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EFFECTS OF QUARANTINE ON TRANSMISSION DYNAMICS OF LASSA FEVER

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ABSTRACT
In this paper, a mathematical model of Lassa fever is formulated. The model includes quarantine as a control strategy and allows re-infection. The model is shown to be well-posed. The disease free equilibrium is shown to be locally asymptotically stable whenever the basic reproduction number is less than unity and unstable otherwise. Numerical simulations have been used to show the impact of the control measure.
Keywords: Quarantine, re-infection, immunity, reproduction number, stability.

INTRODUCTION

Lassa fever, a viral hemorrhagic fever transmitted by rats, is endemic in West Africa (Carey et al., 1972; Frase, 1974; Monath et al., 1973; Monath et al., 1974). After an incubation period of 6 to 21 days, an acute illness with multi-organ involvement develops. Nonspecific symptoms include fever, facial swelling, and muscle fatigue, as well as conjunctivitis and mucosal bleeding. Its symptoms include muscle pain, ulcers of the mucous membranes, headache, internal bleeding and inflammation of the throat. It also causes the destruction of internal tissues; lungs, heart and kidney failure (WHO, 2016). Furthermore, it is an infectious, often fatal, viral disease marked by high fever, which accounts for up to one-third of deaths in hospitals within the affected regions and 10% to 16% of total cases (CDC, 2014; CDC, 2015). It kills approximately 5,000 people per year (Richmond and Baglole, 2003).

The recognized human arenavirus infection history in Africa began in 1969 with the death of two medical missionaries mysteriously and the near-fatal illness of a third (Buckley et al., 1970; Frame et al., 1970; Frame, 1975). An arenavirus which was isolated from two of these patients is given the name of Lassa virus after the town of Lassa, Nigeria, where the disease, known as Lassa fever occurred.

Lassa virus is transmitted from animals; specifically it spreads to humans from a rodent known as natal multimammate mouse (Mastomys natalensis) or African rat. This is probably the most common mouse in equatorial Africa, ubiquitous in human households and eaten as a delicacy in some areas (Richmond and Baglole, 2003). Infection in the rodent population is in a persistent asymptomatic state. The virus is probably transmitted by contact with the feces or urine of animals accessing grain stores in residences (Richmond and Baglole, 2003).

The possibility that Lassa virus could be used as a biological weapon has raised the profile of the need for greater understanding of Lassa fever and for more effective control and treatment programmes (Richmond and Baglole, 2003). Because of its high case fatality rate, ability to spread easily by human-to-human contact, and potential for aerosol release, Lassa virus is classified as a Bio-safety Level 4 (BSL4) and NIAID Bio-defense category A agent. The potential use of Lassa virus as a biological weapon directed against civilian or military targets necessitates the development of counter-threat measures, such as diagnostic assays, vaccines and therapeutics. Moreover, the impact of the disease in endemic regions of West Africa is immense, and therefore means to diagnose, treat and prevent this viral hemorrhagic fever will provide a significant public health benefit (CDC, 2015; WHO 2016). Re-infection occurs in Lassa fever as strengthened by (Richmond and Baglole, 2003).

Many mathematical models have been designed and used to assess the effect of preventive measures on the spread of Lassa virus in a given community. This study extends the works of (James et al., 2015a; James et al., 2015b; Lo lacono et al., 2015) by *inter alia*,

[i.] Incorporating environmental contribution to the transmission which is not considered in (James et al., 2015a; Lo lacono et al., 2015);
[ii.] The environment is considered to be saturated;
[iii.] Incorporating quarantine as control measure (James et al., 2015b);

[iv.] Recovered individuals have temporary immunity (Richmond and Baglole, 2003);
[v.] Latency period is incorporated while it was neglected in (James et al., 2015a, James et al., 2015b);
[vi.] Using incidence rate for both human (constant rate was used in (James et al., 2015a) and rodents population (constant rate was used in (James et al., 2015b)).
The paper is organized as follows. The model with quarantine is formulated in Section 2, analyzed in Section 3 and numerical simulation is presented in Section 4.

Model Formulation

The total human population, $N_H(t)$, is divided into susceptible individuals $S_H(t)$, asymptomatic individuals $E_H(t)$, symptomatic individuals $I_H(t)$ and individuals in quarantine receiving treatment $Q(t)$, so that:
$N_H(t) = S_H(t) + E_H(t) + I_H(t) + Q(t)$.
Whereas, the total population of rodents, at time t denoted by $N_R(t)$, is divided into two compartments for susceptible rodents and infected rodents, such that:
$N_R(t) = S_R(t) + I_R(t)$.
The susceptible population with risk of Lassa virus infection $S_H(t)$ is generated by recruitment of humans at a constant rate Π (all humans recruited into the population are assumed to be at risk of Lassa-infection), infected individuals recover at a rate τ_1 and quarantine individuals recover at a rate τ_2. The population is decreased by infection at a rate λ_H, moving from the susceptible class to exposed class at a rate λ_H and natural death at a rate μ_H. Thus,
$\frac{dS_H}{dt} = \Pi + \tau_1 I_H + \tau_2 Q - \lambda_H S_H - \mu_H S_H$.
The population of asymptomatic humans E_H is generated by Lassa infection at the rate λ_H. It is reduced by the development of clinical symptoms of Lassa at a rate γ_1 and natural death at the rate μ_H.
$\frac{dE_H}{dt} = \lambda_H S_H - (\gamma_1 + \mu_H) E_H$.
The population of symptomatic individuals is increased at the rate γ_1 and diminished by recovery at the rate τ_1, quarantine at the rate γ_2, natural death at the rate μ_H and death induced by the disease at a rate δ. Thus,
$\frac{dI_H}{dt} = \gamma_1 E_H - (\tau_1 + \gamma_2 + \delta + \mu_H) I_H$.
The population of quarantine individuals is generated as a result of quarantining the symptomatic individuals at the rate γ_2 and diminished by recovery of individuals in the quarantine at the rate τ_2, death induced by the disease δ and natural death μ_H. Thus,
$\frac{dQ}{dt} = \gamma_2 I_H - (\tau_2 + \delta + \mu_H) Q$.
The population of pathogens P in the environment is generated as a result of shedding from the infected rodents at a rate α. It is diminished by natural death of the pathogens, so that
$$\frac{dP}{dt} = \alpha I_R - \mu_P P$$
The population of susceptible rodents S_R is assumed to follow a logistic growth rate $b_L(1 - \frac{N_R}{K})$, where b_L is the maximum rate of growth of rodents and $K > N_R$ is the carrying capacity (which is related to availability of food and space). This shows that the growth of rodents is density dependent. The rodents population $S_R$decreased by Lassa fever infection and natural death at the rates λ_R and μ_R, respectively. Therefore,
$\frac{dS_R}{dt} = b_L(1 - \frac{N_R}{K}) - \lambda_R S_R - \mu_R S_R$.
The population of infected rodents I_R is generated following the infection of susceptible rodents at the rate λ_R and decreased only because of natural death. Hence,
$\frac{dI_R}{dt} = \lambda_R S_R - \mu_R I_R$.
The model for the Lassa fever is described by the following system of differential equations while the flow diagram of the model is shown in Figure 1. The parameters and associated variables are presented in tables 1 and 2.

$$\frac{dS_H}{dt} = \Pi + \tau_1 I_H + \tau_2 Q - \lambda_H S_H - \mu_H S_H.$$
$$\frac{dE_H}{dt} = \lambda_H S_H - (\gamma_1 + \mu_H) E_H.$$
$$\frac{dI_H}{dt} = \gamma_1 E_H - (\tau_1 + \gamma_2 + \delta + \mu_H) I_H.$$
$$\frac{dQ}{dt} = \gamma_2 I_H - (\tau_2 + \delta + \mu_H) Q.$$
$$\frac{dP}{dt} = \alpha I_R - \mu_P P$$
$$\frac{dS_R}{dt} = b_L(1 - \frac{N_R}{K}) - \lambda_R S_R - \mu_R S_R.$$
$$\frac{dI_R}{dt} = \lambda_R S_R - \mu_R I_R.$$

where, $\lambda_H = \beta_H I_H + \beta_{EH} \frac{P}{\kappa_c + P} + \beta_{RH} I_R$ and $\lambda_R = \beta_R I_R + \beta_{HR} I_H$.

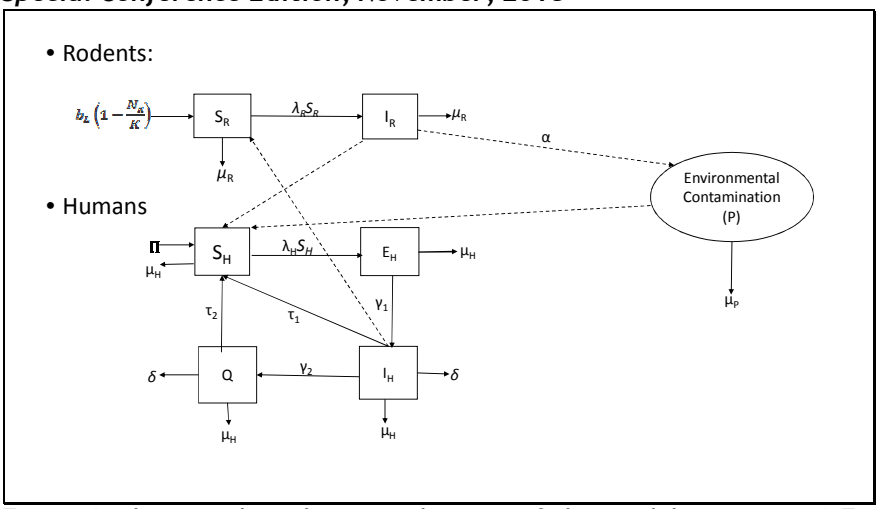

Figure 1: showing the schematic diagram of the model equations 1-7 where solid arrows indicate transitions and dashed arrow indicates interaction. Expressions next to arrows show the *per capita* flow rate between compartments.

Table 1: Description of the state variables of the model

Variable	Interpretation
N_H	Total population of humans
S_H	Population of susceptible humans with risk of Lassa virus infection
E_H	Population of humans exposed to Lassa virus
I_H	Population of Lassa-infected humans with symptoms of Lassa fever
Q	Population of individuals in quarantine
N_R	Total population of rodents
S_R	Population of susceptible rodents
I_R	P population of pathogens in the contaminated environment and air

Table 2: Description of parameters of the model.

Parameter	Interpretation
Π	Recruitment rate for humans.
λ_H	Rates of Lassa force of infection in humans.
λ_R	Rates of Lassa force of infection in rodents.
μ_H, μ_R, μ_P	Natural death rates of humans, rodents and pathogens, respectively.
$\beta_R, \beta_{RH}, \beta_{EH}, \beta_H, \beta_{HR},$	Transmission rates from infected rodents to susceptible rodents, rodents to susceptible humans, contaminated environment and air to susceptible humans, infected humans to susceptible humans and from humans to susceptible rodents, respectively.
α	Rates of shedding from rodent to environment.
τ_1	Recovery rate of infected individuals
τ_2	Recovery rate of individuals in quarantine
γ_1	Progression rate of expose humans to infected class
γ_2	Progression rate of infected humans to quarantine class
K	Carrying capacity for rodents
δ	Disease-induced death rate for humans
b_L	Maximum rate of growth of rodents

Some of the main assumptions made in the formulation of the model are as follows;
[i.] Homogeneous mixing of the human and rodents populations such that there are equal chances of transmitting the virus. Transmission patterns which are possible includes: rodent-to-rodent, rodent-to-human, human-to-human, human-to-rodent, environment-to-human and rodent contaminate the environment (Lo lacono et al., 2015);
[ii.] Successful treatment against Lassa fever does not guarantee permanent immunity against Lassa re-infection (Richmond and Baglole, 2003);
[iii.] Natural recovery is possible (Ajayi, 2014);
[iv.] Infected humans can transmit the disease via human-rodent infection (Lo lacono et al., 2015);

[v.] The virus does not kill the vector (i.e. they die naturally (James et al., 2015a);

The model (1) extends the works in (James et al., 2015a; James et al., 2015b; Lo lacono et al., 2015) by *inter alia*,

[i.] Incorporating environmental contribution to the transmission;

[ii.] The environment is considered to be saturated;

[iii.] Incorporating quarantine as control measure (James et al., 2015b);

[iv.] The contribution of individuals is considered negligible;

[v.] The population of the reservoir (rodents) is divided into susceptible and infected classes;

[vi.] Recovered individuals have temporary immunity (Richmond and Baglole, 2003);

[viii.] Latency period is incorporated while it was neglected in (James et al., 2015a, James et al., 2015b);

[viii.] Using a logistic rate for susceptible rodents (constant rate was used in (James et al., 2015a, James et al., 2015b));

[ix.] Using incidence rate for both human (constant rate was used in (James et al., 2015a) and rodents population (constant rate was used in (James et al., 2015a, James et al., 2015b));

2.1 Basic properties of the model.

Here, we first prove that a solution to the initial-value problem of system (1) exists and in fact, the solution is unique.

Theorem 2.1

Let$(S_{H0}, E_{H0}, I_{H0}, Q_0, P_0, S_{R0}, I_{R0}) \in \mathbb{R}$ be given.

There exist,t_0 and continuously differentiable functions $(S_H(\mathrm{t}),\ E_H(\mathrm{t}),\ I_H(\mathrm{t}),Q(t),\ P(t),S_R(\mathrm{t}),I_R(\mathrm{t}): [0, t_0) \to \mathbb{R})$ such that the ordered heptads $(S_H(\mathrm{t}),\ E_H(\mathrm{t}),\ I_H(\mathrm{t}),Q(t),\ P(t),S_R(\mathrm{t}),I_R(\mathrm{t}))$ satisfies model (1) and$(S_H(\mathrm{t}),\ E_H(\mathrm{t}),\ I_H(\mathrm{t}),Q(t),\ P(t),S_R(\mathrm{t}),I_R(\mathrm{t}))(0) = (S_{H0}, E_{H0}, I_{H0}, Q_0, P_0, S_{R0}, I_{R0})$.

Proof

The Classical Picard-Lindelof theorem will be utilized to prove the result. Since the system of ordinary differential equations is autonomous, it is enough to show that the function $f: \mathbb{R}^7 \to \mathbb{R}^7$ is defined by

$$f(y) = \begin{bmatrix} \Pi + \tau_1 y_3 + \tau_2 y_4 - \lambda_H y_1 - \mu_H y_1 \\ \lambda_H y_1 - (\gamma_1 + \mu_H) y_2 \\ \gamma_1 y_2 - (\tau_1 + \gamma_2 + \delta + \mu_H) y_3 \\ \gamma_2 y_3 - (\tau_2 + \delta + \mu_H) y_4 \\ \alpha y_7 - \mu y_5 \\ b_L \left(1 - \frac{N_R}{K}\right) - \lambda_R y_6 - \mu_R y_6 \\ \lambda_R y_6 - \mu_R y_7 \end{bmatrix}$$

where, $\lambda_H = \beta_H y_3 + \beta_{EH} \frac{y_5}{\kappa_C + y_5} + \beta_{RH} y_7$ and $\lambda_R = \beta_R y_7 + \beta_{HR} y_3$ is locally Lipchitz in its y argument. In fact, it is enough to show that the Jacobian matrix

$$\nabla f(y) = \begin{bmatrix} A & B \\ C & D \end{bmatrix}$$

where,

$$A = \begin{bmatrix} -(\lambda_{\mathrm{H}} + \mu_{\mathrm{H}}) & 0 & \tau_1 - \beta_{\mathrm{H}} y_1 \\ \lambda_{\mathrm{H}} & -(\gamma_1 + \mu_{\mathrm{H}}) & \beta_{\mathrm{H}} y_1 \\ 0 & \gamma_1 & -(\tau_1 + \gamma_2 + \delta + \mu_{\mathrm{H}}) \end{bmatrix}, B = \begin{bmatrix} \tau_2 & -\frac{\beta_{EH} \kappa_C y_1}{(\kappa_C + y_5)^2} 0 & \beta_{\mathrm{RH}} y_1 \\ 0 & \frac{\beta_{EH} \kappa_C y_1}{(\kappa_C + y_5)^2} & 0 & \beta_{\mathrm{RH}} y_1 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

$$C = \begin{bmatrix} 0 & 0 & \gamma_2 \\ 0 & 0 & \alpha \\ 0 & 0 & 0 \\ 0 & 0 & \beta_{\mathrm{HR}} y_6 \end{bmatrix}, D = \begin{bmatrix} -(\tau_1 + \delta + \mu_{\mathrm{H}}) & 0 & 0 & 0 \\ 0 & -\mu_{\mathrm{P}} & 0 & 0 \\ 0 & 0 & -(\frac{b_L}{K} + \lambda_R + \mu_{\mathrm{R}}) & -\frac{b_L}{K} + \beta_{\mathrm{R}} y_6 \\ 0 & 0 & \lambda_R & -\mu_{\mathrm{R}} + \beta_{\mathrm{HR}} y_6 \end{bmatrix}$$

is linear in y and therefore locally bounded for every y$\in \mathbb{R}^7$ and so $f$is locally Lipschitz in y. By the Picard-Lindelop Theorem, there exists a unique solution, $y(\mathrm{t})$, to the ordinary differential equation $y'(t) = f(y(t))$ with initial value $y(0) = y_0$ on $[0, t_0]$ for some time $t_0 > 0$. Moreover, for positive initial data it can be shown that solutions remain positive as long as they exist. A lucky by product of the result above is that the obtained solutions are also bounded.

Theorem 2.2 (Boundedness and Positivity).

Suppose the initial conditions of the model (1) satisfy $(S_{H0} > 0, E_{H0} > 0, I_{H0} > 0, Q_0 > 0, P_0 > 0, S_{R0} > 0, I_{R0} > 0)$. If the unique solution obtained by Theorem 2.1 on the interval $[0, t_0]$ exist for some $t_0 > 0$, then the functions $S_H(\mathrm{t})$, $E_H(\mathrm{t})$, $I_H(\mathrm{t}),Q(t)$, $P(t)$, $S_R(\mathrm{t})$, $I_R(\mathrm{t})$ will be bounded and remain positive for all $t \in [0, t_0]$.

Proof

Let $S_H(\mathrm{t})$, $E_H(\mathrm{t})$, $I_H(\mathrm{t})$, $Q(t)$, $P(t)$, $S_R(\mathrm{t})$,$I_R(\mathrm{t})$ initially have positive values. From Theorem 2.1 there exists at t^* such that the solution exists on $[0, t^*]$.

Assuming $T^*$is denoted as the largest time, for which all populations remain positive, that is,

$T^* = \sup\{t \in [0, t^*] : S_H(\mathrm{s}), E_H(\mathrm{s}), I_H(\mathrm{s}), Q(s), P(s), S_R(\mathrm{s}), I_R(\mathrm{s}) > 0, \forall s \in [0, t_0]\}$

Now on the interval $[0, T^*]$ we can estimate the population values knowing that all constants in the system are positive. Using this and the positivity of solutions on $[0, T^*]$, we can place lower bounds on $\frac{dE_H}{dt}, \frac{dI_H}{dt}, \frac{dQ}{dt}. \frac{dP}{dt}, \frac{dI_R}{dt}$ since

$\frac{dE_H}{dt} = \lambda_{\mathrm{H}} S_{\mathrm{H}} - (\gamma_1 + \mu_{\mathrm{H}}) E_{\mathrm{H}} \geq -(\gamma_1 + \mu_{\mathrm{H}}) E_{\mathrm{H}}$

$\frac{dI_H}{dt} = \gamma_1 E_{\mathrm{H}} - (\tau_1 + \gamma_2 + \delta + \mu_H) I_H \geq -(\tau_1 + \gamma_2 + \delta + \mu_H) I_H$

$\frac{dQ}{dt} = \gamma_2 I_H - (\tau_2 + \delta + \mu_H) Q \geq -(\tau_2 + \delta + \mu_H) Q$

$\frac{dP}{dt} = \alpha I_R - \mu_P P \geq -\mu_P \mathrm{P}$

$\frac{dI_R}{dt} = \lambda_R S_R - \mu_R I_R \geq -\mu_R I_R$

Using separation of variables the populations above at $t \in [0, T^*]$ have their solutions obtained respectively as

$E_H(t) \geq E_H(0) e^{-(\gamma 1 + \mu_H) t}$,

$I_H(t) \geq I_H(0) e^{-(\tau_1 + \gamma_2 + \delta + \mu_H) t}$,

$Q(t) \geq Q(0) e^{-(\tau_2 + \delta + \mu_H) t}$,

$P(t) \geq P(0) e^{-\mu_p t}$

$I_R(t) \geq I_R(0) e^{-\mu_R t}$

Similarly, we can place upper bound on $\frac{dS_H}{dt}$ and $\frac{dS_R}{dt}$ so that

$\frac{dS_H}{dt} = \Pi + \tau_1 I_{\mathrm{H}} + \tau_2 Q - \lambda_{\mathrm{H}} S_{\mathrm{H}} - \mu_{\mathrm{H}} S_{\mathrm{H}} \leq \Pi + \tau_1 I_{\mathrm{H}} + \tau_2 Q$

$S_H(\mathrm{t}) \leq c_1(1 + \mathrm{t})$, where the constant c_1 satisfies $c_1 \geq \max[\Pi, K_1]$, $K_1 = S_H(0) + \frac{\tau_1 I_H(0)}{(\tau_1 + \gamma_2 + \delta + \mu_H)} + \frac{\tau_2 Q(0)}{(\tau_2 + \delta + \mu_H)}$.

$\frac{dS_R}{dt} = b_L(1 - \frac{N_R}{K}) - \lambda_R S_R - \mu_R S_R \leq b_L(1 - \frac{N_R}{K}) \leq b_L$

$S_R(\mathrm{t}) \leq S_R(0) + b_L t$,

$S_R(\mathrm{t}) \leq C_2(1 + \mathrm{t})$, where the constant C_2 satisfies $C_2 \geq \max[b_L, S_R(0)]$

Now, summing some of the equations $\frac{dE_H}{dt}, \frac{dI_H}{dt}, \frac{dP}{dt}, \frac{dI_R}{dt}$ and place bounds on this sum, we have

$$\frac{d(E_H + I_H + P + I_R)}{dt} \leq \lambda_H S_H + \gamma_1 E_H + \alpha I_R + \lambda_R S_R$$

There is a bound on S_H and S_R, simplifying after substituting λ_H and λ_R we have,

$\frac{d(E_H + I_H + P + I_R)}{dt} \leq C_3(1 + t) I_H + (C_4(1 + t) + \alpha) I_R + \gamma_1 E_H + \beta_{EH} P$,

where the constants C_3 and C_4 are, respectively, $(C_1\beta_H + C_2\beta_{HR})$ and $(C_1\beta_{RH} + C_2\beta_R)$ also $(\kappa_c + P > P)$, C_5 satisfies $C_5 \geq \max[C_4, \alpha]$ and C_6 satisfies $C_6 \geq \max[C_3, C_5, \gamma_1, \beta_{EH}]$. Consequently, the inequality becomes

$\frac{d(E_H + I_H + P + I_R)}{dt} \leq C_6(1 + t)(E_H + I_H + P + I_R)$

$(E_H + I_H + P + I_R)(t) \leq C_7 e^{t^2}$

for $t \in [0, T^*]$ where $C_7 > 0$ depends on $C_6 > 0$, $E_{H0}, I_{H0}, P_0, S_{R0}$ and I_{R0} only. Since $E_H(t)$ is positive, we can place an upper bound on $I_H(t)$, $P(t)$, $I_R(t)$

$C_7 e^{t^2} \geq (E_H + I_H + P + I_R) \geq I_H(t)$

$C_7 e^{t^2} \geq (E_H + I_H + P + I_R) \geq P(t)$

$C_7 e^{t^2} \geq (E_H + I_H + P + I_R) \geq I_R(t)$

Moreover, since $I_H(t)$, $P(t)$ and $I_R(t)$ are positive it follows that $E_H(t)$ is as well, hence

$C_7 e^{t^2} \geq (E_H + I_H + P + I_R) \geq E_H(t)$

Furthermore, adding the first four equations gives:

$\frac{dN_H}{dt} = \Pi - \mu_H N_H - \delta(I_H + Q)$

Then, $\Pi - \mu_H N_H - \delta(I_H + Q) \leq \frac{dN_H}{dt} \leq \Pi - \mu_H N_H$

so that

$$\frac{\Pi}{\mu_H+\delta} \le \lim_{t\to\infty}\inf N_H(t) \le \lim_{t\to\infty}\sup N_H(t) \le \frac{\Pi}{\mu_H}$$

This implies that, $N_H(t)$ is bounded which shows the individual classes including $Q(t)$ is bounded. Hence, $S_H(t)$ and $S_R(t)$ can be examined and bound each from below, using

$\frac{dS_H}{dt} = \Pi + \tau_1 I_H + \tau_2 Q - \lambda_H S_H - \mu_H S_H \geq -\lambda_H S_H - \mu_H S_H$.

Substituting λ_H and the bound on $I_H(t),\ P(t),\ I_R(t)$ that is, e^{t^2}, it becomes

$$\frac{dS_H}{dt} \geq -C_9(1+e^{t^2})S_H$$

for $t \in [0, T^*]$ where C_9 satisfies $C_9 \geq \max[\mu_H, C_8]$ and $C_8 \geq \max[\beta_H, \beta_{EH}, \beta_R]$, so

$\frac{dS_H}{dt} + C_9(1+e^{t^2})S_H \geq 0$. It is known that $\frac{d}{dt}(S_H(t) + e^{C_9\int_0^t(1+e^{\tau^2})d\tau}) \geq 0$

hence for $t \in [0, T^*]$, $S_H(t) > S_H(0)e^{-C_9\int_0^t(1+e^{\tau^2})d\tau}$

Now for $S_R(t)$

$$\frac{dS_R}{dt} = b_L\left(1-\frac{N_R}{K}\right) - \lambda_R S_R - \mu_R S_R \geq -b_L\left(\frac{S_R+I_R}{K}\right) - \lambda_R S_R - \mu_R S_R$$

$$\geq -b_L\left(\frac{S_R}{K}\right) - b_L\left(\frac{I_R}{K}\right) - \lambda_R S_R - \mu_R S_R$$

Substituting λ_R with the bounds established earlier on I_H and I_R, gives

$\frac{dS_R}{dt} \geq -C_{12}(1+e^{t^2})S_R$, for $t \in [0, T^*]$

where C_{12} satisfies $C_{12} \geq \max[C_{10}, C_{11}]$, and $C_{10} = \left(\frac{b_L}{K} + \mu_R\right)$, $C_{11} = C_7\beta_R + C_8\beta_{HR}$

hence, $\frac{dS_R}{dt} + C_{12}(1+e^{t^2})S_R \geq 0$ and it follows that

$\frac{d}{dt}\left(S_R(t) + e^{C_{12}\int_0^t(1+e^{\tau^2})d\tau}\right) \geq 0$ hence for $t \in [0, T^*]$,

$S_R(t) > S_R(0)e^{-C_{12}\int_0^t(1+e^{\tau^2})d\tau}$

Thus the values of S_H, E_H, I_H, Q, P, S_R and I_R remain strictly positive for all $[0, T^*]$, including at time T^*. By continuity, there must exist a $t > T^*$ such that S_H, E_H, I_H, Q, P, S_R and I_R are still positive. This contradicts the definition of T^* ($T^* = \sup\{t\ [0, t^*] : S_H(s), E_H(s), I_H(s), Q(s), P(s), S_R(s), I_R(s) > 0, \forall s \in [0, t_0]\}$)

and shows that the model (1) are strictly positive on the entire interval $[0, t^*]$. Furthermore, on the same interval, all of the functions remain bounded, so the interval of existence can be extended further. In fact, the bounds on S_H, E_H, I_H, Q, P, S_R and I_R derived above hold on a compact time interval. Thus, the time interval may be extended on which the solution exists to $[0, t_0]$ for any $t_0 > 0$ and from the above argument, the solutions remain bounded and positive on $[0, t_0]$.

With this, a general idea that the model is sound was obtained and can stay with certainty that it remains biologically valid as long as it begins with biologically-reasonable (i.e, positive) initial data. Following (Hethcote, 2000), the model is mathematically well-posed and epidemiologically realistic, since all the variables remain nonnegative for all $t > 0$. Hence, it is sufficient to consider the dynamics of the model (1) in *D*.

Lemma 2.3.

The following biologically feasible region of the model equation (1)

$D = (S_H, E_H, I_H, Q, P, S_R, I_R \in \mathbb{R}^{+7} : S_H + E_H + I_H + Q \leq \frac{\Pi}{\mu_H} : S_R + I_R \leq \frac{b_L}{\mu_R})$

is positively invariant and attracting.

Proof. It follows from the fact that

$\frac{dN_H(t)}{dt} = \Pi - \mu_H N_H(t)$ and $\frac{dN_R(t)}{dt} = b_L - \left(\frac{b_L}{K} + \mu_R\right)N_R(t) \geq b_L - \mu_R N_R(t)$

so, that $\frac{dN_H(t)}{dt} < 0$, and $\frac{dN_R(t)}{dt} < 0$ if $N_H(t) > \frac{\Pi}{\mu_H}$ and $N_R(t) > \frac{b_L}{\mu_R}$

Thus, a standard comparison theorem as in (Lakshmikantham et al., 2015) can be used to show that

$N_H(t) \leq N_H(0)e^{-\mu_H(t)} + \frac{\Pi}{\mu_H}(1 - e^{-\mu_H(t)})$ and

$N_R(t) \leq N_R(0)e^{-\mu_R(t)} + \frac{b_L}{\mu_R}(1 - e^{-\mu_R(t)})$.

In particular, $N_H(t) \leq \frac{\Pi}{\mu_H}$ and $N_R(t) \leq \frac{b_L}{\mu_R}$ if $N_H(0) \leq \frac{\Pi}{\mu_H}$ and $N_R(0) \leq \frac{b_L}{\mu_R}$ respectively. Thus, D is positively-invariant.

Furthermore, if $N_H(t) > \frac{\Pi}{\mu_H}$ and $N_R(t) > \frac{b_L}{\mu_R}$ then either the solution enters D infinite time, or $N_H(t)$ approaches $\frac{\Pi}{\mu_H}$ and $N_R(t)$ approaches $\frac{b_L}{\mu_R}$ and the infected variables approaches zero. Here D is attracting (i.e. all solutions in $\mathbb{R}^{+7}$ eventually approach, enter or stay in D). Hence the model (1) is epidemiologically well-posed in D as in (Hethcote, 2000).

Analysis of the model

It is instructive, however, to analyze system (1) first of all. This is done below.

Local asymptotic stability of disease-free equilibrium (DFE)

The human-rodent model (1) has a DFE, obtained by setting the right-hand sides of the equations in the model to zero, given by

$\varepsilon_{0L} = (S_H{}^*, E_H{}^*, I_H{}^*, Q^*, P^*, S_R{}^*, I_R{}^*) =$
$(\frac{\Pi}{\mu_H}, 0,0,0,0, \frac{b_L K}{b_L + K\mu_R}, 0)$.

The linear stability of ε_{0L} will be investigated using the next generation operator method on the system (1). The matrices F (for the new infection terms) and V (for the remaining transition terms) associated with the model are given, respectively, by (noting that $S_H{}^* = \frac{\Pi}{\mu_H}$ and $S_R{}^* = \frac{b_L K}{b_L + K\mu_R}$

The F and V matrix were obtained using the notation of (vanden and Watmough, 2002) for the new infection terms and the remaining transfer terms respectively, and used to compute the spectral radius $\mathcal{R}_0$ as

$$F = \begin{pmatrix} 0 & \beta_H S_H{}^* & 0 & \frac{\beta_{EH}}{\kappa_c} S_H{}^* & \beta_{RH} S_H{}^* \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \beta_{HR} S_R{}^* & 0 & 0 & \beta_R S_R{}^* \end{pmatrix}, \quad V = \begin{pmatrix} k_1 & 0 & 0 & 0 & 0 \\ -\gamma_1 & k_2 & 0 & 0 & 0 \\ 0 & -\gamma_2 & k_3 & 0 & 0 \\ 0 & 0 & 0 & \mu_P & -\alpha \\ 0 & 0 & 0 & 0 & \mu_R \end{pmatrix}$$

$$\mathcal{R}_0 = \frac{X + \sqrt{Y^2 + Z}}{2}$$

Where

$X = \left(\frac{\beta_H \gamma_1}{k_1 k_2} \frac{\Pi}{\mu_H} + \frac{\beta_R}{\mu_R} \frac{b_L K}{b_L + K\mu_R}\right)$, $Y = \left(\frac{\beta_H \gamma_1}{k_1 k_2} \frac{\Pi}{\mu_H} - \frac{\beta_R}{\mu_R} \frac{b_L K}{b_L + K\mu_R}\right)$, $Z = \left(\frac{\beta_{HR} \gamma_1}{k_1 k_2} \frac{b_L K}{b_L + K\mu_R}\right)\left(\frac{\beta_{RH}}{\mu_R} \frac{\Pi}{\mu_H} + \frac{\beta_{EH} \alpha}{\kappa_c \mu_P \mu_R} \frac{\Pi}{\mu_H}\right)$

$k_1 = (\gamma_1 + \mu_H)$, $k_2 = (\tau_1 + \gamma_2 + \delta + \mu_H)$, $k_3 = (\tau_2 + \delta + \mu_H)$

The threshold quantity $\mathcal{R}_0$ is the basic reproduction number for Lassa fever (Anderson and May, 1982; Anderson and May 1991; Hethcote, 2000). It represents the average number of secondary cases that one infectious human (or rodent) would generate over the duration of the infectious period if introduced into a completely susceptible human (rodent) population.

Lemma 3.1

The DFE ε_{0L}, of system (1) is locally asymptotically stable (LAS) if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.

Simulations

The numerical simulation was conducted using $ODE15s$ in-built in $MATLAB$ where averted cases were computed for $\mathcal{R}_0 < 1$ and $\mathcal{R}_0 > 1$, also four graphs were obtained; graph of infected humans with and without quarantine when $\mathcal{R}_0 = 0.8764$ as depicted in Figure 2; graph of averted cases when $\mathcal{R}_0 < 1$ and AVERTION=4.7128×10^9 labeled Figure 3. Moreover, graph of infected humans with and without quarantine when $\mathcal{R}_0 = 3.1481$ labelled Figure 4 and graph of averted cases, AVERTION=4.7128×10^9 label Figure 5. The parameter values in table 4were used to get the figures below.

Table 4: Description of parameters of the model

Parameter	Interpretation	Range/Baseline value	Reference
Π	Recruitment rate for humans	$64{,}787{,}478$	(Richmond and Baglole, 2003)
μ_H, μ_R, μ_P	Natural death rates of humans, rodents and pathogens respectively	$0.018182, 0.1858,$ 16248.088819	(CIA, 2008; Oliff, 2003; Stephenson, 1984)
β_R, β_{RH}, β_{EH}, β_H and β_{HR}.	Transmission rates from infected rodents to susceptible rodents, rodents to susceptible humans, ingesting pathogens from the contaminated environment and air to susceptible humans, infected humans to susceptible humans and from humans to susceptible rodents, respectively,	0.43, 0.43, Estimate, 0.4, Estimate. Dimensionless	(Elizabeth et al., 2014; Elizabeth et al., 2014; Estimate; Elizabeth et al., 2014; Estimate;)
α	Rates of shedding from rodent to environment	$10^3 - 10^5 (\text{TCID})_{50/ml}$	(McCormick, 1987)
κ_c	Concentration of the pathogens in the contaminated environment and air	$10^3 - 10^5 (\text{TCID})_{50/ml}$	(McCormick, 1987)
τ_1	Re-infection rate of humans from infected	[0.01,0.18]	(Richmond and Baglole, 2003)
τ_2	Re-infection rate of humans from isolated humans	[0.01,0.18]	(Richmond and Baglole, 2003)
γ_1	Progression rate of expose humans to infected class	0.7869	(Richmond and Baglole, 2003)
γ_2	Progression rate of infected humans to isolated class	$[0.05,0.08]$	(McCormick, 1987)
K	Carrying capacity for rodents	946	(McCormick, 1987)
δ	Disease-induced death rate for humans	$[0.0452,0.1133]$	(NCDC, 2018)
b_L	Maximum rate of growth of rodent population	$1.502\ per\ head$ $per\ 28\ days$	(Oliff, 1953)

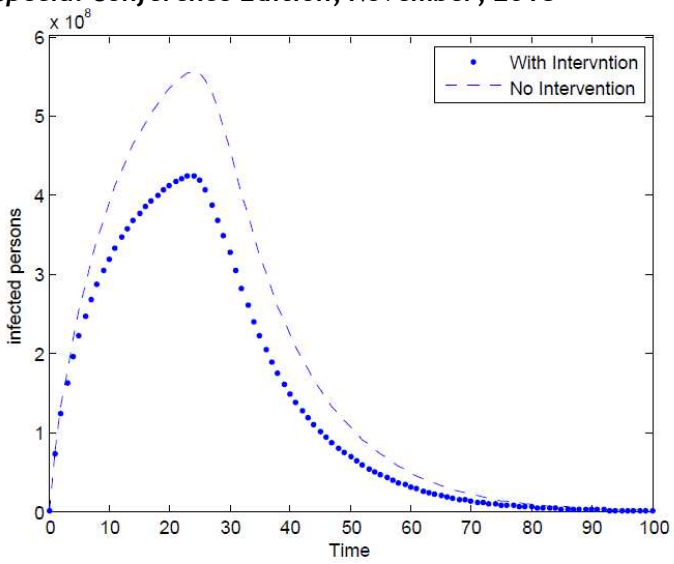

Figure 2. Graph of infected humans with and without intervention when $\mathcal{R}_0 < 1$ at $\beta_H = 4 \times 10^{-11}$

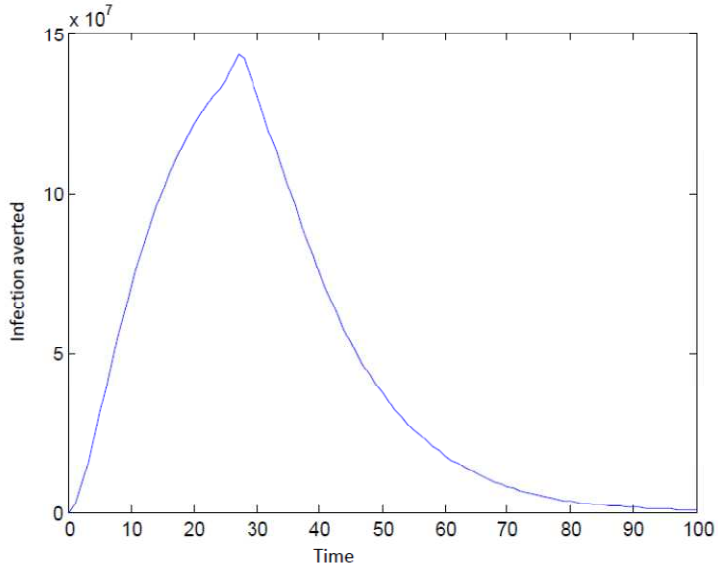

Figure 3. Graph of averted cases, $\mathbf{AVERTION} = \mathbf{4.7128 \times 10^9}$

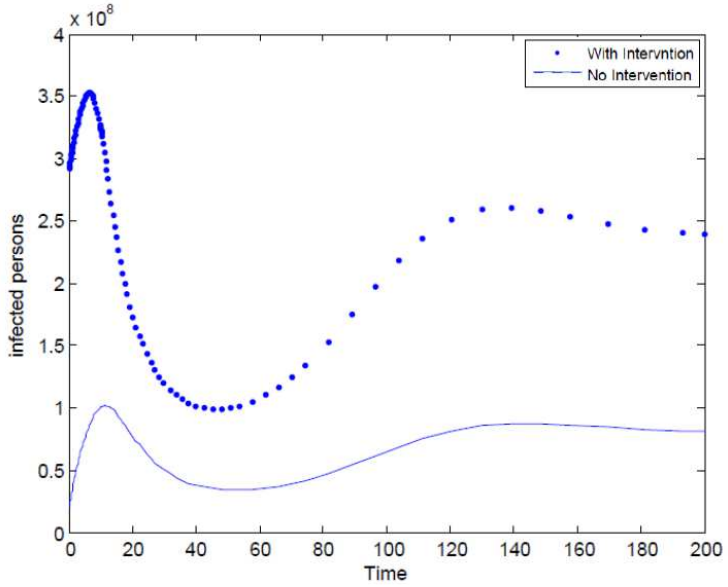

Figure 4. Graph of infected humans with and without quarantine when $\boldsymbol{\mathcal{R}_0} > 1$ at $\beta_H = 4 \times 10^{-14}$

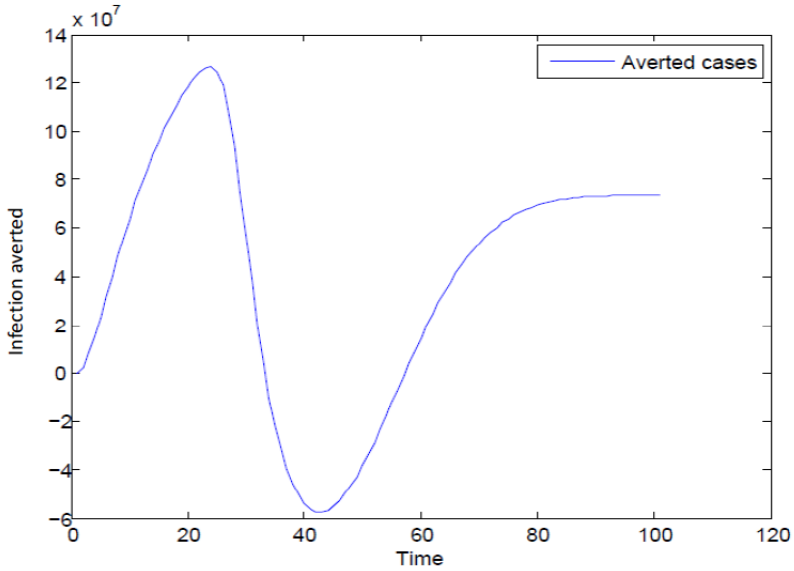

Figure 5. Graph of averted cases, $\boldsymbol{AVERTION = 4.7128 \times 10^9}$

CONCLUSION

In this work, a mathematical model is developed and analyzed to study the transmission and control of Lassa fever. Mathematically we modeled Lassa fever as 7-dimensional system of non-linear ordinary differential equation. We first show that there exists a domain where our model is well posed mathematically and epidemiologically. The model incorporates quarantine and re-infection parameters. The DFE point of the model is obtained and analyzed for stability. We obtained an important threshold parameter called basic reproductive number $\mathcal{R}_0$. Numerical simulations, using the parameter values in table 4 show that the associated reproduction number $\mathcal{R}_0 < 1$, and decrease when quarantine is implemented as shown in Figure 2. Thus, the outlook of the effective control of Lassa virus is greatly enhanced if a control strategy based on using quarantine of the infected and infectious human is implemented, which shows the averted cases in Figure 3. But when $\mathcal{R}_0 . > 1$, the Figure 4 and Figure 5 shows the infected humans with and without quarantine when $\mathcal{R}_0 > 1$ at $\beta_H = 4 \times 10^{-14}$, and the averted cases respectively.

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