) + k\phi)(\epsilon(\mu + \nu) + \mu + \delta),  
M_5 = \epsilon(\mu + c + \sigma)(\beta(d + n\tau) + k\phi), \quad M_6 = \sigma(d + n\tau)(\mu + \delta).  
\]

Direct calculation for \( I \geq 0 \) shows
\[
\frac{dS(I)}{dI} = \frac{M_1 M_2 - M_0 M_3 - 2M_0 M_4 I - M_1 M_4 I^2}{(M_2 + M_3 I + M_4 I^2)^2} < 0,  
\]
and then \( S \) and \( V \) is monotonically decreasing for \( I > 0 \). Combining Equations (5) and (6), we can define the equation:
\[
f(I) \triangleq S + \epsilon V - \frac{S_0 + \epsilon V_0}{R_0} = 0.  
\]

From the Equation (7), we can find that the function \( f(I) \) is also monotonically decreasing for \( I > 0 \). As the function \( f(0) = S_0 + \epsilon V_0 - \frac{S_0 + \epsilon V_0}{R_0} > 0 \) and \( f(\frac{A}{\mu}) < 0 \) when \( R_0 > 1 \), the model (2) has a unique endemic equilibrium \( P^*(S^*, V^*, E^*, I^*, B^*) \).

3. The global stability of the disease-free and endemic equilibrium

In this section, we investigate the global stability of disease-free equilibrium and the endemic equilibrium of model (2). It is important for us to understand the extinction and persistence of the disease.

**Theorem 1.** If \( R_0 \leq 1 \), then the disease-free equilibrium \( P_0 \) of system (2) is the global asymptotically stable in \( \Omega \).
Proof: For the disease-free equilibrium \( P_0 \), model (2) can be rewritten as follows:

\[
\begin{align*}
\frac{dS}{dt} &= S(A(\frac{1}{S} - \frac{1}{S_0}) + \delta(S - S_0)(\frac{V}{S} - \frac{V_0}{S_0}) - \beta(E + I) - \phi B), \\
\frac{dV}{dt} &= V(\nu(\frac{S}{V} - \frac{S_0}{V_0}) - \epsilon \beta(E + I) - \epsilon \phi B), \\
\frac{dE}{dt} &= (\beta(E + I) + \phi B)(S_0 + \epsilon V_0 + S + \epsilon V - S_0 - \epsilon V_0) - (\sigma + \mu)E, \\
\frac{dI}{dt} &= \sigma E - (\mu + c)I, \\
\frac{dB}{dt} &= k(E + I) - (d + n\tau)B.
\end{align*}
\]

Since \( R_0 \leq 1 \), so \( \frac{((d + n\tau)\beta + k\phi)(S_0 + \epsilon V_0)}{(d + n\tau)(\mu + c)} < 1 \), we define the Lyapunov function

\[
L(S, V, E, I, B) = S - S_0 - S_0 \ln \frac{S}{S_0} + V - V_0 - V_0 \ln \frac{V}{V_0} + E + \frac{\phi(S_0 + \epsilon V_0)}{d + n\tau} B
\]

\[
+ \frac{(d + n\tau)(\mu + \sigma) - ((d + n\tau)\beta + k\phi)(S_0 + \epsilon V_0)}{(d + n\tau)\sigma} I.
\]

Then the derivative of \( L \) along solutions of model (8) is

\[
\frac{dL}{dt} = A(S - S_0)(\frac{1}{S} - \frac{1}{S_0}) + \delta(S - S_0)(\frac{V}{S} - \frac{V_0}{S_0}) + \nu(V - V_0)(\frac{S}{V} - \frac{S_0}{V_0})
\]

\[
+ \beta(S_0 + \epsilon V_0)(E + I) + \phi(S_0 + \epsilon V_0) B - (\sigma + \mu)E
\]

\[
+ \frac{(d + n\tau)(\mu + \sigma) - ((d + n\tau)\beta + k\phi)(S_0 + \epsilon V_0)}{(d + n\tau)\sigma} I
\]

\[
- \frac{(d + n\tau)(\mu + \sigma) - ((d + n\tau)\beta + k\phi)(S_0 + \epsilon V_0)}{(d + n\tau)\sigma} (\mu + c) I
\]

\[
+ \frac{k\phi(S_0 + \epsilon V_0)}{d + n\tau} (E + I) - \phi(S_0 + \epsilon V_0) B
\]

\[
= \frac{(\mu + c)(\mu + \sigma)}{\sigma}(R_0 - 1)I + 2A + \delta V_0 + \nu S_0 - A \frac{S_0}{S}
\]

\[
- \mu S_0 - \delta V_0 \frac{S_0}{S} - \nu S_0 \frac{V}{V_0} - \mu V_0 \frac{V}{V_0}
\]

\[
= \frac{(\mu + c)(\mu + \sigma)}{\sigma}(R_0 - 1)I + \mu V_0(3 - \frac{V}{V_0} - \frac{S_0}{S} - \frac{V_0 S}{V S_0})
\]

\[
+ \delta V_0(2 - \frac{V S}{V_0 S} - \frac{V_0 S}{V S_0}) + \mu S_0(2 - \frac{S}{S_0} - \frac{S_0}{S})
\]

\[
\leq 0.
\]

Therefore, the equality \( \frac{dL}{dt} = 0 \) holds if and only if \( S = S_0, V = V_0 \) or \( I = 0 \). Since \( P_0 \) is the only invariant set of model (1) in \( \{(S, V, E, I, B) \in \Omega : \frac{dL}{dt} = 0\} \), thus the disease-free equilibrium \( P_0 \) is global asymptotic stability in \( \Omega \) by LaSalle’s Invariance Principle. \( \square \)
In the next subsection, we analyze the global asymptotic stability of the endemic equilibrium.

Let

\[ s = \frac{S}{S^*}, \quad v = \frac{V}{V^*}, \quad e = \frac{E}{E^*}, \quad i = \frac{I}{I^*}, \quad b = \frac{B}{B^*}. \]

The model (2) is transformed into the following form

\[
\begin{aligned}
\frac{ds}{dt} &= s\left(\frac{A}{S^*}\left(\frac{1}{s} - 1\right) + \frac{\delta V^*}{S^*}(\frac{v}{s} - 1) - \beta E^*(e - 1) - \beta I^*(i - 1) - \phi B^*(b - 1)\right), \\
\frac{dv}{dt} &= v\left(\frac{\nu S^*}{V^*}(\frac{s}{v} - 1) - \epsilon \beta E^*(e - 1) - \epsilon \beta I^*(i - 1) - \epsilon \phi B^*(b - 1)\right), \\
\frac{de}{dt} &= \beta s e (s - 1) + \epsilon \beta V^* e (v - 1) + \frac{\beta s_i}{E^*} e (\frac{si}{e} - 1) + \frac{\epsilon \beta V^* I^*}{E^*} e (\frac{vi}{e} - 1) + \phi \frac{s_i}{E^*} e (\frac{vi}{e} - 1), \\
\frac{di}{dt} &= \frac{\sigma E^*}{I^*} i (\frac{\mu}{i} - 1), \\
\frac{db}{dt} &= \frac{k}{B^*} b (E^*(\frac{\epsilon}{b} - 1) + I^*(\frac{i}{b} - 1)).
\end{aligned}
\]

(9)

It is easy to find that model (9) has a unique endemic equilibrium \( P_*(1,1,1,1,1) \), and that the global stability of \( P_* \) is the same as that of \( P^* \), so we will investigate the global stability of \( P_* \) instead of \( P^* \).

Defining the Lyapunov function

\[
L(s, v, e, i, b) = S^*(s - 1 - \ln s) + V^*(v - 1 - \ln v) + E^*(e - 1 - \ln e) + \frac{(S^* + \epsilon V^*) I^* (\beta E^* + \beta I^* + \phi B^*)}{\sigma E^* (E^* + I^*)} (i - 1 - \ln i) + \frac{\phi (S^* + \epsilon V^*) B^*}{k (E^* + I^*)} (b - 1 - \ln b).
\]

For the equilibrium state \( P_* \), we have the following equations:

\[
\begin{aligned}
\frac{dL}{dt} &= (s - 1)\left(\frac{1}{s} - 1\right) + \delta V^* \left(\frac{v}{s} - 1\right) - \beta E^* e (e - 1) - \beta I^* (i - 1) - \phi B^* (b - 1)\right).
\end{aligned}
\]

(10)
\[+(v - 1)(\nu S^* \left(\frac{s}{v} - 1\right) - \epsilon \beta V^* E^*(e - 1) - \epsilon \beta V^* I^*(i - 1) - \epsilon \phi V^* B^*(b - 1))\]
\[+(e - 1)(\beta S^* E^*(s - 1) + \epsilon \beta V^* E^*(v - 1) + \beta S^* I^*(\frac{si}{e} - 1) + \epsilon \beta V^* I^*(\frac{vi}{e} - 1))\]
\[+\phi S^* B^*(\frac{sb}{e} - 1) + \epsilon \phi V^* B^*(\frac{vb}{e} - 1))\]
\[+(S^* + \epsilon V^*)I^*\left(\beta E^* + \beta I^* + \phi B^*\right)\frac{(i - 1)\left(\frac{e}{i} - 1\right)}{E^* + I^*}\]
\[+\frac{\phi(S^* + \epsilon V^*)B^*}{E^* + I^*}(b - 1)(E^*(\frac{e}{b} - 1) + I^*(\frac{i}{b} - 1))\]
\[= 2A + \delta V^* + \nu S^* + M_1 + \phi(S^* + \epsilon V^*)B^* - (A + \delta V^* - \beta S^* I^* - \phi S^* B^* - \nu S^*)s\]
\[\quad - (\nu S^* - \delta V^* - \epsilon \beta V^* I^* - \epsilon \phi V^* B^*)v - \frac{A}{s} - \delta V^* \frac{v}{s} - \nu S^* \frac{s}{v}\]
\[\quad - M_1 \frac{e}{i} - M_2 \frac{e}{b} - M_2 I^* \frac{i}{b} - \beta S^* I^* \frac{si}{e} - \epsilon \beta V^* I^* \frac{vi}{e}\]
\[\quad - \phi S^* B^* \frac{sb}{e} - \epsilon \phi V^* B^* \frac{vb}{e}\]
where \(M_1 = \frac{(S^* + V^*)I^*(\beta E^* + \beta I^* + \phi B^*)}{E^* + I^*}\), \(M_2 = \frac{\phi(S^* + \epsilon V^*)B^*}{E^* + I^*}\).

From the equation (10), we can obtain
\[
\frac{dL}{dt} = 2A + \delta V^* + \nu S^* + M_1 + \phi(S^* + \epsilon V^*)B^* - (\mu S^* + \beta S^* E^*)s - \frac{A}{s}
\quad - (\mu V^* + \epsilon \beta V^* E^*)v - \delta V^* \frac{v}{s} - \nu S^* \frac{s}{v} - M_2 \frac{e}{b} - M_2 I^* \frac{i}{b}
\quad - M_1 \frac{e}{i} - \beta S^* I^* \frac{si}{e} - \epsilon \beta V^* I^* \frac{vi}{e} - \phi S^* B^* \frac{sb}{e} - \epsilon \phi V^* B^* \frac{vb}{e}.
\]

After some algebraic manipulations, we have
\[
\frac{dL}{dt} = (\mu S^* + \beta S^* E^*)(2 - \frac{1}{s} + \frac{v}{s} - \frac{s}{v}) + \beta S^* I^*(3 - \frac{1}{s} - \frac{e}{i} - \frac{si}{e})
\quad + (\mu V^* + \epsilon \beta V^* E^*)(3 - \frac{1}{s} - \frac{v}{s} - \frac{s}{v}) + \frac{\phi S^* B^* E^*}{E^* + I^*}(3 - \frac{1}{s} - \frac{e}{b} - \frac{sb}{e})
\quad + \frac{\phi S^* B^* I^*}{E^* + I^*}(4 - \frac{1}{s} - \frac{e}{i} - \frac{si}{e}) + \epsilon \beta V^* I^*(4 - \frac{1}{s} - \frac{vi}{e} - \frac{e}{i})
\quad + \frac{\epsilon \phi V^* B^* I^*}{E^* + I^*}(5 - \frac{1}{s} - \frac{e}{i} - \frac{si}{e}) + \frac{\epsilon \phi V^* B^* E^*}{E^* + I^*}(4 - \frac{1}{s} - \frac{vi}{e} - \frac{e}{i})
\quad \leq 0.
\]
The equality \( \frac{dL}{dt} = 0 \) holds only for \( s = v = 1, e = i = b \), which corresponds to the set \( \bar{\Omega} = \{(S, V, E, I, B) : S = S^*, V = V^*, \frac{E}{S^*} = \frac{I}{V^*} = \frac{B}{B^*}\} \subset \Omega \). This means that \( P^* \) is the maximum invariant set of model (1) in \( \bar{\Omega} \), and then the endemic equilibrium \( P^* \) is global asymptotic stability in \( \Omega \).

According to the above discussion, we can derive the following theorem:

**Theorem 2.** For system (2), if \( R_0 > 1 \), then the endemic equilibrium \( P^* \) exists and is the global asymptotic stability.

**Remark** Biologically speaking, Theorem 1 shows that elimination of brucellosis is independent of initial sizes of the populations, and the disease will be eliminated only if the epidemiological threshold \( R_0 \leq 1 \). From Theorem 2, we can see that when \( R_0 > 1 \), the disease persists in the sheep population no matter how large the initial population is.

4. The application of the model to the prevention of brucellosis transmission in Inner Mongolia

In this section, based on the reported human brucellosis data in Inner Mongolia, using least square method, we carry out parameter estimation of model (1) and make some sensitivity analysis on some parameters.

From the bulletin of China’s major zoonotic epidemics, we can obtain the data on human brucellosis cases. However, data monitoring can not be easily conducted since there are too many sheep and little monitoring budget. Therefore, we can only rely on the existing facts to make some rational assumptions to fit data. The values of parameters are listed in Table 1. For the initial values needed for fitting data, we can directly obtain \( S_h(0) = 2.384 \times 10^7 \) [37]. In Inner Mongolia, there are 44.5 and 53.18 million sheep exposed to brucellosis in 2004 and 2005 respectively. Before 2011, each adult sheep is only vaccinated once a year, and the vaccination rate is about 31.6%. Hence we estimate that the number of vaccinated sheep is 8.44 million \((44.5 \times 0.316 \times (1 - 0.4))\), that is, \( V(0) = 8.44 \times 10^6 \). Based on actual survey, the true prevalence of sheep is about 2.5% in 2005 (unpublished data), and we estimate \( I(0) = 1.33 \times 10^6, E(0) = 0, S(0) = 4.341 \times 10^7 \). We use the data fitting to obtain \( B(0) = 6 \times 10^6 \).

Using model (1), we evaluate the human brucellosis data in Inner Mongolia from 2005 to 2010 and make a prediction about the trend of human brucellosis infection. Fig.2 shows that the simulation of our model with reasonable parameter values provides a good match.
Fig. 2: Simulation of human brucellosis cases over time in Inner Mongolia of China. The smooth curve represents the solution $I_{ab}$ of model (1) and the stars are the reported data of human cases.

Fig. 3: $R_0$ in terms of $\nu$ and $d$

with the data on infected human brucellosis cases in Inner Mongolia from 2005 to 2010. Moreover, with the current control measures, it can be predicted by our model that the human brucellosis cases will continue increasing in the next few years. With the simulated parameter values, we estimate that $R_0 = 1.8$, which indicates that human brucellosis will persist in Inner Mongolia with the current control and prevention measures.

Fig. 3(a) depicts the influence of $\nu$ (adult sheep vaccination rate) on $R_0$. Though vaccinating susceptible sheep is an effective measure to decrease $R_0$, $R_0$ cannot become less than one even if the vaccination rate $\nu$ is 100%. From Fig. 3(b) and Fig. 4(b), we can see that the effect of decaying rate of brucella $d$ and disinfection rate $n\tau$ is relatively little on $R_0$. Fig. 4(a)
represents the relationship between $R_0$ and the mortality caused by brucellosis, which shows that the influence of parameter $c$ on $R_0$ is greater than parameters $n\tau$ and $\nu$. As Fig.5 shows, the more disinfection and vaccination are given, the less infection will be caused. However, human brucellosis cases cannot ultimately be reduced below the initial cases even though disinfection rate and vaccination rate are 100%. Thus, we can conclude that under current situation, eliminating infected sheep in time can effectively decrease $R_0$ below 1 and is the most effective strategy to eradicate brucellosis in Inner Mongolia. However, giving only one vaccination to adult sheep a year is far from enough to eradicate brucellosis.

5. Discussion

As a zoonotic and chronic disease, brucellosis has become a serious public health problem
which can not be ignored in China. In this paper, based on the characteristics of the brucellosis infection in Inner Mongolia of China, we proposed an SEIVB dynamic model for the sheep-human transmission of brucellosis. By validating our model, we can conclude that human brucellosis cases would gradually increase in the next a couple of years, which
implies that brucellosis cannot be eradicated with the current strategies. By carrying out some sensitivity analyses of the basic reproduction number on various parameters, we find that the vaccination rate of adult sheep and eliminating rate of infected sheep play important roles in the prevention of brucellosis. However, from Fig.5(a), we see that although acute infection cases can be reduced by giving vaccination to adult sheep, brucellosis cannot be eventually eradicated if vaccination to adult sheep is only once a year. Furthermore, from Fig.6(a), we can see that, even if vaccination is given twice a year and the vaccination rate is 100% (which is almost impossible), $R_0$ is relatively close to one ($R_0 = 0.93$), which means that brucellosis will continue persisting a very long time in Inner Mongolia. Therefore, vaccinating adult sheep alone is not adequate to eradicate brucellosis. Eliminating infected sheep can effectively control brucellosis, but this results in a huge financial burden on the herdsman in Inner Mongolia, so the strategy to cull infectious animals is difficult to carry out for Inner Mongolia Autonomous Region government.

While brucella infection causes disease primarily in adults (sexually mature), young animals may be infected but generally show only a weak and transient serological response. Generally speaking, young sheep turn sexually mature within 3-6 months. Therefore, immune young sheep timely in the first year of birth is very necessary. In 2011, the government of Inner Mongolia Autonomous Region began to give vaccination to all sheep twice a year, which implied that part of the recruitment of sheep population would be classified into the vaccinated compartment rather than the susceptible compartment. That is, in the model (1), the number of young sheep to be classified into the vaccinated compartment is $Aν$. Fig.6(b) indicates that $R_0$ will be below 1 if the vaccination rate is more than 86% every year, and if the vaccination rate reaches 1.8 (vaccinating twice a year), $R_0$ will be reduced to 0.64. Fig.7(a) shows that human brucellosis cases will first increase and then reduce even though the vaccination rate is greater than 0.86. Simultaneously, Fig.7(a) reveals that the larger the vaccination rate to all sheep is, the smaller public health hazard will be. Comparing Figs.7(a) and (b), we can find that combining the strategy of disinfection with vaccination is more effective than vaccination alone.

To sum up, only when both animal brucellosis surveillance and prevention are emphasized and strengthened, human brucellosis epidemic in Inner Mongolia of China could be effectively controlled. We also can claim that our model can be applied to study the brucellosis spread in other regions, such as the provinces of Shanxi, Heilongjiang, Jilin, etc. where brucellosis
is also prevalent.

Meanwhile, we cannot deny the limitations of the research, which may influence the generality of the model. Firstly, the influence of season was not taken into account, while brucellosis may have different infection rates and different transmission ways in different seasons. Secondly, regular sheep brucellosis surveillance has not been carried out for some reasons in China, so the data such as the positive rate of sheep was limited. We leave these for further research.

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