



VCU

Virginia Commonwealth University
VCU Scholars Compass

Theses and Dissertations

Graduate School

2008

An SCIR Model of Meningococcal Meningitis

Kalimah Vereen

Virginia Commonwealth University

Follow this and additional works at: <https://scholarscompass.vcu.edu/etd>



Part of the [Physical Sciences and Mathematics Commons](#)

© The Author

Downloaded from

<https://scholarscompass.vcu.edu/etd/710>

This Thesis is brought to you for free and open access by the Graduate School at VCU Scholars Compass. It has been accepted for inclusion in Theses and Dissertations by an authorized administrator of VCU Scholars Compass. For more information, please contact libcompass@vcu.edu.

© Kalimah J. Vereen, 2008

All Rights Reserved

AN SCIR MODEL OF MENINGOCOCCAL MENINGITIS

A Thesis submitted in partial fulfillment of the requirements for the degree of Master of Science at Virginia Commonwealth University.

by

KALIMAH J. VEREEN

Bachelor of Science, Virginia Commonwealth University, 2008

Director: DR REBECCA SEGAL

ASSISTANT PROFESSOR, DEPARTMENT OF MATHEMATICS

Virginia Commonwealth University
Richmond, Virginia
May 2008

Acknowledgement

I would like to thank my advisor Dr. Rebecca Segal for being there to answer all my questions no matter how basic they may have been. She made me feel at ease with her easygoing personality and open door policy. I would like to also thank the members of my committee, Dr. Moa Apagodu and Dr. Ghislaine Mayer, for being a part of my thesis writing experience.

I would like to thank my mother and father for encouraging me during the rough times, my brother and sister for requiring that I set a good example, my kids for understanding that “mommy has to go to school a lot” and the rest of my family for being my family. I love you!

Last but not least I would like to thank my fellow graduate teaching assistants for all their help, whether it was a borrowed book or a little advice.

Table of Contents

	Page
Acknowledgements	ii
List of Figures	v
Chapter	
1 Introduction	1
Anatomy	1
Infection.....	2
Epidemiology.....	5
2 Review of Infection Modeling Literature	8
Classic SIR Model	8
Polio SIR Model with Vaccine.....	13
SEIR Model with Vertical Transmission.....	20
Influenza SIRC Model.....	21
3 Development and analysis of the meningitis model	24
Meningitis Model	24
Reproduction Number	28
Equilibriums	30
Stability Nature of Disease Free Equilibrium.....	32
Existence of Endemic Equilibrium.....	33
4 Model Parameters and Results	34
Euler's Method	34

Parameter Values	35
Explanation of model behavior.....	37
5 Conclusions and Future Works	43
Conclusions	43
Future Works	44
References	47
Appendices.....	50
A Matlab Program.....	50

List of Figures

	Page
Figure 1: Meninges of the Central Nervous System	1
Figure 2: Meningitis Belt	6
Figure 3: Graph 1; ($\beta = .2$, $p = .2$)	37
Figure 4: Graph 2; ($\beta = .2$, $p = .685$)	38
Figure 5: Graph 3; ($\beta = .2$, $p = .97$)	38
Figure 6: Graph 4; ($\beta = .6$, $p = .2$)	39
Figure 7: Graph 5; ($\beta = .6$, $p = .885$)	40
Figure 8: Graph 6; ($\beta = .6$, $p = .97$)	40
Figure 9: Graph 7; ($\beta = .9$, $p = .2$)	41
Figure 10: Graph 8; ($\beta = .9$, $p = .93$)	42
Figure 11: Graph 9; ($\beta = .9$, $p = .97$)	42

Abstract

SCIR Model of Meningococcal Meningitis

By Kalimah Vereen, B.S.

A Thesis submitted in partial fulfillment of the requirements for the degree of Master of Science at Virginia Commonwealth University.

Virginia Commonwealth University, 2008

Major Director: Dr. Rebecca Segal
Assistant Professor, Department of Mathematics

A model for meningitis is developed by adding a class of carriers to the basic SIR model. This model is used to analyze the impact a vaccination program can have on the health of the population of epidemic prone countries. Analysis of the model shows the local stability of the disease free equilibrium, the existence of an endemic equilibrium and computation of the reproduction number, \mathcal{R}_0 . Using a MATLAB program we simulate a time course of the model using parameters gathered from the World Health Organization. The numerical solution demonstrates that our reproduction number was correct. We then concluded that a high infection transmission rate requires a high vaccine rate.

CHAPTER 1 Introduction

1.1 Anatomy

The meninges are the membranes that cover the central nervous system. The purpose of the meninges and the cerebrospinal fluid is to protect and provide nourishment to the central nervous system. The meninges are made of three layers. They are the dura mater, the arachnoid mater, and the pia mater. The pia mater is the membrane closest to the brain and the arachnoid mater is the middle of the meninges. These two are quite delicate and are separated by a small gap, the subarachnoid space, which contains cerebrospinal fluid. This fluid acts as a shock absorber within the nervous system. The dura mater is thick and durable and closest to the skull. It surrounds the other two parts of the meninges and protects the brain and spinal cord. (Woodburne & Burkel, 1988)

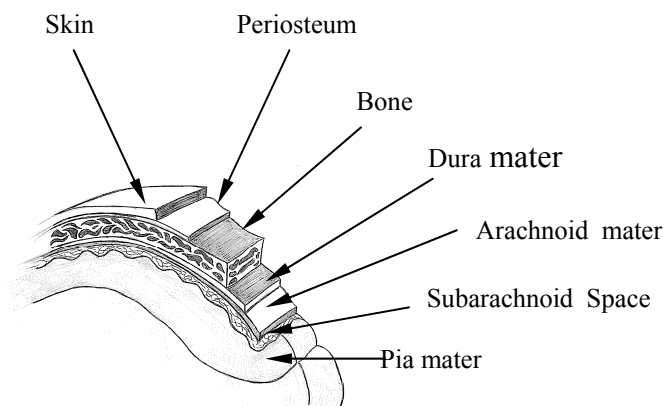


Figure 1: Meninges of the central nervous system; Recreation of meninges image: <http://en.wikipedia.org/wiki/Meninges>

1.2 Infection

Meningitis is the inflammation of the meninges. This disease can be caused by different organisms. Bacteria and viruses are the most common causes of meningitis. When these organisms are in the cerebrospinal fluid, everything in this immediate area will become inflamed. The introduction of bacteria in the meninges will almost surely cause meningitis. Sometimes the presence of this bacterium is the result of bacteria traveling from an infection in some other part of the body.

Bacterial meningitis occurs more often than viral. In fact more than 80% of all meningitis cases are caused by three distinct types of bacteria. The types are *Neisseria meningitidis*, *haemophilus influenzae*, and *Streptococcus pneumoniae*. *Neisseria meningitidis*, which causes meningococcal meningitis, occurs the most frequently of the three.

This paper will deal with bacterial meningitis caused by *Neisseria meningitidis*. This is a very serious form of meningitis. It has a high mortality rate if not treated. It has been reported that the fatality rate in developed countries was about 70-80% before successful treatments were discovered, such as antibiotics, which caused the rate to drop to 25%. (Martcheva & Crispino-O'Connell, 2002)

Transmission of meningitis passes through several stages. First an individual has to be susceptible to the disease. The three main bacterial causes of meningitis are present in the environment. When a susceptible individual comes into contact with any of these

bacteria or another infected individual they can then experience carriage of the bacterium.

Once they are a carrier, they can then develop the disease.

Carriage of *Neisseria meningitidis* does not necessarily lead to the development of the disease. (Martcheva & Crispino-O'Connell, 2002) The relationship between the last two stages is not fully understood. (Cartwright, 1995) At any given time about 10% of the general population will become carriers of the bacterium. (Martcheva & Crispino-O'Connell, 2002) The carriage rate is higher in new military recruits', schools, prisons and other isolated or semi isolated places. The rate is also higher if you have had contact with someone with the disease. (Cartwright, 1995) In a closed community, carrier rates can approach 100%. In a New Zealand study, a military trainee was found to have meningococcal meningitis. Of the 47 trainees in the patient's dormitory 85% were carriers of the bacteria. (Vedros, 1987)

Meningococcus, another term for *Neisseria meningitidis*, naturally resides in the human nasopharynx (throat, area behind mouth). (Cartwright, 1995) The bacteria can then gain entrance into the blood stream by way of the nasopharynx. Sinus, otogenic (starting at the ear), or paranasal (beside the nasal cavity) infections are some of the ways that the bacteria can enter the blood stream. (Kloss, 1996) Once bacteria are inside the blood, they have the ability to defeat the body's defense mechanisms that would normally fight off infection. (Bartfield, 2000) After entering the bloodstream the bacteria may find its way to the cerebrospinal fluid and end up in the meninges. It takes about 4 days for the bacteria to go from the nasopharynx to the meninges. (Kloss, 1996) Bacteria can also be introduced directly into the cerebrospinal fluid due to trauma or problems with a

neurosurgical procedure. However this process is less common and not usually involved in creating an epidemic. (Bartfield, 2000) Once this bacterium is inside the meninges it causes the meninges to become inflamed. The inflammation of the cervical nerves causes Nuchal rigidity. This is the inability to move the head forward and is often used for diagnosis. (Kloss, 1996)

The key to surviving meningococcal meningitis is early identification of the bacterium causing the disease. (Kloss, 1996) A lumbar puncture must be done in order to diagnose a patient with bacterial meningitis. The lumbar puncture is the process of retrieving cerebrospinal fluid from the subarachnoid space. Once a patient is evaluated and determined to have bacterial meningitis antibiotics should be administered immediately. (Bartfield, 2000)

Meningococcal meningitis can last for a period of 1 to 3 days. (Vedros, 1987) In the beginning those infected with the disease will experience symptoms that may mimic flu symptoms. They may have a fever and feel poorly. Very quickly these symptoms will become specific to meningitis. A patient may experience nausea, headache, confusion, or other problems with consciousness. (Martcheva & Crispino-O'Connell, 2002) Two-thirds of the patients will develop a rash. (Vedros, 1987) An infected person's health can rapidly go downhill within 24 hours. This decline may happen quicker for children. (Martcheva & Crispino-O'Connell, 2002)

Since this disease is associated with a high fatality rate if not treated early, antibiotics should be administered promptly if symptoms are visible and evaluation cannot be done immediately. (Bartfield, 2000) Penicillin was found to be a great tool in fighting

the bacterium causing meningococcal meningitis and it is still used today. (Kloss, 1996)

When the disease is identified and treated early most patients will go back to a normal state of consciousness within two days and any sign of the meninges being irritated will be gone after four days. (Vedros, 1987)

1.3 Epidemiology

When meningococcal disease was first detected there was no way to study the ailment since it was hardly reported. This changed early in the 20th century when countries started requiring notification. However this introduced a new problem of under notification. Scientist suggests that data on meningococcal disease may only reflect 65% of the actual occurrence of the disease. Fatal cases are reported more often which can lead to an over estimate of the mortality rate compared to the disease occurrence rate.

Notification did help scientist to discover that meningococcal disease was a problem in overcrowded areas such as cities. This crowding effect was also seen in the military. (Cartwright) In World War I, there were 5,839 cases of meningococcal meningitis in the army with a fatality rate of 39%. (Nelson, 1942) Early on when trying to prevent the spread of the disease in the military it was determined that spacing the troops appropriately was a big help. Meningococcal disease has not affected the military as much since World War II. This may be due to the vaccination required or preventive measures that make sure living spaces are sanitary. (Cartwright, 1995)

The last major epidemic in the U.S. occurred in 1943. (Kloss, 1996) Endemically (regular occurrence of meningitis), the rate in the United States of America is 1 out of

100,000 people, with the disease occurring mostly among children under the age of five. In European countries the estimate is similar with 1-3 per 100,000 people with the same age constraint. (Cartwright, 1995)

Meningitis epidemics are not a great threat to the United States of America and European Countries. However in developing countries it can be considered a major cause of death. A good example of this is the area referred to as the meningitis belt in Africa.



Figure 2: Meningitis Belt; <http://wwwn.cdc.gov/travel/yellowBookCh4-Menin.aspx>

Sub-Saharan African countries experience a high death rate due to meningitis epidemics in children under 15. These countries have been identified as having recurring meningitis

epidemics every 5 to 12 years. These reoccurring epidemics spread throughout the continent from east to west. This pattern was first described about 40 years ago. (Teyssou & Rouxie. 2007)

The last major epidemic to hit the African meningitis belt occurred in 1996 to 1997 affecting about 10 countries. In this epidemic 250,000 people were infected with the disease killing around 25,000. This type of epidemic creates social and economic problems in these countries.

One of the most recent epidemic of meningococcal disease occurred in Burkina Faso. Meningitis had spread to 22 districts in the country by March 20, 2007. One million people had been vaccinated and it was planned that 3 million more would be vaccinated in the next few days. At that time almost 600 of the 7000 infected died. This particular epidemic was also reported to have reached the Democratic Republic of Congo with 7000 cases, Sudan with 700 cases and Uganda with 3000 cases. (Kieny, 2007)

CHAPTER 2 Review of Infection Modeling Literature

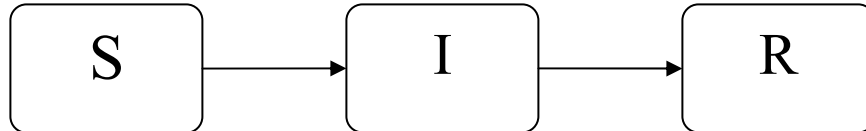
2.1 Classic SIR model

Before developing and analyzing a model for meningitis we first examine the classic SIR, (susceptible, infected, removed), model. In addition we will reflect on ways others have utilized and altered the basic SIR model to model specific diseases. Some of the diseases that have been modeled using a variation of SIR model include polio, influenza, mumps, and SARS.

In the paper “*A Contribution to the Mathematical Theory of Epidemics*” Kermack and McKendrick (1927) introduce the idea of generalizing the process of analyzing the spread of contagious epidemics. Today this generalization is known as an SIR model. In a basic SIR model three groups are considered. These three groups are identified as 1) *S*-susceptible 2) *I*-infected and 3) *R*-removed. The modeling of the disease process begins by considering an infected person coming into contact with a group of ‘healthy’ or susceptible people that are at risk of becoming infected. A portion of these susceptible people will then become infected, moving to the group of people who are infected. Once an infected person dies or recovers from the disease they then become a part of the group of people who are no longer infected. When there is an epidemic the number of susceptible people decreases. The model describes the progression of an epidemic considering everyone is

equally likely to become infected. Immunity after infection is assumed, meaning individuals do not return to the susceptible group once infected.

In a basic SIR model the flow of the disease can be represented as



The classic Kermack-McKendrick model is comprised of three ordinary differential equations (ODE's).

$$\frac{dS}{dt} = -rSI \quad (2.1)$$

$$\frac{dI}{dt} = rSI - aI \quad (2.2)$$

$$\frac{dR}{dt} = aI \quad (2.3)$$

These ODE's are based on three assumptions. The first assumption is that the infective class grows at some rate r that is proportional to the number of infected and susceptible individuals. The rate of moving from S to I depends on interaction of the two groups. The susceptible class decreases by the same rate. The second assumption is that the rate, a , by which infectives are removed from the infective class and become a part of the recovered class, is constant. The third assumption is that as soon as a susceptible becomes infected, that individual has the ability to infect others. Since r and a represent rates they are both positive.

Since S , I , and R represent population values only nonnegative solutions are considered. When dealing with the model the total population, N , is considered constant. At any given time an individual in the population is susceptible, infected or recovered so $S(t) + I(t) + R(t) = N$. When thinking of an epidemic we can assume that in the beginning of an epidemic the number of susceptibles and infectives are both greater than 0 and there is no one in the recovered class. This leads to initial conditions associated with an epidemic model being

$$S(0) = S_0 > 0, I(0) = I_0 > 0, \text{ and } R(0) = 0. \quad (2.4)$$

Despite its basic nature this model can help provide us with valuable information about an epidemic. When considering an epidemic situation the main concerns are 1) How fast will the infective class grow? 2) When will the infective class decrease? 3) When will the epidemic be over? These questions can be answered by knowing the rate at which an infection will reproduce. This rate is known as the basic reproduction rate, \mathfrak{R}_0 , of the infection.

The reproduction rate for the basic SIR model can be derived by analyzing simple facts about $S(t)$ and $I(t)$. From (2.1) we know that the class of susceptibles is decreasing. This information can be acquired from the fact that $\frac{dS}{dt} \leq 0$. Since the class of susceptibles is decreasing we know that $S(t) \leq S_0$. Following this fact we can propose that if $S(0) < \frac{a}{r}$ then $S(t) < \frac{a}{r}$, which means individuals are recovering faster than individuals are infecting. Rearranging the last inequality we obtain $rS(t) < a$, which implies

$rS(t) - a \leq 0$ for all $t \geq 0$. We can then conclude that this would then cause the infected class to decrease. This can be written as the following implication: If $S(0) < \frac{a}{r}$ then

$\frac{dI}{dt} = I(rS(t) - a) \leq 0$ for all $t \geq 0$. We can also gather from this that if $rS(t) > a$ then $I(t)$

will initially increase. The relative removal rate is $\frac{a}{r}$ and the infection's contact rate is the

reciprocal $\frac{r}{a}$. Analyzing the values of our parameters that will make $I(t)$ negative or

positive is related to finding \mathfrak{R}_0 . The rate at which the infection will reproduce is the

product of the infection's contact rate and the number of susceptibles at time zero. We can

now give a formula for \mathfrak{R}_0 that applies to the basic SIR model.

$$\mathfrak{R}_0 = \frac{rS_0}{a} \quad (2.5)$$

In the case where $I(t)$ is decreasing, $\mathfrak{R}_0 < 1$ and the infection will die out. When $I(t)$ is increasing then $\mathfrak{R}_0 > 1$ and we are dealing with an epidemic.

When modeling an epidemic we should also consider equilibrium points and their stability nature. In the classic SIR model it is possible to eliminate $\frac{dR}{dt}$ because of the

relationship $S(t) + I(t) + R(t) = N$. $R(t)$ can be written as a function of $S(t)$, $I(t)$ and N

and therefore becomes unnecessary. However we will call on $R(t)$ again in order to

examine $S(t)$. Now if we contemplate the equations $\frac{dS}{dt}$ and $\frac{dI}{dt}$ we can come up with

some important information concerning an epidemic.

$$\frac{dI}{dS} = \frac{(rS-a)I}{-rSI} \Rightarrow \frac{dI}{dS} = -1 + \frac{a}{rS} \Rightarrow dI = (-1 + \frac{a}{rS})dS \quad (2.6)$$

Integrating we get

$$I(t) = -S(t) + \frac{a}{r} \ln S(t) + c \quad (2.7)$$

The constant c can be found by rearranging the above equation and using our initial conditions.

$$c = I_0 + S_0 - \frac{a}{r} \ln S_0 \quad (2.8)$$

We then end up with

$$I(t) = -S(t) + \frac{a}{r} \ln S(t) + I_0 + S_0 - \frac{a}{r} \ln S_0 \quad (2.9)$$

$S(t)$ can be obtained in the same manner by considering $\frac{dS}{dR}$.

$$\frac{dS}{dR} = \frac{-rSI}{aI} \Rightarrow \frac{1}{S} dS = -\frac{r}{a} dR \quad (2.10)$$

Integrating we get

$$S(t) = e^{-\frac{r}{a}R+c} \quad (2.11)$$

$$c = \ln(S_0) + \frac{r}{a} R_0 = \ln(S_0) \quad (2.12)$$

We then end up with

$$S(t) = S_0 e^{-\frac{r}{a}R} \quad (2.13)$$

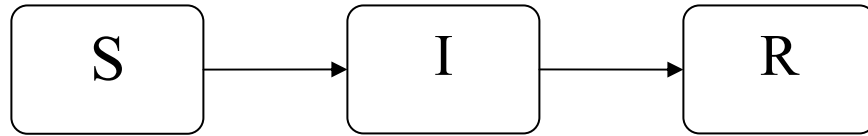
Now dealing with the two differential equations, $\frac{dS}{dt}$ and $\frac{dI}{dt}$, we consider some important cases within a general epidemic. A system of ordinary differential equations has equilibrium when $\frac{dX}{dt} = 0$ for all X 's in the system. Since $\frac{dS}{dt} = -rSI$ we know that the class of susceptibles experiences an equilibrium if either $S(t) = 0$ or $I(t) = 0$. $S(t) = 0$ is not a valid solution since from the solution, $S(t) = S_0 e^{-\frac{r}{a} I}$, it can be shown that as $t \rightarrow \infty$, $S(t) \rightarrow 0$ but will never be zero. $I(t) = 0$ is the case where no one in the population is infected therefore no additional infections are occurring. Examining $\frac{dI}{dt} = rSI - aI$, we see that $I(t)$ is zero if either $S(t) = \frac{a}{r}$ or $I(t) = 0$. The point at which a derivative equals 0 is a maximum or a minimum. $S(t) = \frac{a}{r}$ happens to be I_{\max} , which relates to the severity of an epidemic. I_{\max} will be the time when the most people are infected during the entire epidemic. After $I(t)$ reaches I_{\max} the number infected will start to decrease. The only equilibrium for the system is $I(t) = 0$, where no disease is present. (Murray, 2002)

2.2 Polio SIR Model with Vaccine

The vaccination process for many diseases involves using a virus that has been altered in such a way that the virus loses most of its ability to cause the disease. If a small proportion of the population is treated with this type of vaccine the virus may actually

experience an increase in power. The paper “*Circulating Vaccine Derived Polio Viruses and their Impact on Global Polio Eradication*”, uses an SIR model to examine the risk associated in using a live vaccine for polio.

In this SIR model it is assumed that recovered individuals become immune to the virus which means that they do not return to the susceptible class. This immunity is also considered to be permanent. Individuals belonging to the susceptible class that receive vaccination become immune and immediately join the recovered class. It is also assumed that the infection does not cause death. All the assumptions that were associated with the classic SIR model hold here as well. The model can be represented by the same flow chart used for the classic SIR.



The model is written as

$$\frac{d\tilde{S}}{dt} = (1-p)\nu N - \frac{\beta}{N} \tilde{I}\tilde{S} - \mu\tilde{S} \quad (2.14)$$

$$\frac{d\tilde{I}}{dt} = \frac{\beta}{N} \tilde{I}\tilde{S} - (\mu + \gamma)\tilde{I} \quad (2.15)$$

$$\frac{d\tilde{R}}{dt} = p\nu N + \gamma\tilde{I} - \mu\tilde{R} \quad (2.16)$$

The parameters associated with the model are p - proportion vaccinated, ν - birth rate, β - transmission rate, μ - natural death rate, and γ - recovery rate. All rates are between 0 and 1.

As it was in the classic SIR model the total population is $N = \tilde{S} + \tilde{I} + \tilde{R}$. For convenience

the SIR model is scaled by the population, N , so $1 = S + I + R$, where $S = \frac{\tilde{S}}{N}$, $I = \frac{\tilde{I}}{N}$,

and $R = \frac{\tilde{R}}{N}$. The model is considering a relatively short time scale and it assumes no

population growth so the estimate $\mu = \nu$ is used. So all μ 's within the system are replaced

with ν 's. For $X = S, I$, or R , we have $X = \frac{\tilde{X}}{N}$, and also

$$\frac{dX}{dt} = \frac{1}{N} \frac{d\tilde{X}}{dt} - \frac{X}{N^2} \frac{dN}{dt} \quad (2.17)$$

Since the total population, N , is constant then $\frac{dN}{dt} = 0$. The differential equation becomes

$$\frac{dX}{dt} = \frac{1}{N} \frac{d\tilde{X}}{dt} \quad (2.18)$$

For S

$$\frac{dS}{dt} = \frac{1}{N} \frac{d\tilde{S}}{dt} \Rightarrow \frac{dS}{dt} = (1-p)\nu - \beta IS - \nu S \quad (2.19)$$

For I

$$\frac{dI}{dt} = \frac{1}{N} \frac{d\tilde{I}}{dt} \Rightarrow \frac{dI}{dt} = \beta IS - \gamma I - \nu I \quad (2.20)$$

For R

$$\frac{dR}{dt} = \frac{1}{N} \frac{d\tilde{R}}{dt} \Rightarrow \frac{dR}{dt} = p\nu + \gamma I - \nu R \quad (2.21)$$

With the condition $1 = S + I + R$, our system is over determined. We can drop the $\frac{dR}{dt}$

equation leaving the two equations

$$\frac{dS}{dt} = (1-p)\nu - \beta IS - \nu S \quad (2.22)$$

$$\frac{dI}{dt} = \beta IS - \gamma I - \nu I \quad (2.23)$$

To find \mathfrak{R}_0 we once again examine the parameters that control whether or not $\frac{dI}{dt}$ is

positive or negative.

$$\frac{dI}{dt} = \beta IS - \gamma I - \nu I \Rightarrow \frac{dI}{dt} = I[\beta S - (\gamma + \nu)]$$

I is never negative, so the term $\beta S - (\gamma + \nu)$ determines when $\frac{dI}{dt}$ is negative or positive.

$\frac{dI}{dt}$ is negative when $\beta S < \gamma + \nu$. In order for this inequality to hold, it needs to be true

for all values of S . Well we know that $0 < S \leq 1$. In order for $\frac{dI}{dt} < 0$ for all values of S we

need $\beta < \gamma + \nu$. Considering $\beta S < \gamma + \nu$ we know that as S decreases so does the value of βS , which means max S gives max βS . So if the highest value of βS is less than $\gamma + \nu$ then so are all other values of βS . Well the highest value of S is 1. So if $\beta(1) < \gamma + \nu$ then so are all other values of βS . This gives us the stronger inequality

$$\beta < \gamma + \nu \quad (2.24)$$

$\frac{dI}{dt}$ is positive when $\beta S > \gamma + \nu$. However this situation is not quite the same as the one

preceding. $\beta > \gamma + \nu$ implies $\beta S > \gamma + \nu$ only when $S > \frac{\gamma + \nu}{\beta}$. So given a particular S_0 ,

$\frac{dI}{dt}$ will increase until $S = \frac{\gamma + \nu}{\beta}$, where it will then start to decrease. During the period

that $\frac{dI}{dt}$ increases the number of secondary infections can be given as

$$\beta > \gamma + \nu \quad (2.25)$$

From this information a reproductive ratio, \mathfrak{R}_0 can be defined as

$$\mathfrak{R}_0 = \frac{\beta}{\gamma + \nu} \quad (2.26)$$

The system (2.22) & (2.23) has two equilibriums. They were found by finding solutions

of $\frac{dS}{dt} = 0$ and $\frac{dI}{dt} = 0$.

For $\frac{dS}{dt} = 0$ we get

$$S = \frac{(1-p)\nu}{\beta I - \nu} \text{ or } I = \frac{(1-p)\nu - \nu S}{\beta S} \quad (2.27)$$

For $\frac{dI}{dt} = 0$ we get

$$S = \frac{\gamma + \nu}{\beta} \text{ or } I = 0 \quad (2.28)$$

An equilibrium occurs when all differential equations in the system are zero. This gives the disease free equilibrium, (DFE),

$$S_1^* = 1 - p, I_1^* = 0 \quad (2.29)$$

and the endemic equilibrium

$$S_2^* = \frac{\gamma + \nu}{\beta}, I_2^* = \frac{\nu}{\gamma + \nu} \left[1 - \left(\frac{\gamma + \nu}{\beta} \right) - p \right] \quad (2.30)$$

Theorem (1.1); (Allen 2007)

Assume the functions $f(x, y)$ and $g(x, y)$ have continuous first-order partial derivatives in x and y on some open set in \mathbf{R}^2 that contains the point (x^, y^*) . Then the equilibrium point (x^*, y^*) of the nonlinear system*

$$x_{t+1} = f(x_t, y_t), y_{t+1} = g(x_t, y_t),$$

Is locally asymptotically stable if the eigenvalues of the Jacobian matrix J evaluated at the equilibrium satisfy $|\lambda_i| < 1 \xleftrightarrow{\text{iff}} |Tr(J)| < 1 + \det(j) < 2$.

The equilibrium is unstable if some $|\lambda_i| > 1$.

In order to find \mathfrak{R}_0 , we look at the case in which there is no immunity is observed. This means $p = 0$. The lack of immunity causes the DFE to change such that

$$S_1^* = N = 1, I_1^* = 0 \quad (2.31)$$

The Jacobian matrix for this S-I system is

$$J(S, I) = \begin{pmatrix} \beta I - \nu & \beta S \\ \beta I & \beta S - \gamma - \nu \end{pmatrix} \quad (2.32)$$

The Jacobian matrix at the DFE is

$$J(1, 0) = \begin{pmatrix} -\nu & \beta \\ 0 & \beta - \gamma - \nu \end{pmatrix} \quad (2.33)$$

This gives us the eigenvalues

$$\lambda_1 = -\nu \text{ and } \lambda_2 = \beta - \gamma - \nu \quad (2.34)$$

From the theorem it is clear that the DFE is locally asymptotically stable if $|\lambda_{1,2}| < 1$. Since

$|\lambda_1| = \nu$ and ν is the parameter representing the birth rate we can conclude that $0 < \lambda_1 < 1$.

The second eigenvalues is satisfied as long as $\frac{\beta}{1 + \gamma + \nu} < 1$ and $\beta < \gamma + \nu$. $\frac{\beta}{1 + \gamma + \nu} < 1$

holds for all values of β , γ , and ν since β is a rate and therefore will never be greater than

$1 + \gamma + \nu$. The reproduction number \mathfrak{R}_0 , determines whether or not $\beta > \gamma + \nu$. If $\mathfrak{R}_0 < 1$

then $\beta < \gamma + \nu$ and the DFE is stable. If $\mathfrak{R}_0 > 1$ then $\beta > \gamma + \nu$ and the DFE unstable.

Writing the endemic equilibrium is in terms of \mathfrak{R}_0 , gives

$$S_2^* = \frac{1}{\mathfrak{R}_0}, \quad I_2^* = \frac{\nu}{\lambda + \nu} \left(1 - \frac{1}{\mathfrak{R}_0} - p \right) \quad (2.35)$$

I_2^* is further simplified by defining two new variables

$$f = \frac{\nu}{\gamma + \nu} \text{ and } p_{crit} = 1 - \frac{1}{\mathfrak{R}_0} \quad (2.36)$$

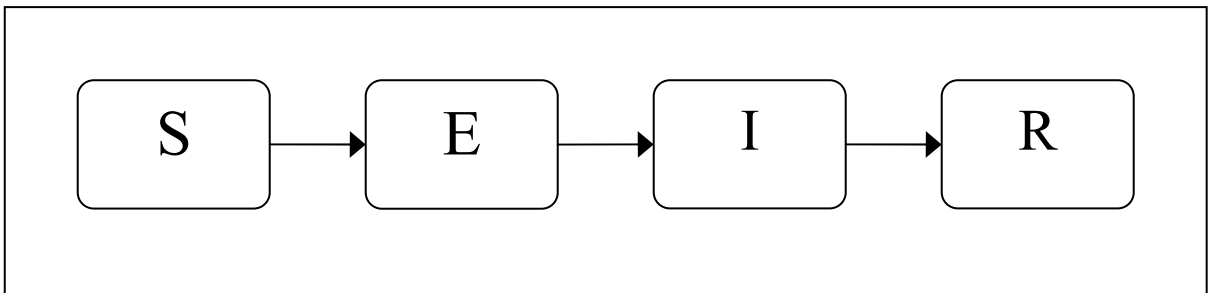
The endemic equilibrium is now expressed as

$$S_2^* = \frac{1}{\mathfrak{R}_0}, I_2^* = f(p_{crit} - p) \quad (2.37)$$

Since we are dealing with a biological system, $I \geq 0$ it is observed that I_2^* can only exist when $p < p_{crit}$ which are the only values for which I_2^* will be positive. If $p > p_{crit}$, the endemic equilibrium does not exist, and the DFE is globally asymptotically stable. So, values that are close to the equilibrium will stay close and all solutions approach the DFE. However if $p < p_{crit}$ then all solutions such that $I_0 > 0$ will approach the endemic equilibrium. Therefore p_{crit} is the minimum level of vaccination needed in order to prevent the perseverance of the disease. (Wagner & Earn, 2007)

2.3 SEIR Model with Vertical Transmission

The paper, *Global Dynamics of an SEIR Epidemic Model With Vertical Transmission*, studies an SEIR model that considers horizontal (normal contact) and vertical (by birth), transmission of disease. This model is intended to model human diseases such as hepatitis B, Chagas disease, and AIDS. It is assumed that a portion of the population is infectious at birth. The exposed class is included to take into account the infected population that is not infectious. It is then assumed that a portion of the offspring associated with infected class will be infected at birth, and will enter the exposed class. The model's flow is represented as:



The model is given as

$$\frac{dS}{dt} = b - \lambda IS - pbE - qbI - bS \quad (2.38)$$

$$\frac{dE}{dt} = \lambda IS + pbE + qbI - (\varepsilon + b)E \quad (2.39)$$

$$\frac{dI}{dt} = \varepsilon E - (\gamma + b)I \quad (2.40)$$

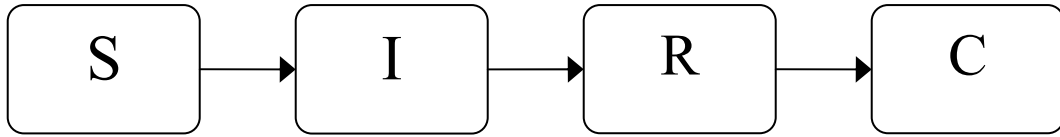
$$\frac{dR}{dt} = \lambda I - bR \quad (2.41)$$

Where the parameters are b - birth rate, λ - rate at which infected individual recover, p - latent portion infected at birth, q - infectious portion infected at birth, and ε - rate at which infected recover. The model can easily be changed by eliminating certain parameters to fit specific diseases. The basic reproduction number \mathfrak{R}_0 , a function of p and q is then proven to completely determine the global dynamics of the model. If $\mathfrak{R}_0 \leq 1$ then the DFE is globally asymptotically stable and if $\mathfrak{R}_0 > 1$ then the unique endemic equilibrium is globally asymptotically stable within the feasible region.

2.4 Influenza SIRC Model

An SIRC model is developed and analyzed in *The SIRC Model and Influenza A*. In this paper a fourth class (C), cross-immune, is added to the classic SIR model representing individuals that have recovered after being infected by different strains of the influenza A

virus. The idea behind this model is that an individual will move from the infectious class to the recovered class after recovering from whichever strain is dominant at the time of their infection. Then after some time when there is a new dominant strain the individual will move into the cross-immune class because they will only have partial immunity to the new strain. The flow of the model is represented as:



This is represented by the model

$$\frac{dS}{dt} = \mu(1 - S) - \beta SI + \gamma C \quad (2.42)$$

$$\frac{dI}{dt} = \beta SI + \sigma \beta CI - (\mu + \alpha)I \quad (2.43)$$

$$\frac{dR}{dt} = (1 - \sigma)\beta CI + \alpha I - (\mu + \delta)R \quad (2.44)$$

$$\frac{dC}{dt} = \delta R - \beta CI - (\mu + \gamma)C \quad (2.45)$$

Where the parameters are μ - mortality rate, β - contact rate, α - time spent by individual in I, δ - time spent by individual in R, γ - time spent by individual in C, and σ - portion of cross-immune individuals that become infected. The reproduction number,

\mathfrak{R}_0 , is given as $\mathfrak{R}_0 = \frac{\beta}{\mu + \alpha}$ after analyzing the stability of the DFE,

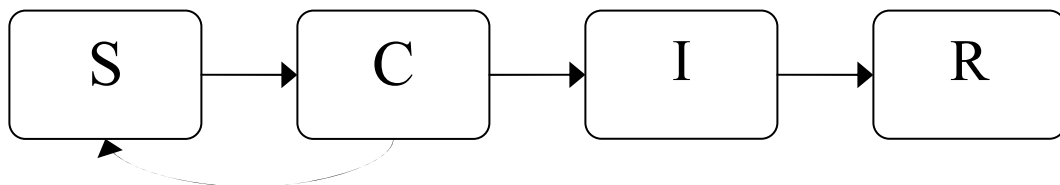
$(S^*, I^*, R^*, C^*) = (1, 0, 0, 0)$. Again, the DFE is asymptotically stable if and only if $\mathfrak{R}_0 < 1$.

If $\mathfrak{R}_0 > 1$ then the DFE is instead a saddle node and there exist a unique endemic equilibrium.

CHAPTER 3 Development and Analysis of the Meningitis Model

3.1 Meningitis Model

When developing a model for meningitis it was essential to first consider the different classes involved. At any given time an individual is a member of one of the four classes S - Susceptible, C - Carrier, I - infected, or R -Removed. A proportion of the susceptible class will come into contact with carriers. Individuals in the carrier class are able to infect others without suffering from the disease themselves. They will then either become infected or move back to the susceptible class. Individuals in the infected class come directly from the carrier class. The removed class consists of those in the infected class that have either recovered from the disease or died, and the individuals who are vaccinated. The flow of the disease is as follows:



This is represented by the model

$$\frac{d\tilde{S}}{dt} = (1-p)\nu N - \frac{\beta}{N}\tilde{C}\tilde{S} + \gamma_1\tilde{C} - \mu_1\tilde{S} \quad (3.1)$$

$$\frac{d\tilde{C}}{dt} = \frac{\beta}{N}\tilde{C}\tilde{S} - \gamma_1\tilde{C} - \alpha\tilde{C} - \mu_1\tilde{C} \quad (3.2)$$

$$\frac{d\tilde{I}}{dt} = \alpha\tilde{C} - \gamma_2\tilde{I} - \mu_2\tilde{I} - \mu_1\tilde{I} \quad (3.3)$$

$$\frac{d\tilde{R}}{dt} = p\nu N + \gamma_2\tilde{I} + \mu_2\tilde{I} - \mu_1\tilde{R} \quad (3.4)$$

The parameters of the model are p - proportion vaccinated, β - transmission rate, α - infection rate of carriers, γ_1 - rate at which carriers return to the susceptible class, γ_2 - infected recovery rate, μ_1 - natural death rate, and μ_2 - rate of death due to infection. The rate of change in the susceptible class, with respect to time, is given by the proportion of people vaccinated, $(1-p)\nu N$ plus those that return to the susceptible class from the carrier class minus those interacting with individuals belonging to the carrier class, $\frac{\beta}{N}\tilde{C}\tilde{S}$ and the natural death of individuals in the susceptible class, $\mu_1\tilde{S}$. In the carrier class this rate of change is given by the proportion of the susceptible class interacting with the carrier class, $\frac{\beta}{N}\tilde{C}\tilde{S}$ minus those returning to the susceptible class, $\gamma_1\tilde{C}$ those leaving the carrier class by becoming infected, $\alpha\tilde{C}$ and those leaving the carrier class due to natural death,

$\mu_1 \tilde{C}$. The variation in the infected class is given by the portion of carriers that become infected, $\alpha \tilde{C}$ minus the portion of the infected class that either recover, $\gamma_2 \tilde{I}$ die from infection, $\mu_2 \tilde{I}$ or experience natural death, $\mu_1 \tilde{I}$. The change in the recovery class is the sum of the portion of individuals that have been vaccinated, $p\nu N$ the recovered individuals from the infected class, $\gamma_2 \tilde{I}$ and those that die from natural causes, $\mu_1 \tilde{R}$. It is assumed that individuals in this class cannot reacquire the disease.

For the SCIR model the total population at any given time is $N = \tilde{S} + \tilde{C} + \tilde{I} + \tilde{R}$. This model is considering a time period of no more than a few years. Since we are dealing with a short time scale the population can be considered constant. So the estimate $\mu_1 = \nu$ is used. Looking at the four differential equations we see that when we combine all four everything cancels out with the exception of $(1-p)\nu N$, $p\nu N$, $-\mu_1 \tilde{S}$, $-\mu_1 \tilde{C}$, $-\mu_1 \tilde{I}$, & $-\mu_1 \tilde{R}$. The estimate, $\mu_1 = \nu$ helps to ensure that $\frac{dS}{dt} + \frac{dC}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0$. Since $\mu_1 = \nu$ we can rewrite the equation replacing all μ_1 's with ν 's. Now when we add the few that didn't cancel out we obtain

$(1-p)\nu N + p\nu N - \nu \tilde{S} - \nu \tilde{C} - \nu \tilde{I} - \nu \tilde{R} = \nu N - \nu(\tilde{S} + \tilde{C} + \tilde{I} + \tilde{R})$ which becomes 0 from the fact $N = \tilde{S} + \tilde{C} + \tilde{I} + \tilde{R}$.

Similar to the method used in the analysis of the polio model the meningitis model, the class populations are scaled by the total population, N , so $1 = S + C + I + R$, where

$S = \frac{\tilde{S}}{N}$, $C = \frac{\tilde{C}}{N}$, $I = \frac{\tilde{I}}{N}$, and $R = \frac{\tilde{R}}{N}$. For $X = S, C, I$, or R , we have $X = \frac{\tilde{X}}{N}$, and equation

$\frac{dX}{dt} = \frac{1}{N} \frac{d\tilde{X}}{dt} - \frac{X}{N^2} \frac{dN}{dt}$ (2.17) holds. Since the total population, N , is constant $\frac{dN}{dt} = 0$. So

equation $\frac{dX}{dt} = \frac{1}{N} \frac{d\tilde{X}}{dt}$ (2.18) holds. We are now able to simplify the SCIR model.

For S , $\frac{dS}{dt} = \frac{1}{N} \frac{d\tilde{S}}{dt}$

$$\frac{dS}{dt} = (1-p)\nu - \beta CS + \gamma_1 C - \nu S \quad (3.5)$$

For C , $\frac{dC}{dt} = \frac{1}{N} \frac{d\tilde{C}}{dt}$

$$\frac{dC}{dt} = \beta CS - \gamma_1 C - \alpha C - \nu C \quad (3.6)$$

For I , $\frac{dI}{dt} = \frac{1}{N} \frac{d\tilde{I}}{dt}$

$$\frac{dI}{dt} = \alpha C - \gamma_2 I - \mu_2 I - \nu I \quad (3.7)$$

For R , $\frac{dR}{dt} = \frac{1}{N} \frac{d\tilde{R}}{dt}$

$$\frac{dR}{dt} = p + \gamma_2 I + \mu_2 I - \nu R \quad (3.8)$$

The fact that $1 = S + C + I + R$ allows us to drop R since it can be expressed as a function of S , C , and I . This simplification makes the model easier to analyze. We are left with three differential equations.

$$\frac{dS}{dt} = (1-p)\nu - \beta CS + \gamma_1 C - \nu S \quad (3.9)$$

$$\frac{dC}{dt} = \beta CS - \gamma_1 C - \alpha C - \nu C \quad (3.10)$$

$$\frac{dI}{dt} = \alpha C - \gamma_2 I - \mu_2 I - \nu I \quad (3.11)$$

3.2 Reproduction Number

As discussed before the reproduction number represents the number of secondary infections caused by the average infectious individual. The reproduction number for this model is found by using a method described in the van den Driessche and Watmough,

(2002), paper. The variable x is used to represent all classes so $x = \left(\frac{dS}{dt}, \frac{dC}{dt}, \frac{dI}{dt} \right)^T$.

Then $\mathcal{F}(x)$ represents the rate at which new infections appear. While $\mathcal{V}^+(x)$ and $\mathcal{V}^-(x)$ are the rates at which individuals enter and leave each class. From this new variables are defined such that

$$F = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(x_0) \right] \text{ and } V = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(x_0) \right] \text{ with } 1 \leq i, j \leq m. \quad (3.12)$$

where m represents the number of classes in which individuals are infectious. The reproduction number is then defined as

$$\mathfrak{R}_0 = \rho(FV^{-1}), \quad (3.13)$$

where $\rho(A)$ represents the maximum eigenvalue of matrix A .

Using this method for the meningitis model gives

$$\mathfrak{F}(x) = \begin{pmatrix} 0 \\ \beta CS \\ 0 \end{pmatrix} \quad (3.14)$$

$$\mathfrak{V}(x) = \begin{pmatrix} -(1-p)\nu - \gamma_1 C + \nu S \\ \alpha C + \gamma_1 C + \nu C \\ -\alpha C + \gamma_2 I + \mu_2 I + \nu I \end{pmatrix} \quad (3.15)$$

Since C and I are the only classes in which individuals are infectious $m = 2$ and we obtain

$$F = \begin{pmatrix} \beta & 0 \\ 0 & 0 \end{pmatrix} \quad (3.16)$$

$$V = \begin{pmatrix} \gamma_1 + \alpha + \nu & 0 \\ -\alpha & \gamma_2 + \mu_2 + \nu \end{pmatrix} \quad (3.17)$$

$$V^{-1} = \begin{pmatrix} \frac{1}{\gamma_1 + \alpha + \nu} & 0 \\ \frac{\alpha}{(\gamma_1 + \alpha + \nu)(\gamma_2 + \mu_2 + \nu)} & \frac{1}{\gamma_2 + \mu_2 + \nu} \end{pmatrix} \quad (3.18)$$

From this we obtain

$$FV^{-1} = \begin{pmatrix} \frac{\beta}{\gamma_1 + \alpha + \nu} & 0 \\ 0 & 0 \end{pmatrix} \quad (3.19)$$

The eigenvalues associated with FV^{-1} are 0, and $\frac{\beta}{\gamma_1 + \alpha + \nu}$ which gives us the

reproduction number,

$$\mathfrak{R}_0 = \frac{\beta}{\gamma_1 + \alpha + \nu}$$

3.3 Equilibriums

The system (3.9), (3.10) & (3.11) has two equilibriums. These equilibrium points are

found by finding the intersection of the solutions of $\frac{dS}{dt} = 0$, $\frac{dC}{dt} = 0$ and $\frac{dI}{dt} = 0$.

For $\frac{dS}{dt} = 0$ we get

$$S = \frac{(1-p)\nu + \gamma_1 C}{\beta C + \nu} \text{ or } C = \frac{(1-p)\nu - \nu S}{\beta S - \gamma_1} \quad (3.20)$$

For $\frac{dC}{dt} = 0$ we get

$$C = 0 \text{ or } S = \frac{\gamma_1 + \alpha + \nu}{\beta} \quad (3.21)$$

For $\frac{dI}{dt} = 0$ we get

$$C = \frac{(\gamma_2 + \mu_2 + \nu)I}{\alpha} \text{ or } I = \frac{\alpha C}{\gamma_2 + \mu_2 + \nu} \quad (3.22)$$

From these six equations we are able to determine our two equilibriums. To find the first

equilibrium, we consider $\frac{dC}{dt} = 0$ and the case in which $C = 0$. Using this information in

the case $\frac{dI}{dt} = 0$ and $I = \frac{\alpha C}{\gamma_2 + \nu}$ we see that I would also become zero. We then consider

$C = 0$ where it intersects (3.20) as it is placed inside equation $S = \frac{(1-p)\nu + \gamma_1 C}{\beta C + \nu}$. This

gives $S = 1 - p$ which is the population that has not been vaccinated. Since there are no individuals who are infected or carriers this represents a disease free equilibrium. In this case the DFE is:

$$S_1^* = 1 - p, C_1^* = 0, I_1^* = 0 \quad (3.23)$$

Now taking the other nullcline from $\frac{dC}{dt} = 0, S = \frac{\gamma_1 + \alpha + \nu}{\beta}$ we use it to solve for C in

terms of our parameters in equation $C = \frac{(1-p)\nu - \nu S}{\beta S - \gamma_1}$ from (3.20). We

obtain $C = \frac{\nu}{\alpha + \nu} \left(1 - p - \frac{\gamma_1 + \alpha + \nu}{\beta}\right)$. We then look at $\frac{dI}{dt} = 0$ and use

$C = \frac{\nu}{\alpha + \nu} \left(1 - p - \frac{\gamma_1 + \alpha + \nu}{\beta}\right)$ to solve $I = \frac{\alpha C}{\gamma_2 + \mu_2 + \nu}$ for I in terms of our parameters.

From this we get $I = \frac{\alpha \nu}{(\alpha + \nu)(\gamma_2 + \mu_2 + \nu)}$. Since there no other places where the nullclines

will intersect this gives us the unique endemic equilibrium:

$$\begin{aligned} S_2^* &= \frac{\gamma_1 + \alpha + \nu}{\beta}, C_2^* = \frac{\nu}{\alpha + \nu} \left(1 - p - \frac{\gamma_1 + \alpha + \nu}{\beta}\right), \\ I_2^* &= \frac{\alpha \nu}{(\alpha + \nu)(\gamma_2 + \mu_2 + \nu)} \left(1 - p - \frac{\gamma_1 + \alpha + \nu}{\beta}\right) \end{aligned} \quad (3.24)$$

3.4 Stability Nature of Disease Free Equilibrium

To understand how the parameters affect the meningitis model we analyze the stability nature of our DFE when immunity is not involved using theorem 1.1. We first find the Jacobian matrix for the S - C - I system. The matrix is

$$J(S, C, I) = \begin{pmatrix} -\beta C - \nu & -\beta S + \gamma_1 & 0 \\ \beta C & \beta S - \gamma_1 - \alpha - \nu & 0 \\ 0 & \alpha & -\gamma_2 - \mu_2 - \nu \end{pmatrix} \quad (3.25)$$

Since we are dealing with the case in which there is no immunity our DFE becomes

$$S_1^* = 1, C_1^* = 0, I_1^* = 0 \quad (3.26)$$

At the DFE, with no immunity, this becomes

$$J(S_1^*, C_1^*, I_1^*) = \begin{pmatrix} -\nu & -\beta + \gamma_1 & 0 \\ 0 & \beta - \gamma_1 - \alpha - \nu & 0 \\ 0 & \alpha & -\gamma_2 - \mu_2 - \nu \end{pmatrix} \quad (3.27)$$

This gives the eigenvalues

$$\lambda_1 = -\nu, \lambda_2 = -\gamma_2 - \mu_2 - \nu, \text{ and } \lambda_3 = \beta - \gamma_1 - \alpha - \nu$$

In order for the DFE to be locally asymptotically stable we need $|\lambda_{1,2,3}| < 1$. It is obvious

that $|\lambda_1| < 1$ since $\lambda_1 = -\nu$. $|\lambda_2| < 1$ and $|\lambda_3| < 1$ hold if $\gamma_2 + \mu_2 + \nu < 1$ and $|\beta - \gamma_1 - \alpha - \nu| < 1$

respectively.

3.5 Existence of endemic equilibrium

To understand how vaccination affects the model we then turn to the endemic equilibrium, (3.24). First we write our endemic equilibrium in terms of the reproduction number, \mathfrak{R}_0 .

$$S_2^* = \frac{1}{\mathfrak{R}_0}, \quad C_2^* = \frac{\nu}{\alpha + \nu} \left(1 - p - \frac{1}{\mathfrak{R}_0}\right), \quad I_2^* = \frac{\alpha \nu}{(\alpha + \nu)(\gamma_2 + \mu_2 + \nu)} \left(1 - p - \frac{1}{\mathfrak{R}_0}\right) \quad (3.28)$$

We then define a few new variables to simplify the equilibrium. So we let

$$f = \frac{\nu}{\alpha + \nu}, \quad g = \frac{\alpha}{\gamma_2 + \mu_2 + \nu}, \quad \text{and} \quad p_{crit} = 1 - \frac{1}{\mathfrak{R}_0} \quad (3.29)$$

With this simplification the endemic equilibrium becomes

$$S_2^* = \frac{1}{\mathfrak{R}_0}, \quad C_2^* = f(p_{crit} - p), \quad I_2^* = fg(p_{crit} - p) \quad (3.30)$$

Since this is a biological situation both C_2^* and I_2^* have to be positive. So C_2^* and I_2^* will only exist when $p < p_{crit}$. This means that in order to control a meningitis epidemic individuals have to be vaccinated at a rate, p , greater than p_{crit} .

CHAPTER 4 Model Parameters and Results

4.1 Euler's Method

A visual representation is very useful for understanding the model. Matlab is used to graph the dynamics of the system. The graphs show how each class changes with respect to time and how they change relative to each other. The Matlab program is written using Euler's method. This method solves differential equations numerically. Starting with initial conditions, Euler's Method approximates solutions at different times by using tangent lines to approximate the derivative.

For the system we are trying to solve numerically, the slope of each tangent line is given by the change in each class with respect to time. If we let y represent each class the slope is given by $\frac{dy}{dt}$. So we have

$$\frac{dy}{dt} = f(t, y), \quad y(t_0) = y_0 \quad (4.1)$$

In the case of the tangent line at y_0 the slope is given by $f(y_0) = y'$. This is a good approximation since points on the tangent line sufficiently close to y_0 will have solutions that are very close to solutions of y' . The tangent line at y_0 is then

$$y = y_0 + f(y_0) * (t - t_0) \quad (4.2)$$

This is a linearization of the unknown solution about t_0 . To specify a particular portion of our solution curve that we want the tangent line to approximate we define a segment of the t axis that starts at t_0 and ends at a distance greater than t_0 . Let dt be the positive increment that represents this segment. We can then replace y by y_1 and t by $t_1 = t_0 + dt$ in equation (4.2) which gives

$$y_1 = y_0 + dt f(t_1, y_1) \quad (4.3)$$

The point (t_1, y_1) gives an approximation to the point $(t_1, y(t_1))$ on the solution curve. This approximation depends on the size of segment dt . Smaller values of dt will result in more accurate approximations. The step of using a tangent line to approximate the solution curve at a certain point can then be repeated for (t_1, y_1) . From this step we obtain

$$y_2 = y_1 + dt f(t_1, y_1) \quad (4.4)$$

The relationship between $y_1, y_2, y_3 \dots y_n$ can be represented by the recursive general formula

$$y_{n+1} = y_n + hf(x_n, y_n) \quad (4.5)$$

This recursive formula is used to express the meningitis model inside the Matlab program. See Appendix A.

4.2 Parameter Values

In order to run the Matlab program parameters have to be defined. It is assumed that this model would be used in epidemic situation. We will use data from outbreaks in

the meningitis belt of Africa to define our parameters. The total time discussed for the model will be in years with the change in time, dt representing days. The parameter, p , which represents the percent vaccinated, will be varied to see how this variable affects the model. As mentioned in the introduction, carrier rates are about 10% in any given population but will approach 100% in an epidemic situation. With this we assume that β can be .1 to .99. We will examine different values of β ; .2, .6 and .9. and then look at values of p less than, equal, and greater than p_{crit} for each β . In a study done the mean carriage time was 30 days, so γ_1 , the rate at which carriers return to the susceptible population is .033. (Mueller et al, 2007) The time it takes infected individuals to recover from the disease, is about 1 to 3 days, so we take $\gamma_2 = .3$. (Vedros, 1987) It is assumed that the population does not change by a significant amount and the birth and death rate, ν is assumed to be 1%. In 2006 the African meningitis belt, with a population of about 300 million, experienced about 250,000 cases of infection which resulted in 25,000 deaths. From this we see that death from infection occurs about 10% this gives $\mu_2 = .1$. Also since this is an epidemic situation we know that the number of carriers would be very high leading to the assumption that only a very small portion of carriers actually become infected. So we let the infection rate of carrier, α be 2%. At t_0 it can be assumed that S_0 is less than $1 - p$. R_0 is equivalent to the proportion that has been vaccinated, p . Since $S + C + I + R = 1$, the values of C_0 and I_0 combined should equal $1 - S_0 - R_0$.

4.3 Graphs

We investigate the effect of β and the impact on the model. Letting

$\beta = \{.2, .6, .9\}$ we wish to see how different vaccination rates affect long term

population distribution. We choose $p = .2 < p_{crit}$ (for all β values examined), $p = p_{crit}$, and

$p = .97 > p_{crit}$ (for all β values examined)

Case $\beta = .2$; (Low Transmission)

$$\mathcal{R}_0 = \frac{.2}{.063} \cong 3.17 \text{ so } p_{crit} = 1 - \frac{.063}{.2} \cong .685$$

In this case we consider

- 1) $p = .2, S_0 = .5, C_0 = .2, I_0 = .1$
- 2) $p = .685, S_0 = .2, C_0 = .08, I_0 = .035$
- 3) $p = .97, S_0 = .02, C_0 = .007, I_0 = .003$

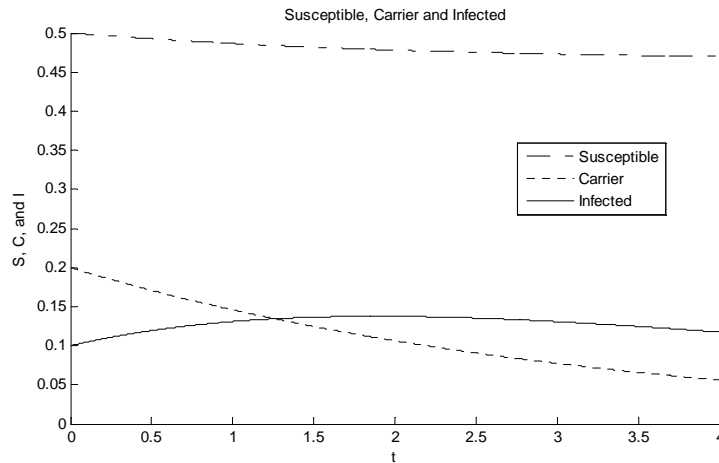


Figure 3: Graph of Susceptible, Carrier and Infected Class with:

$$p = .2, S_0 = .5, C_0 = .2, I_0 = .1$$

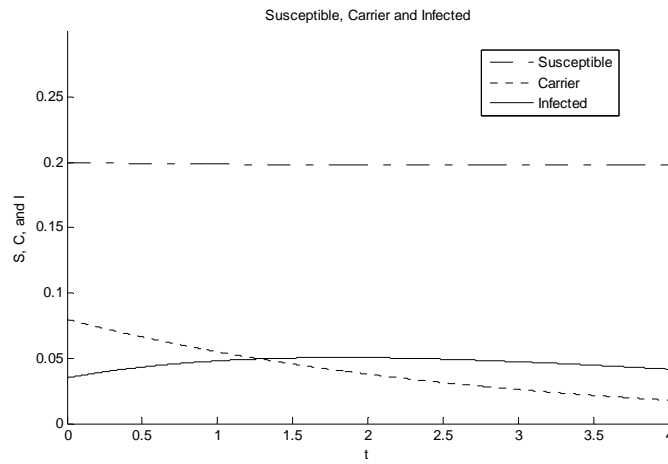


Figure 4: Graph of Susceptible, Carrier and Infected Class with:

$$p = .685, S_0 = .2, C_0 = .08, I_0 = .035$$

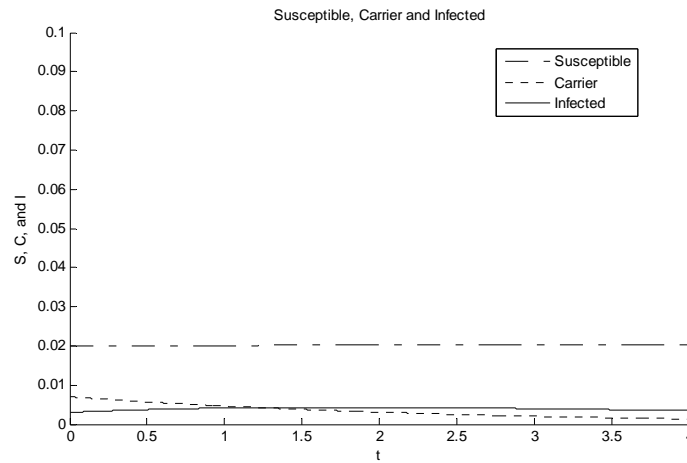


Figure 5: Graph of Susceptible, Carrier and Infected Class with:

$$p = .97, S_0 = .02, C_0 = .007, I_0 = .003$$

Case $\beta = .6$; (Moderate Transmission)

$$\mathfrak{R}_0 = \frac{.55}{.063} \cong 8.73 \text{ so } p_{crit} = 1 - \frac{.063}{.55} \cong .885$$

In this case we consider

- 1) $p = .2$, $S_0 = .5$, $C_0 = .2$, $I_0 = .1$
- 2) $p = .885$, $S_0 = .2$, $C_0 = .08$, $I_0 = .035$
- 3) $p = .97$, $S_0 = .02$, $C_0 = .007$, $I_0 = .003$

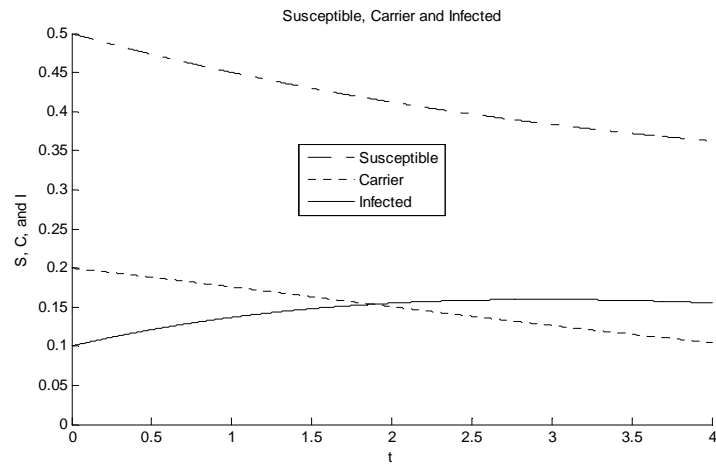


Figure 6: Graph of Susceptible, Carrier and Infected Class with:

$$p = .2, S_0 = .5, C_0 = .2, I_0 = .1$$

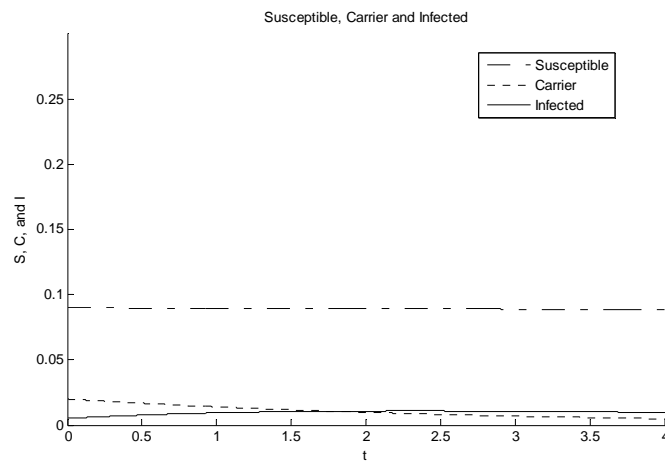


Figure 7: Graph of Susceptible, Carrier and Infected Class with:

$$p = .885, S_0 = .09, C_0 = .02, I_0 = .005$$

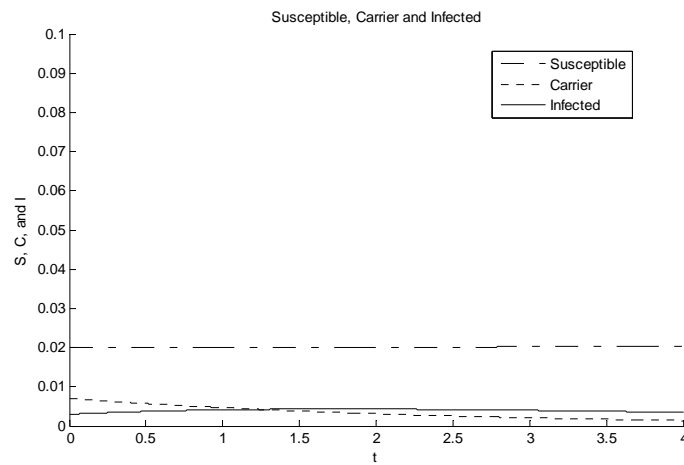


Figure 8: Graph of Susceptible, Carrier and Infected Class with:

$$p = .97, S_0 = .02, C_0 = .007, I_0 = .003$$

For $\beta = .9$; (High Transmission)

$$\mathcal{R}_0 = \frac{.9}{.063} \cong 14.29 \text{ so } p_{crit} = 1 - \frac{.063}{.9} \cong .93$$

In this case we will consider $p = .7$, $p = .93$, and $p = .95$

$$1) \ p = .2, \ S_0 = .5, \ C_0 = .2, \ I_0 = .1$$

$$2) \ p = .93, \ S_0 = .2, \ C_0 = .08, \ I_0 = .035$$

$$3) \ p = .97, \ S_0 = .02, \ C_0 = .007, \ I_0 = .003$$

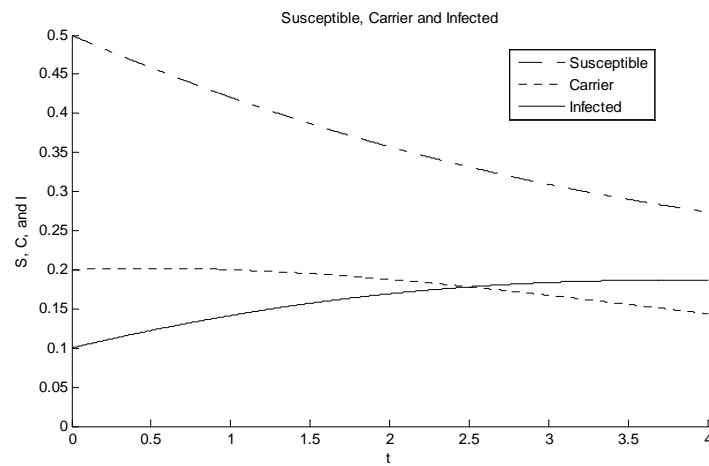


Figure 9: Graph of Susceptible, Carrier and Infected Class with:

$$p = .2, \ S_0 = .5, \ C_0 = .2, \ I_0 = .1$$

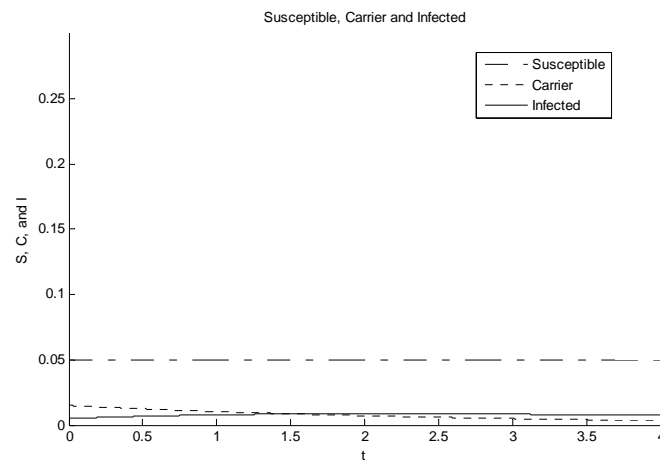


Figure 10: Graph of Susceptible, Carrier and Infected Class with:

$$p = .93, S_0 = .05, C_0 = .015, I_0 = .005$$

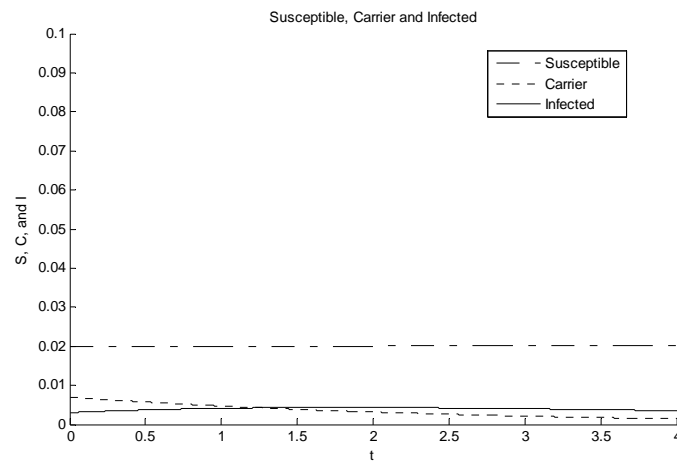


Figure 11: Graph of Susceptible, Carrier and Infected Class with:

$$p = .97, S_0 = .02, C_0 = .007, I_0 = .003$$

CHAPTER 5 Conclusion and Future Works

5.1 Conclusion

We developed an SCIR model to capture spread of meningitis and found where the system had equilibrium states. Criteria that lead to the disease free equilibrium being locally asymptotically stable and the existence of the endemic were also determined. The model was solved numerically using Euler's method.

From the graphs we draw the following conclusions. When p is less than p_{crit} the susceptible class will experience a decrease. This decrease occurs at a faster rate as β is increased. The infected class grows when vaccine levels are low. Choosing $p = p_{crit}$ allows the susceptible class to stay fairly constant. This implies that the calculation of \mathcal{R}_0 is correct. The infected class increases at a rate very close to the rate the carrier class decreases. The susceptible class again stays constant when p is greater than p_{crit} , while the infected class experiences the same increasing behavior as before. However for $p > p_0$, the decrease in C and the increase in I as well as their actual values are very small to the point that they can be considered negligible. In conclusion vaccinations rate needs to increase to stop spread in a highly populated area.

5.2 Future Works

Many of the parameters considered in the model were defined through estimates of the very limited data. More research is needed to define parameters such as the rate at which carriers become infected. This is also true for the parameter representing death from infection. It was estimated that 10% of the population will die over the course of the epidemic but this may not be accurate for daily death rates. The availability of better parameter estimates will increase the likelihood that this model closely mimics an actual epidemic situation. Also an option to consider is whether to change the interaction of individuals in the susceptible class with those in the carrier class, $\frac{\beta}{N} \tilde{C} \tilde{S}$ to the interaction of individuals in the susceptible class with those in both the carrier and infected classes,

$$\frac{\beta}{N} \tilde{S}(\tilde{C} + \tilde{I}).$$

To make a stronger case for vaccine use it should be proven that the disease free equilibrium, DFE is globally asymptotically stable when the endemic equilibrium does not exist. A future study of this model may use the method considered by Korobeinikov, (2004), while proving the global properties for SEIR and SEIS epidemic models. The proofs discussed in the paper Lyapunov functions and Global Properties for SEIR and SEIS epidemic models involve finding a Lyapunov function as defined below

Definition 5.11. (*Allen 2007*)

A positive definite function $V(X, Y)$ in an open neighborhood, Ω of the origin is

said to be a *Lyapunov function* for the autonomous differential system, $\frac{dx}{dt} = f(x, y)$,

$\frac{dy}{dt} = g(x, y)$, if $\frac{dV(x, y)}{dt} \leq 0$ for all $(x, y) \in \Omega - \{(0, 0)\}$. If $\frac{dV(x, y)}{dt} < 0$ for all

$(x, y) \in \Omega - \{(0, 0)\}$ then the function $V(X, Y)$ is called a *strict Lyapunov function*.

and the following theorem.

Theorem (5.1); (Allen 2007)

(Lyapunov's Stability Theorem). Let $(0, 0)$ be an equilibrium of the autonomous system (5.22) and let V be a positive definite function in a neighborhood Ω of the origin.

- (i) *If $dV(x, y)/dt \leq 0$ for $(x, y) \in \Omega - \{(0, 0)\}$, then $(0, 0)$ is stable.*
- (ii) *If $dV(x, y)/dt < 0$ for $(x, y) \in \Omega - \{(0, 0)\}$, then $(0, 0)$ is asymptotically stable.*
- (iii) *If $dV(x, y)/dt > 0$ for $(x, y) \in \Omega - \{(0, 0)\}$, then $(0, 0)$ is unstable.*

Dealing with the $\{S, E, I\}$ system associated with the SEIR model the author

suggests a Lyapunov function $W(S, E, I)$ such that $\frac{dW}{dt} \leq 0$ for all $(S, E, I) \in \{\mathbf{R}_+^3 \setminus \Sigma\}$. In

order to prove the global stability of the meningitis model's DFE one would have to find a Lyapunov function that corresponds with the $\{S, C, I\}$ system.

In addition to proving global stability of the DFE and providing more information on parameters, the time delay of a vaccine for meningitis could be considered. The vaccines available for the treatment of meningitis have different time period for which they will become effective. This model assumes that an individual is immune as soon they are vaccinated.

References

References

- Anon, "Meningococcal Meningitis." Media centre. May 2003. World Health Organization. 18 Apr 2008 <<http://www.who.int/mediacentre/factsheets/fs141/en/>>.
- Allen, Linda J. S. An Introduction to Mathematical Biology. 1st. Upper Saddle River, NJ: Pearson Education inc, 2007.
- Bartfield, Allison A. "Bacterial Meningitis." International Journal of Infectious Diseases 7: No.2 (2000): 49-54.
- Cartwright, Keith, eds. Meningococcal Disease. 1st. Baffins Lane, Chichester, West Sussex; England: John Wiley & Sons Ltd, 1995.
- Casagrandi, Renato, Luca Bolzoni, Simon A. Levin and Viggo Andreasen. "The SIRC model and influenza A." Mathematical Biosciences 300 (2006): 152-169.
- Frosch, Matthias and Martin C.J. Maiden, eds. Handbook of Meningococcal Disease. 1st. Weinheim, Germany: Wiley-VCH, 2006.
- Jin, Yu, Wendi Wang and Shiwu Xiao. "An SIRS model with a nonlinear incidence rate." Chaos Solitons & Fractals 34 (2007): 1482-1497.
- Kermack, W.O.. "A Contribution to the Mathematical Theory of Epidemics." Proceedings of the Royal Society of London. Series A, Containing Papers of a Mathematical and Physical Character 115 (1927): 700-721.
- Kieny, Marie Paule. "Meningococcal Meningitis in the African Meningitis Belt Epidemiology and Vaccine." Vaccine 25S (2007): A1-A2.
- Kloss, Deborah. "Caring for the Patient with Meningococcal Meningitis." The American Journal of Nursing 96: No.4 (1996): 16F-16L.
- Korobeinikov, Andrei. "Lyapunov functions and Global Properties for SEIR and SEIS Epidemic Models." Mathematical Medicine and Biology 21(2004): 75-83.

- LI, Michael Y, Hal L. Smith and Liancheng Wang. "Global Dynamics of an SEIR Epidemic Model with Vertical Transmission." Journal for the Society for Industrial and Applied Mathematics 62(2001): 58-69.
- Martcheva, Maia. "The Transmission of Meningococcal Infection: A mathematical Study." Journal of Mathematical Analysis and Applications 283(2003): 251-275.
- Mueller, Judith E., Lassana Sangare, Berthe-Marie, Njanpop-Lafourcade, Zekiba Tarnagda, Yves Traore, Seydou Yaro, Raymond Borrow, Bradford D. Gessner and Pierre Nicolas . "Molecular Characteristics and." Emerging Infectious Diseases 13, No. 6(2007): 847-854.
- Murray, James Dickson. Mathematical Biology; I: An Introduction. 3rd. Berlin-Heidelberg: Springer-Verlag , 2002.
- Teyssou, Remy and Erwan Muros-Le Rouzic. "Meningitis epidemics in Africa: A Brief Overview." Vaccine 25S (2007): A3-A7.
- van den Driessche, P. and James Watmough. "Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission." Mathematical Biosciences 180(2002): 29-48.
- Wagner, Bradley and David J. D Earn. "Circulating Vaccine Derived Polio Viruses and their Impact on Global Polio Eradication." Bulletin of Mathematical Biology 70 (2008): 253-280.
- Woodburne, Russell T and William E. Burkel. Essentials of Human Anatomy. 8th. New York: Oxford University Press, Inc, 1988.

APPENDIX A

Matlab Program

```

function [S,C,I,R]=SCIR(s0,c0,i0,p,v,b,g1,a,g2,u,dt,t)
%function [S,C,I,R]=SCIR(s0,c0,i0,p,v,b,g1,a,g2,u,dt,t)
X(1,1)=s0;
X(1,2)=c0;
X(1,3)=i0;
tf=t/dt;
for i=1:tf
    x1=X(i,1)+(v*(1-p)-b*X(i,1)*X(i,2)+g1*X(i,2)-v*X(i,1))*dt;
    x2=X(i,2)+(b*X(i,1)*X(i,2)-g1*X(i,2)-a*X(i,2)-v*X(i,2))*dt;
    x3=X(i,3)+(a*X(i,2)-g2*X(i,3)-u*X(i,3)-v*X(i,3))*dt;
    X=[X;x1,x2,x3];
end
t=0:dt:t;
figure
hold
plot(t,X(:,1),'-k');
xlabel('t');
ylabel('S, C, and I');
plot(t,X(:,2),':k');
plot(t,X(:,3),'-k');
axis([0 4 0 .5])
legend('Susceptible','Carrier','Infected','Location','Best');
title('Susceptible, Carrier and Infected')
S=X(tf,1);
C=X(tf,2);
I=X(tf,3);
R=1-S-C-I;

```

VITA

Kalimah Vereen was born August 31, 1981 in Queens, New York. She moved to Richmond, Virginia in 2001 to pursue her education. She received her Associate of Science degree from J. Sargeant Reynolds Community College in 2003. Two years later she received her Bachelor of Science degree from Virginia Commonwealth University majoring in Mathematical Sciences with a concentration in Applied Mathematics. Kalimah is currently a graduate teaching assistant in the department of Mathematics at Virginia Commonwealth University.