A DETERMINISTIC MATHEMATICAL MODEL OF LASSA FEVER DISEASE DYNAMICS

BY

ONUORAH MARTINS ONYEKWELU

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CERTIFICATION

This thesis titled A DETERMINISTIC MATHEMATICAL MODEL OF LASSA FEVER DISEASE DYNAMICS by Onuorah Martins Onyekwelu

M.TECH/SSSE/2006/1584 meets the regulations governing the award of the degree of M.Tech, the federal University of Technology, Minna and is approved for its contribution to scientific knowledge and literary presentation.

Dr. N.I. Akinwande .....

Supervisor Signature and Date

Dr. N.I. Akinwande .....

Head of Department Signature and Date

Mathematics / Computer Science

Prof. M. Galadima .....

Dean, School of Science Signature and Date

and Science Education

Prof. S.L. Lamai .....

Dean, Postgraduate School Signature and Date

DEDICATION

This project is dedicated to my sweet heart Obinna

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ABSTRACT

In this work, we propose a Deterministic Mathematical Model of Lasa fever disease dynamics. The model is represented by a set of ordinary differential equations. The first two equations represent the human population which is partitioned into the susceptible class S(t), and the infected class I(t) and the last equation represents the vector or virus carrier population V(t). The equilibrium states were obtained and analysed for stability. The result of the analysis shows that the zero equilibrium state is stable if the birth rate of the Mastomys Natelences (vector) is les than the total death rate of the vector. However, the non-zero equilibrium was found to be unstable meaning that the disease can not be eradicated once it enters a population.

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CHAPTER ONE-INTRODUCTION

1.1 Background to the study

Mathematical model is an abstract representation of a phenomenon in order to gain a better understanding of the phenomena. It uses mathematical statements to represent relevant variable factors of the real life problem/ situation under study. The model is analyzed by means of special schemes which may be analytical or numerical. The analysis of the model gives better understanding of the real life problem. The problems such as the existence of equilibrium state and stability are of great interest to mathematical models of population dynamics as pointed out by Akinwande (1999).

Lassa fever is a zoonotic disease, that is, it can be transmitted from an infected animal to human. The animal host of lassa fever is rat species known as mastomy (mastomy natalensis) in particular. The infected mastomy do not become ill but can shed the virus in their excreta (urine and faeces). The fever is therefore transmitted through exposure to infected mastomys (through their excreta or consuming contaminated food) and through direct contact with the blood, urine, faeces, or other body secretions of a person infected with Lassa virus.

Human to human transmission occur in both community and health care settings, where the virus is spread through contaminated medical equipment, example is re-used needles. Lassa fever occurs in all age groups and in both men and women. Those leaving in rural areas where mastomys are usually found are at high risk of getting infected with the virus. Health care workers are at risk if proper nursing and infection control practices are not maintained. At present there is no vaccine for the virus, and an antiviral drug- Riverbrin is used for treatment.

In this work, we propose a deterministic mathematical model of the dynamics of Lassa fever disease represented by three ordinary differential equations. The first two equations represent the human population which is partitioned into the susceptible class S(t), the infected class I(t) and the last equation represents the vector population V(t). It is assumed that a portion of the Susceptible class may move to the Infected class as a result of interaction with the Infected class or the Vector. As well a portion of the Infected class may move to the Susceptible class as a result of recovery. And finally we assume that the virus can not kill the Vector (*Mastomys natalensis).*

This work has been divided into five chapters. The first chapter is the introduction. In chapter two we review some literatures that are related to this work. The model equations and their underlying assumptions are presented

in chapter three. The zero and non zero equilibrium as well as the characteristic equation are obtained in chapter three. Chapter four contains the stability analysis of the equilibrium states and chapter five contains the conclusion and the recommendations.

1.2 Objectives of the study.

"In the regulation of population, boundedness and stability of equilibrium are two concepts most likely to be given prominence" Sowunmi (2000).

The objective of the study can be summarized as follows:

(i) To formulate a mathematical model of Lassa fever disease dynamics.

(ii) To solve for the equilibrium state and obtain the characteristic equation for the model.

(iii) To analyze the equilibrium states for stability or other-wise in order to gain an insight into the Lassa fever disease.

1.3 Significance of the Study

The studies of population have been of great relevance to the growth of a nation or economy over the years because of the practical influence it has on human life. "Population plays a very important role in the economic success of a nation to the extent that it can not survive without adequate understanding of her population dynamics" Ogbu (2007). Population studies are important for both short and long term planning in fields such as health agriculture, social services and environment preservation; such studies provide the information needed for the formulation of government policies so as to achieve economic and social objectives.

The study will help to understand the dynamics of the disease. This becomes very important as the disease affects human population in some West African countries.

1.4 Scope and Limitation of the Study

The scope of this research work covers only the dynamics of the disease as areas like epidemic and endemic situations, effects of vaccine and biological properties of the virus are beyond the scope. Availability and access to intellectual works, time and cost are some of the limitations encountered in the course of this work.

1.5 Epidemiology of Lassa fever

Epidemiology is the medical that involves the study of the incidence and distribution of diseases in large populations, and the conditions influencing the spread and severity of diseases. Initially, epidemiology concerned itself with infectious diseases. The first prominent epidemiological investigation was conducted in 1849 by the English physician John Snow, who observed that the London cholera epidemic occurred chiefly in regions served by the broad street pump. After the pump was shut down the epidemic subsided. Modern epidemiology may focus on the effect of age, such as the susceptibility of older persons to respiratory deaths during influenza epidemics; of sex, such as the greater incidence of heart attack among men. Modern epidemiologists are still involved with tracing the causes of diseases. One example is the finding that a previously unknown microorganism called pneumophila was responsible for an out break of respiratory disease at an American Legion convention in Philadelphia in 1976.

In this section, we look at the epidemiology of Lassa fever disease under the following: the nature of the virus and transmission, human to human transmission, symptoms and diagnosis.

1.5.1 Nature of virus and transmission

Lassa fever is an acute viral hemorrhagic fever first described in 1969 in the Nigerian town of Lassa in the Yedseram River valley. The fever is caused by Lassa virus which belongs to the Arena virus family, and classified as group V(-)ssRNA. Most of the viruses associated with VHFs are zoonotic, which means they reside in an animal or insect host and are dependent on that host for their survival

Lassa virus is zoonotic (transmitted from animals), in that it spreads to man from rodents, specifically multi-mammate rats (*Mastomys natalensis*). In these rats infection is in a persistent asymptomatic state. The virus is shed in their excreta (urine and feces), which can be aerosolized. In fatal cases, Lassa fever is characterized by impaired or delayed cellular immunity leading to fulminant viremia.

Infection in humans typically occurs via exposure to animal excrement through the respiratory or gastrointestinal tracts. Inhalation of tiny particles of infective material (aerosol) is believed to be the most significant means of exposure. It is possible to acquire the infection through broken skin or mucous membranes that are directly exposed to infective material

1.5.2 Human to human transmission

Like other hemorrhagic fevers, Lassa fever can be transmitted directly from one human to another.

- **Person-to-person contact.** You can contract the virus if you come in contact with the blood, throat secretions or urine of an infected person, especially during the acute fever stage of the illness.
- **Sexual contact.** Because the virus can be transmitted in semen long after infection, experts recommend that men who have recovered from Lassa fever refrain from sexual activity for at least three months.
- **Contaminated needles and syringes.** This form of transmission is most likely to occur through an accidental needle stick or in a hospital in a developing nation where equipment may be used on more than one person.
- Transmission through breast milk has also been observed.
- **Airborne route**. Inhalation of tiny particles of infective material (aerosol) is believed to be the most significant means of exposure.

1.6 Mathematical modeling

Mathematical Modeling, which is by defined Benyah (2005) as the process of creating a mathematical representation of some phenomenon in order to gain a better understanding of that phenomenon. It has become an important an important scientific techniques over the last 20 years. Mathematical modeling provides essential tools to capture a set of assumptions and to follow them to their precise logical conclusions. They allow us to generate new hypothesis, suggest experimental and measure crucial parameter. Essentially, any real situation in the physical and biological world, whether natural or technological, can be subjected to analysis by modeling if it can be described in quantitative terms. Thus optimization and control theory can be used to model industrial process, traffic pattern, sediment transport in streams and other situations. Information and communication theory can be used to model massage transmission, linguistic characteristic, and the likes; while dimension analysis and computer simulation may be used to model atmospheric circulation pattern, stress distribution in engineering structures, the growth and development of land forms, and host of others.

Once a model has been developed and used to answer questions, it can be critically examined and often modified to obtain a more accurate reflection of

1.5.3 Symptoms and diagnosis

In 80% of cases the disease is in-apparent, but in the remaining 20% it takes a complicated course. After an incubation period of six to twenty-one days, an acute illness with multiorgans involvement develops. Non-specific symptoms include fever, facial swelling, and muscle fatigue, as well as conjunctivitis and mucosal bleeding. The other symptoms arising from the affected organs are:

- Gastrointestinal tract
    - Nausea
    - Vomiting (bloody)
    - Diarrhea (bloody)
    - Stomach ache
    - Constipation
    - Dysphagia (difficulty in swallowing)
    - Hepatitis
- Cardiovascular system
    - Pericarditis
    - Hypertension
    - Hypotension
    - Tachycardia (abnormally high heart rate)

- Respiratory tract
    - Cough
    - Chest pain
    - Dyspnea (difficulty in breathing often cause by heart or lung disease)
    - Pharyngitis
    - Pleuritis
- Nervous system
    - Encephalitis
    - Meningitis

1.5.4 Symptoms and Diagnosis

Occasionally, patients have tinnitus, epistaxis, bleeding from the gums and venipuncture sites, maculopapular rash, cough, and dizziness. Twenty percent of patients develop **sensorineural hearing loss, often permanent**. In patients who will recover, defervescence occurs; fatally ill patients often develop shock, delirium, rales, pleural effusion, and, occasionally, generalized seizures. Pericarditis occasionally occurs. The degree of fever and the aminotransferase levels correlate with disease severity. Late sequelae include alopecia, iridocyclitis, and *transient blindness*

Lassa fever is suspected in patients with possible exposure who have a viral prodrome followed by unexplained disease of any organ system except the CNS. If suspected, liver function tests, urinalysis, serologic tests, and possibly CBC should be obtained. Proteinuria is common and may be massive. AST and ALT levels rise (10× normal), as do LDH levels. The most rapid diagnostic test is PCR, although demonstrating either Lassa IgM antibodies or a 4-fold rise in IgG antibody titer using an indirect fluorescent antibody technique is also diagnostic. Although the virus can be grown in cell culture, cultures are not routine. Due to the risk of infection, particularly in patients with hemorrhagic fever, cultures must be handled only in a biosafety level 4 laboratory. Chest x-rays, obtained if lung involvement is suspected, may show basilar pneumonitis and pleural effusions.

the observed reality. Mathematical model is an evolving process, as new is gained the process begins again as additional factors are considered. Generally, the success of a model depends on how easily it can be used and how accurate its predictions are.

1.6.1 Overview of mathematical models

"To explain a phenomenon is to find a model that fits into the basic framework of the theory and that allows us to derive analogues for the messy and complicated phenomenological laws which are true of it" Cartwright (1983).

The term model is used in many different situations and many different ways. Model may be defined as a simplified or idealized description or conception of a particular system, situation or process Edmond (1999). It may be categorized according to the medium in which they are expressed. Some types of models that have been identified in the philosophy of science literature are ; Mental model, Iconic model, Analog model, and Mathematical model.

Mental model: of a situation provides subjective description of how a person thinks about a situation. The model includes, beliefs, assumptions,

1.6.4 Mathematical model with differential equation

A differential equation is an equation containing one or more derivatives of the unknown function. Differential equation form very important mathematical toll used in developing models of physical and biological processes as well as formulating significant problems in the social sciences. They have been the subject of a great deal of research for more than 10 decades.

Mathematical modeling through ordinary differential equation arises when the problem being modeled involves continuous variable(s), and there are reasonable hypothesis about the rates of change of the dependent variable and independent variables. When there are more than one dependent continuous variable and only one independent variable, the hypothesis may result in a model which is a system of first order ordinary differential equations, that is $\frac{dy}{dx} = f(x,t)$. The model will be an ordinary differential equation of the second order if we have a hypothesis about the rate of change of $\frac{dy}{dx}$, in which case we have $\frac{d^2x}{dt^2} = f(x^!x,t)$.

If there are more than one dependent variable and only one independent variable, the hypothesis may result in a model which is a system of first or higher order differential equation

1.7 Equilibrium and Stability

1.7.1Equilibrium

Equilibrium is the state of a system whose configuration or large scale properties do not change over time. For example, if a hot penny is dropped into a cup of cold water, the system of the water and the penny will reach equilibrium when both are at the same temperature. At that point, the large scale properties of the system, namely, the temperature of the water and the penny, will not change over time. As another example, in mechanics a system is at equilibrium if the net force acting on the body is zero. In the case of a stationary body, the large scale properties of the position of the body will remain unchanged over time. If the dynamics of a system is described by a differential equation (or a system of differential equations), then equilibria can be estimated by setting a derivative (all derivatives) to zero.

Example: consider the Logistic model $\frac{dN}{dt} = r_0 N\left(1 - \frac{N}{K}\right)$

To find equilibria we need to solve the equation: $\frac{dN}{dt} = 0$:

Thus $r_0 N\left(1 - \frac{N}{K}\right) = 0$. this equation has two roots:$N = 0$ and $N = K$.

CHAPTER TWO – LITERATURE REVIEW

2.1 Introduction

Biomathematics is an interdisciplinary field of academic study which aims at modelling natural and biological processes using mathematical techniques and tools. Works in biomathematics dates back to 19th century, the Lokta-Volterra predator- prey equations and evolution game theory developed by John Maynard Smith are examples. The purpose of this chapter is to review some scientific literatures are that related to mathematical Epidemiology (the study of infectious disease affecting population) Lassa fever disease. Over the years various model of viral spread has been proposed and analysed and provide important result that can be applies to health policy decision.

Akinwande, (2007a) in his papers on Model of Avian Influenza (bird flu) dynamics involving human interaction concludes that once the epidemics is allowed into a population, the tendency for wiping out the population is imminent. Since in his model analysis, the zero state is stable while the non zero state is unstable

Okuonghae (2006) et'el, in their work on Lassa fever examined the steady state of their model fro epidemics and endemic situations. They also formulated a second model which incorporated the effects of vaccination on a

300-500,000 cases annually with approximately 5,000 deaths Fisher et al (2004). Outbreaks of the disease have been observed in Nigeria, Liberia, Sierra Leone, Guinea, and the, Central African Republic, but it is believed that human infections also exist in Democratic Republic of the Congo, Mali, and Senegal. Its primary animal host is the Natal Multimammate Mouse (*Mastomys natalensis*), an animal indigenous to most of Sub-Saharan Africa. Geisbert et al (2005). Although the rodents are also a source of protein for peoples of these areas, the virus is probably transmitted by the contact with the feces and urine of animals accessing grain stores in residences Werner (2004).

2.2.2 Virus Replication

Lassa fever is caused by the *Lassa virus*, a member of the Arenaviridae family; it is an enveloped, single-stranded, bisegmented RNA virus, Fisher-Hoch et al (2004).

Replication for Lassa virus is very rapid, while also demonstrating temporal control in replication. There are two genome segments. The first step involved is making mRNA copies of the - sense genome. This ensures that there is adequate proteins, which are required for replication. The N and L proteins

are made from the mRNA produced. The - sense genome then makes viral complementary RNA (vcRNA) copies of itself which are + sense. The vcRNA is a template for producing - sense progeny but mRNA is also synthesized from it. The mRNA synthesized from vcRNA translate the G (spike) proteins and Z proteins. Thus, with this temporal control, the spike proteins are produced last, making the infection further undetected by the host immune system.

Lassa virus will infect almost every tissue in the human body. It starts with the mucosa, intestine, lungs and urinary system, and then progresses to the vascular system.

2.3 Prevalence and Prognosis

2.3.1Prevalence

The dissemination of the infection can be assessed by prevalence of antibodies to the virus in populations of:

Sierra Leone 8–52%

Guinea 4–55%

Nigeria approx. 21%

Like other hemorrhagic fevers, Lassa fever can be transmitted directly from one human to another. It can be contracted by an airborne route or with direct contact with infected human blood, urine, or semen. Transmission through breast milk has also been observed.

2.3.2 Prognosis

Once one is infected, death or survival occurs within 7 to 31 days. About 15%-20% of hospitalized Lassa fever patients will die from the illness. It is estimated that the overall mortality rate is 1%, however during epidemics mortality can climb as high as 50%. The mortality rate is greater than 80% when it occurs in pregnant women during their third trimester; fetal death also occurs in nearly all those cases. Abortion decreases the risk of death to the mother.

Thanks to treatment with Ribavirin, fatality rates are continuing to decline. Work on a vaccine is continuing, with multiple approaches showing positive results in animal trials.

2.4 Transmission and Spread

Lassa fever is a zoonotic disease, that is, it can be transmitted from an infected animal to human. The animal host of lassa fever is rat species known as mastomy (mastomy natalensis) in particular. The infected mastomy do not become ill but can shed the virus in their excreta (urine and faeces).

Infection in humans typically occurs via exposure to animal excrement through the respiratory or gastrointestinal tracts. Inhalation of tiny particles of infective material (aerosol) is believed to be the most significant means of exposure. It is possible to acquire the infection through broken skin or mucous membranes that are directly exposed to infective material. Transmission from person to person has also been established, presenting a disease risk fro health workers.

2.5 Prevention and treatment

2.5.1 Prevention

Control of the *Mastomys* rodent population is impractical, so measures are limited to keeping rodents out of homes and food supplies, as well as maintaining effective personal hygiene. Gloves, masks, laboratory coats, and goggles are advised while in contact with an infected person.

No vaccine against Lassa fever is currently available, though development is underway. The Mozambique virus closely resembles Lassa fever, while lacking its deadly effects. This virus is being considered for possible use as a vaccine.

Researchers at the USAMRIID facility, where military biologists study infectious diseases, have a promising vaccine candidate WHO (2000). They have developed a replication-competent vaccine against Lassa virus based on recombinant vesicular stomatitis virus vectors expressing the Lassa virus glycoprotein. After a single intramuscular injection, test primates have survived lethal challenge, while showing no clinical symptoms, Preston (2002).

2.5.2 Treatment

All persons suspected of Lassa fever infection should be admitted to isolation facilities and their body fluids and excreta properly disposed of.

Early and aggressive treatment using Ribavirin was pioneered by Joe McCormick in 1979. After extensive testing, it was determined that early administration is critical to success. Additionally, Ribavirin is almost twice as effective when given intravenously as when taken by mouth, Chen (2000). Ribavirin is a prodrug which appears to interfere with viral replication by

inhibiting RNA-dependent nucleic acid synthesis, although the precise mechanism of action is disputed, Beltrami (1989). The drug is relatively inexpensive, but the cost of the drug is still very high for many of those in poverty-stricken West African states. Fluid replacement, blood transfusion and fighting hypotension are usually required. Intravenous interferon therapy has also been used.

When Lassa fever infects pregnant women late in their third trimester, it is necessary to abort the pregnancy for the mother to have a good chance of survival, Price (1988). This is because the virus has an affinity for the placenta and other highly vascular tissues. The fetus has only a one in ten chance of survival no matter what course of action is taken; hence focus is always on saving the life of the mother. Following abortion, women should receive the same treatment as other Lassa fever patients.

Siga Technologies is developing an antiviral drug that has been shown effective in treating experimentally infected guinea pigs. In a study conducted at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), treatment with ST-193 once a day for 14 days resulted in significant reduction in mortality (71% of the animals survived at the low dose), whereas all untreated animals and those treated with ribavirin died within 20 days of the infection, Crotty (2002).

CHAPTER THREE – Materials and Method

3.1INTRODUCTION

Lassa fever is a zoonotic disease, that is, it can be transmitted from an infected animal to human. The animal host of Lassa fever is rat species known as mastomy (mastomy natalensis) in particular. The infected mastomy do not become ill but can shed the virus in their excreta (urine and faeces). The fever is therefore transmitted through exposure to infected mastomys (through their excreta or consuming contaminated food) and through direct contact with the blood, urine, faeces, or other body secretions of a person infected with Lassa virus.

Human to human transmission occur in both community and health care settings, where the virus is spread through contaminated medical equipment, example is re-used needles. There is no epidemiological evidence supporting air born spread among humans through aerosol transmission has been demonstrated in the laboratory. Lassa fever occurs in all age groups and in both men and women. In this chapter, we propose a set of ordinary differential equations. The first two equations represent the human population which is partitioned into the susceptible class S(t), the infected class I(t) and the third equation represents the vector population V(t). It is assumed that a

the third equation represents the vector population V(t). It is assumed that a portion of the Susceptible class may move to the Infected class as a result of interaction with the Infected class or the Vector. As well a portion of the Infected class may move to the Susceptible class by way of treatment.

3.1.1 Basic assumptions

Models are representation of relevant variables of a system for a given purpose. Due to the fact that the whole element of a system are not represented, it is necessary to state some assumptions. For the purpose of this research work the following assumptions are made.

(i) Members of the susceptible human population S(t) can move to the infected population I(t) via interaction.

(ii) Members of the infected population I(t)can as well move to the susceptible population via treatment.

(iii) It is assumed that the new births of susceptible S(t) are susceptible.

(iv) Because of high affinity of the Lassa virus with the placenta, the off-springs of the infected is divided between the S(t) and I(t) in the proportion of $(1-\theta)$ and θ respectively.

(v) It is assumed that the virus does not kill the Vector since the Rats are in persistent asymptomatic state i.e their death can be natural or accidental.

3.2 THE MODEL EQUATION

The dynamics of the disease is given by equations (3.1) to (3.3).

$$\frac{dS(t)}{dt} = (\beta_1 - \mu_1)S - (\alpha_1 I - \alpha_2 V)S + (\gamma + (1-\theta)\beta_1) \quad (3.1)$$

$$\frac{dI(t)}{dt} = (\alpha_1 I + \alpha_2 V)S - (\mu_1 + \delta_1 + \gamma)I + \theta\beta_1 I \quad (3.2)$$

$$\frac{dI(t)}{dt} = (\beta_2 - \mu_2 - \delta_2 \quad (3.3)$$

The parameters of the model equation are defined as follows:

β_1 = Natural birth for the susceptible human population

β_2 = Natural birth for the Vector population

μ_1 = Natural death rate for the human population

μ_2 = Natural death rate for the Vector population

δ_1 = Death rate of the human population due to infection

δ_2 = Death rate of vector population do to other factors like harvesting,fire,etc

α_1 = Contracting rate for the susceptible human population as a result of interaction with infected human population

α_2 = Contracting rate for the susceptible human population as a result of interaction with infected vector population

γ = the rate of recovery of the infected human population as a result of treatment

θ = the proportion of the off-springs of the infected human population which are infected at birth $0 < \theta < 1$.

3.3 Equilibrium State of the Model

$S(t) = x$, $I(t) = y$, $V(t) = z$, then equations 3.1 to 3.3 becomes

$$(\beta_1 - \mu_1)x - (\alpha_1 y - \alpha_2 z)x + (\gamma + (1-\theta)\beta_1)y = 0 \quad (3.4)$$

$$(\alpha_1 y + \alpha_2 z)x - (\mu_1 + \delta_1 + \gamma - \theta\beta_1)y = 0 \quad (3.5)$$

$$(\beta_2 - \mu_2 - \delta_2)z \quad (3.6)$$

From equation 3.6,

$$z = 0 \quad (3.7)$$

Substitute $z = 0$ in equations3.4 and 3.5 to have

$$(\beta_1 - \mu_1)x - (\alpha_1 y)x + (\gamma + (1-\theta)\beta_1)y = 0 \quad (3.8)$$

$$\alpha_1 xy - (\mu_1 + \delta_1 + \gamma - \theta\beta_1)y = 0 \quad (3.9)$$

Add equations 3.8 and 3.9

$$(\beta_1 - \mu_1)x - (\alpha_1 y)x + (\gamma + (1-\theta)\beta_1)y + \alpha_1 xy - (\mu_1 + \delta_1 + \gamma - \theta\beta_1)y$$

$$(\beta_1 - \mu_1)x - (\mu_1 + \delta_1 - \beta_1)y = 0$$

$$x = \frac{(\mu_1 + \delta_1 - \beta_1)y}{(\beta_1 - \mu_1)} \quad 3.10$$

From equation 3.9,

$$[\alpha_1 x - (\mu_1 + \delta_1 + \gamma - \theta\beta_1)y] = 0$$

Either $y = 0$

Or

$$\alpha_1 x - (\mu_1 + \delta_1 + \gamma - \theta\beta_1) = 0$$

$$x = \frac{(\mu_1 + \delta_1 + \gamma - \theta\beta_1)}{\alpha_1} \quad 3.11$$

From equation 3.8, if $y = 0, x = 0$

Hence, (0,0,0) is an equilibrium state.

If $y \neq 0$

From equation 3.8,we have

$$(\beta_1 - \mu_1)x + (\gamma + (1-\theta)\beta_1 - \alpha_1 x)y = 0$$

$$(\gamma + (1-\theta)\beta_1 - \alpha_1 x)y = -(\beta_1 - \mu_1)x$$

$$y = -\frac{(\beta_1 - \mu_1)x}{\gamma + (1-\theta)\beta_1 - \alpha_1 x} \qquad 3.12$$

Substitute 3.11 into 3.12, we have

$$y = \frac{-(\beta_1 - \mu_1)\frac{(\mu_1 + \delta_1 + \gamma - \theta\beta_1)}{\alpha_1}}{\gamma + (1-\theta)\beta_1 - \alpha_1 \frac{(\mu_1 + \delta_1 + \gamma - \theta\beta_1)}{\alpha_1}}$$

$$y = \frac{-(\beta_1 - \mu_1)(\mu_1 + \delta_1 + \gamma - \theta\beta_1)}{\alpha_1[\gamma + (1-\theta)\beta_1 - (\mu_1 + \delta_1 + \gamma - \theta\beta_1)]}$$

$$y = \frac{-(\beta_1 - \mu_1)(\mu_1 + \delta_1 + \gamma - \theta\beta_1)}{\alpha_1(\beta_1 - \mu_1 - \delta_1)} \qquad 3.13$$

Equations 3.11,3.13, and3.7 gives $(\overline{x}, \overline{y}, 0)$ as the second equilibrium state

3.4 THE CHARACTERISTIC EQUATION

We perturb the equilibrium states using equations 1.14t0 3.16

$$S(t) = x + p(t); p(t) = \overline{p}e^{\lambda t} \qquad 3.14$$

$$I(t) = y + q(t); q(t) = \overline{q}e^{\lambda t} \qquad 3.15$$

$$V(t) = z + r(t); r(t) = \overline{r}e^{\lambda t} \qquad 3.16$$

where $\overline{p}$, $\overline{q}$,$\overline{r}$ are constants. Substituting equations 3.14, 3.15,3.16 into equations 3.1 to 3.3 i.e

From equation 3.1

$$\frac{dS(t)}{dt} = (\beta_1 - \mu_1)S - (\alpha_1 I - \alpha_2 V)S + (\gamma + (1-\theta)\beta_1)I \qquad (3.1)$$

$$\frac{dS(x + \overline{p}e^{\lambda t})}{dt}$$

$$= (\beta_1 - \mu_1)(x + \overline{p}e^{\lambda t}) - [(\alpha_1(y + \overline{q}e^{\lambda t}) - \alpha_2(z + \overline{r}e^{\lambda t})](x + \overline{p}e^{\lambda t}) + (\gamma + (1-\theta)\beta_1)(y + \overline{q}e^{\lambda t})$$

$$= \beta_1 x + \beta_1 \overline{p}e^{\lambda t} - \mu_1 x - \mu_1 \overline{p}e^{\lambda t} - \alpha_1(y + \overline{p}e^{\lambda t})(x + \overline{q}e^{\lambda t}) + \alpha_2(z + \overline{r}e^{\lambda t})(x + \overline{p}e^{\lambda t}) + \gamma y + \gamma \overline{q}e^{\lambda t} + (1-\theta)\beta_1)y + (1-\theta)\beta_1)\overline{q}e^{\lambda t}.$$

$$\lambda\overline{p}e^{\lambda t} = (\beta_1 - \mu_1)x + (\beta_1 - \mu_1)\,\overline{p}e^{\lambda t} - \alpha_1(yx + y\overline{q}e^{\lambda t} + x\overline{p}e^{\lambda t}\ \overline{p}\,\overline{q}e^{2\lambda t})$$
$$- \alpha_2(zx + z\overline{p}e^{\lambda t} + x\overline{r}e^{\lambda t} + \overline{p}\,\overline{r}e^{2\lambda t}) + \gamma y + \gamma\overline{q}e^{\lambda t} + (1-\theta)\beta_1)y$$
$$+ (1-\theta)\beta_1)\overline{q}e^{\lambda t}$$

$$= (\beta_1 - \mu_1)x + \beta_1\,\overline{p}e^{\lambda t} - \mu_1\,\overline{p}e^{\lambda t} - \alpha_1 yx - \alpha_1 y\overline{p}e^{\lambda t} - \alpha_1 x\overline{q}e^{\lambda t} - \alpha_1\,\overline{p}\,\overline{q}e^{2\lambda t}$$
$$- \alpha_2 zx - \alpha_2 z\overline{p}e^{\lambda t} - \alpha_2 x\overline{r}e^{\lambda t} - \alpha_2\overline{p}\,\overline{r}e^{2\lambda t} + \gamma y + \gamma\overline{q}e^{\lambda t}$$
$$+ (1-\theta)\beta_1)y + (1-\theta)\beta_1)\overline{q}e^{\lambda t}$$

$$= (\beta_1 - \mu_1)x - \alpha_1 yx - \alpha_2 zx + \gamma + y(1-\theta)\beta_1)y + \beta_1\,\overline{p}e^{\lambda t}$$
$$- \mu_1\,\overline{p}e^{\lambda t} - \alpha_1 y\overline{p}e^{\lambda t} - \alpha_1 x\overline{q}e^{\lambda t} - \alpha_1\,\overline{p}\,\overline{q}e^{2\lambda t} - \alpha_2 z\overline{p}e^{\lambda t} - \alpha_2 x\overline{r}e^{\lambda t}$$
$$- \alpha_2\overline{p}\,\overline{r}e^{2\lambda t} + \gamma\overline{q}e^{\lambda t} + (1-\theta)\beta_1)\overline{q}e^{\lambda t}.$$

Neglecting the terms of order 2 in λt and using equation 3.4gives

$$\lambda\overline{p}e^{\lambda t} = \beta_1\,\overline{p}e^{\lambda t} - \mu_1\,\overline{p}e^{\lambda t} - \alpha_1 y\overline{p}e^{\lambda t} - \alpha_1 x\overline{q}e^{\lambda t} - \alpha_2 z\overline{p}e^{\lambda t} - \alpha_2 x\overline{r}e^{\lambda t} + \gamma\overline{q}e^{\lambda t} +$$
$$(1-\theta)\beta_1)\overline{q}e^{\lambda t}.$$

Dividing through by $e^{\lambda t}$ gives

$$\lambda\overline{p} = \beta_1\,\overline{p} - \mu_1\,\overline{p} - \alpha_1 y\overline{p} - \alpha_1 x\overline{q} - \alpha_2 z\overline{p} - \alpha_2 x\overline{r} + \gamma\overline{q} + (1-\theta)\beta_1\,\overline{q}.$$

$$(\beta_1 - \mu_1 - \alpha_1 y - \alpha_2 z)\,\overline{p} - (\alpha_1 x - \gamma + (1-\theta)\beta_1)\overline{q} + \alpha_2 x\overline{r} = 0 \qquad 3.17$$

From equation 3.2

CHAPTER FOUR - Results

4.1 Stability of the zero equilibrium state

At zero equilibrium state i.e x, y, z, (0,0,0)

The characteristic equation 3.15 takes the form

$$\{\beta_2 - \mu_2 - \delta_2 - \lambda\}\{(\beta_1 - \mu_1 - \lambda)(\theta\beta_1 - \mu_1 - \delta_1 - \gamma - \lambda)\} = 0 \qquad 4.1$$

Either

$$(\beta_2 - \mu_2 - \delta_2 - \lambda) = 0 \qquad 4.2$$

or

$$(\beta_1 - \mu_1 - \lambda)(\theta\beta_1 - \mu_1 - \delta_1 - \gamma - \lambda) = 0 \qquad 4.3$$

Now considering 4.2;

$$\lambda_1 = \beta_2 - \mu_2 - \delta_2$$

$\lambda_1 < 0$, if

$$\beta_2 - \mu_2 - \delta_2 < 0$$

i.e $\beta_2 < \mu_2 + \delta_2$

From equation 4.3

From equation 4.3

$\lambda_2 = (\beta_1 - \mu_1)$

$\lambda_2 < 0$ if $\beta_1 < \mu_1\lambda^2 - a\lambda + b = 0.$

From equation 4.4

$\lambda_3 = -(\mu_1 + \delta_1 + \gamma - \theta\beta_1)$

$\lambda_3 < 0$

4.2 Stability of non zero equilibrium state

Recall that at non zero equilibrium state, $x, y \; and \; z$ are given by equations 3.11,3.13 and 3.7 respectively.

Substituting 3.7 $in \; to$ 3.17, we have;

$(\beta_1 - \mu_1 - \alpha_1 y - \lambda)(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1 - \lambda) + (\alpha_1 x + \gamma + (1-\theta)\beta_1)(\alpha_1 y) = 0$

$(\beta_1 - \mu_1 - \alpha_1 y)(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1 - \lambda) - \lambda(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1 - \lambda) +$

$(\alpha_1 x + \gamma + (1-\theta)\beta_1)(\alpha_1 y) = 0$

$\lambda^2 - \lambda(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1) + (\beta_1 - \mu_1 - \alpha_1 y)(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1 - \lambda)$

$+ (\alpha_1 x + \gamma + (1-\theta)\beta_1)(\alpha_1 y) = 0$

$$\lambda^2 - \lambda(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1) - \lambda(\beta_1 - \mu_1 - \alpha_1 y) + (\beta_1 - \mu_1 - \alpha_1 y)(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1) + (\alpha_1 x + \gamma + (1-\theta)\beta_1)(\alpha_1 y) = 0$$

$$\lambda^2 - \lambda(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1 + \beta_1 - \mu_1 - \alpha_1 y) + (\beta_1 - \mu_1 - \alpha_1 y)(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1) + (\alpha_1 x + \gamma + (1-\theta)\beta_1)(\alpha_1 y) = 0$$

$$\lambda^2 - \lambda(\alpha_1 x - 2\mu_1 - \delta_1 - \gamma + \theta\beta_1 + \beta_1 - \alpha_1 y) + (\beta_1 - \mu_1 - \alpha_1 y)(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1) + (\alpha_1 x + \gamma + (1-\theta)\beta_1)(\alpha_1 y) = 0$$

$$\lambda^2 - \lambda(\alpha_1 x - 2\mu_1 - \delta_1 - \gamma + \theta\beta_1 + \beta_1 - \alpha_1 y) + (\beta_1 - \mu_1)(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1) - \alpha_1 y(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1) + (\alpha_1 x + \gamma + (1-\theta)\beta_1)(\alpha_1 y) = 0$$

$$\lambda^2 - \lambda(\alpha_1 x - 2\mu_1 - \delta_1 - \gamma + \theta\beta_1 + \beta_1 - \alpha_1 y) + (\beta_1 - \mu_1)(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1) + \alpha_1 y(-\alpha_1 x + \mu_1 + \delta_1 + \gamma - \theta\beta_1 + \alpha_1 x + \gamma + (1-\theta)\beta_1) = 0$$

$$\lambda^2 - \lambda(\alpha_1 x - 2\mu_1 - \delta_1 - \gamma + \theta\beta_1 + \beta_1 - \alpha_1 y) + (\beta_1 - \mu_1)(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1) + \alpha_1 y(\mu_1 + \delta_1 + 2\gamma - 2\theta\beta_1 + \beta_1) = 0$$

$$\lambda^2 - \lambda[(\beta_1 - \mu_1) - (\mu_1 + \delta_1 + \gamma + \alpha_1 y - \alpha_1 x - \theta\beta_1)] + (\beta_1 - \mu_1)(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1) + \alpha_1 y(\mu_1 + \delta_1 + 2\gamma - 2\theta\beta_1 + \beta_1) = 0 \ldots \quad 4.4$$

Equation 4.4 is of the form $\lambda^2 - a\lambda + b = 0$.

The constants a, b are given by

$$a = -(\alpha_1 x - 2\mu_1 - \delta_1 - \gamma + \theta\beta_1 + \beta_1 - \alpha_1 y) \qquad 4.5$$

$$b = (\beta_1 - \mu_1)(\alpha_1 x - \mu_1 - \delta_1 - \gamma + \theta\beta_1) + \alpha_1 y(\mu_1 + \delta_1 + 2\gamma - 2\theta\beta_1 + \beta_1) = 0$$

4.6

With the variables x, y, z given by equations $3.7, 3.11,$ *and* 3.13 respectively as functions of the parameters of the model equations. The sufficient condition for the stability of the non zero equilibrium state are for $a > 0$ and $b > 0$ cuncrrently.

Substituting $3.7, 3.11,$ *and* 3.13 into 4.5 yields

$$a = -[2\mu_1 - \delta_1 - \gamma + \theta\beta_1 + \beta_1 + \frac{\alpha_1(\mu_1 + \delta_1 + \gamma - \theta\beta_1)}{\alpha_1} \frac{+\alpha_1(\beta_1 - \mu_1)(\mu_1 + \delta_1 + \gamma - \theta\beta_1)}{\alpha_1(\beta_1 - \mu_1 - \delta_1)}]$$

$$a = -[\frac{(\beta_1 - \mu_1)(\mu_1 + \delta_1 + \gamma - \theta\beta_1)}{(\beta_1 - \mu_1 - \delta_1)} + 2\mu_1 - \delta_1 - \gamma + \theta\beta_1 + \beta_1 + \mu_1 + \delta_1 + \gamma - \theta\beta_1]$$

$$a = -[\frac{(\beta_1 - \mu_1)(\mu_1 + \delta_1 + \gamma - \theta\beta_1)}{(\beta_1 - \mu_1 - \delta_1)} + 3\mu_1 + \beta_1]$$

Also substituting 3.7, 3.11, *and* 3.13 into 4.6 yields

$$b = (\beta_1 - \mu_1)\left(\alpha_1 \frac{(\mu_1+\delta_1+\gamma-\theta\beta_1)}{\alpha_1} - \mu_1 - \delta_1 - \gamma + \theta\beta_1\right) -$$

$$\alpha_1[\frac{(\beta_1 - \mu_1)(\mu_1+\delta_1+\gamma-\theta\beta_1)}{\alpha_1(\beta_1 - \mu_1 - \delta_1)}] \quad (\mu_1 + \delta_1 + 2\gamma - 2\theta\beta_1 + \beta_1)$$

$$b = (\beta_1 - \mu_1) - [\frac{(\beta_1 - \mu_1)(\mu_1+\delta_1+\gamma-\theta\beta_1)}{(\beta_1 - \mu_1 - \delta_1)}] \quad (\mu_1 + \delta_1 + 2\gamma - 2\theta\beta_1 + \beta_1)$$

$$b = (\beta_1 - \mu_1) - [(\mu_1 + \delta_1 + 2\gamma - 2\theta\beta_1 + \beta_1)\frac{(\beta_1 - \mu_1)(\mu_1+\delta_1+\gamma-\theta\beta_1)}{(\beta_1 - \mu_1 - \delta_1)}]$$

From the analysis, $a < 0$ while $b > 0$ it follows that the non zero equilibrium state is unstable.

CHAPTER FIVE –Discussion, Conclusion and Recommendation

5.1Conclusion

The result of the model analysis shows that the zero equilibrium state of the model equations is stable when the birth rate of the human population is less than the death rate i.e $\beta_1 < \mu_1$ and the same when the birth rate of the vector is less than the total death rate i.e $\beta_2 < \mu_2 + \delta_2$. Further analysis of equation(4.6); $\lambda^2 - a\lambda + b = 0$ shows that the non zero equilibrium state is unstable since $a < 0\ while\ b > 0$, which means that once the disease enters a population it will be difficult to eradicate it. This confirms the present situation where it is not practicable to control the vector in the prevalence West African states

5.2 Recommendation

Control of the (Vector) *Mastomys* rodent population is impractical, because the vector is a source of protein to some people especially in West African states, so measures are limited to:

1. Keeping rodents out of homes and food supplies
2. Maintaining effective personal hygiene.

3. Gloves, masks, laboratory coats, and goggles are advised while in contact with an infected person.
4. Because the virus can be transmitted in semen long after infection, experts advice that men who have recovered from Lassa fever should refrain from sexual activity for at least three months
5. When Lassa fever infect pregnant women in their late trimester, it is necessary to abort the baby for the mother to have a good chance of survival.
6. The antiviral drug Rivabrin should be administered earlier in the course of the illness and more so, intravenously to speedy recovery.
7. More research and investigation for Lassa fever disease should be geared up in order to fully understand the disease and come up effective vaccine against the disease. Also, the disease is no longer African problem, as the case of transportation to the united states of America and the great Britain has been recorded.
8. The appropriate authorities should create awareness of the disease especially in rural communities where the out break of the disease is eminent as witnessed recently in some northern states of the country.

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