

Reproduction Number of Vertical Transmission of Measles Model

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Abstract

In this model, we study the reproduction number of measles epidemiology, the rate of vertical transmission of measles and antibodies, including the effect of maternal antibody on the spread of measles to the infant. We exempt the vaccinated class due to the finding of Viera Scheibner [2]. We demonstrated that the disease will die out, if the basic reproductive number for the disease free equilibrium $R_0 < 1$. This is the case of a disease-free state, with no infection in the population. Otherwise the disease may become endemic if the basic reproductive number R_0 is bigger than unity. The basic reproduction number at both the disease Free State and the endemic state were obtained and the result shows stability in the effect of mother to child transmission of either disease or immunity.

Keywords: Reproduction number R_0 , Vertical transmission, maternal antibody, Measles Infectious Disease

1 Introduction

Measles is the childhood disease with the highest rate of mortality especially in developing countries, measles like other childhood diseases affect the children and infants much more frequently than the rest of the population.

New-born are afforded protection to measles through maternal antibodies, which may be effective for up to one year after birth. Vaccination against measles is not recommended until these antibodies have waned out (Hethcote, H. W. (2008).)[1]. Measles is one of the most infectious diseases and has severe complications, including pneumonia, encephalitis (inflammation of the brain) and death. Global fight against measles, mumps and rubella has reduced the morbidity rate of measles and decrease the spread of the disease, however, the fight against measles is yet to be won especially in the developing world. One of the challenges yet to be overcome as reported by WHO in 2012 is that about 430 children still die from measles each day, and more than 100,000 are born with congenital rubella syndrome every year (WHO) [5].

In a bid to fight the war against the prevalence of measles, Mathematical modellers develop models to look into the situation to give useful information on the means of solution. Epidemiology is one of the areas in biology to which mathematical modeling has been applied most successfully, it was through the mathematical concept of basic reproductive number that Ronald Ross gained the insight that malaria could be controlled if the mosquito population was sufficiently suppressed (Diekmann O. and Heesterbeek J.A.P. (2000)) [3]. Epidemiology studies the distribution of a disease within a host population.

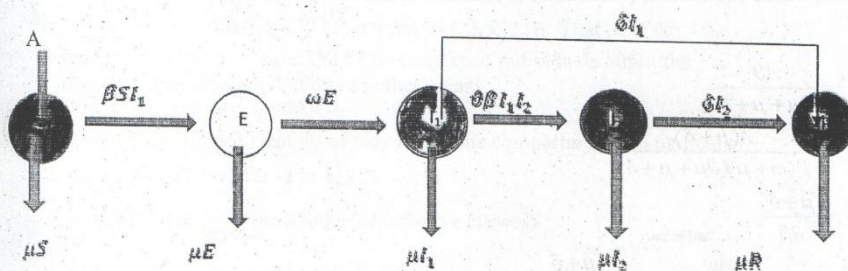
Most models used for infectious diseases are based on partitioning the host population into different classes (compartment) that correspond to the different stages of the infectious process (e.g., susceptible, infectious, and recovered) and the transitions between these classes. After the partitioning, different mathematical concept will be applied to test for the stability of the model and to test for the criteria which give the availability of solution for the system of equations. One of the several means of obtaining a valid analysis of the system of equations arising from the model is the calculation of reproductive number. The reproductive number is an important parameter. It is defined as the average number of secondary infections caused by an infected host over the lifetime of the infection. In a completely susceptible population, this number is known as the basic reproductive number, R_0 . If the reproductive number is larger than one, a single infection can lead to a chain reaction of infections and, eventually, to an epidemic or an endemic state (Bellomo N. et. al. 2007) [4]. If the reproductive number is smaller than one, large epidemics do not occur and the pathogen is bound to disappear from the population. If the basic reproductive number is less than one, the numbers of infected individuals hardly ever become truly large and stochastic effects prevail. If this is the case the disease manifests itself in the form of outbreaks that follow the introduction of the disease into the population. The size and duration of an outbreak can vary enormously through chance events. To capture these dynamics a stochastic formalism is needed.

2 Model Formulation

A deterministic model is applied to study the effect of mother to child transmission of measles disease and its antibodies. A basic model for the epidemiology of measles outbreaks is founded on a subdivision of the host population into classes. The allocation of individuals to classes is not static: hosts can move from one class to another. Whenever this happens we speak of a transition. Examples of transitions are infection, which moves a host from the susceptible to the infected class, and recovery, which moves a host from the infected to the recovered class.

The total population are subdivided into compartment to relate the effect of measles breaking out in a stable population. The recruitment into the population at any time is denoted as A while μ denotes the mortality rate. S denotes the Susceptible class (individual in the population that can contact the disease once in contact with the infectious/infection), E denote the exposed class (individual that already has a contact with the infectious but are yet to show clinical symptom), the Infected class by contraction (I_1); people that were infected through direct contact and they are now infectious (capable of spreading the disease), the infected class by vertical transmission (I_2); and the removed class (R), which consists of people that can no longer be infected either due to permanent immunity obtained from recovery after been infected or people that have been vaccinated twice etc. β is the infection rate (the rate at which the S -class get infected when in contact with the I_1), ω denotes the percentage of exposed class that move into fully infected class after a week to the time of contact, δ is the recovery rate and ϑ is the vertical transmission rate of both the diseases and antibodies.

The flow diagram of the modified model



The system of equations is given as:

$$\frac{dS}{dt} = A - \mu S - \beta SI_1$$

$$\frac{dE}{dt} = \beta SI_1 - (\mu + \omega)E$$

$$\frac{dI_1}{dt} = \omega E - (\mu + \delta)I_1 - \vartheta \beta I_1 I_2$$

$$\frac{dI_2}{dt} = \vartheta \beta I_1 I_2 - (\mu + \delta) I_2$$

$$\frac{dR}{dt} = \delta I_1 + \delta I_2 - \mu R$$

where the parameters are given by

- A - Birth rate and immigration rate
- ϑ - Lateral/Vertical Transmission
- δ - Recovery rate for both classes
- β - Infection rate
- ω - Transmission rate from exposed to infected class
- μ - Natural mortality/death rate
- S - Susceptible class
- E - Exposed class
- I_1 - Infected class by contraction
- I_2 - Infected class by vertical transmission
- R - Recovered class.

3 Disease Eradication

We begin the study by stating the result of the disease free and endemic equilibrium of the model. We note that at disease free, $I_1 = I_2 = 0$ and hence the resulting equations give $A - \mu S = 0$ which give the disease free equilibrium as:

$$S^*, E^*, I_1^*, I_2^*, R^* = \frac{A}{\mu}, 0, 0, 0, 0.$$

The endemic equilibrium (when there is presence of measles infection) was obtained as:

$$S^{**} = \frac{A\vartheta}{\vartheta\mu + \mu + \delta}$$

$$E^{**} = \frac{A(\mu + \delta)}{\beta(\omega + \mu)(\vartheta\mu + \mu + \delta)}$$

$$I_1^{**} = \frac{\mu + \delta}{\vartheta\beta}$$

$$I_2^{**} = \frac{A\omega}{\beta(\omega + \mu)(\vartheta\mu + \mu + \delta)} - \frac{\mu + \delta}{\vartheta\beta}$$

$$R^{**} = \frac{A\omega\delta}{\mu\beta(\omega + \mu)(\vartheta\mu + \mu + \delta)}$$

We now proceed to obtain the reproduction number of the model as follows.

3.1 Reproductive Number

The behaviour of the model can also be studied using the technique known as the next generation matrix method. The technique due to Diekmann (1990) constructs an $n \times n$ matrix from the system of equations of the model by considering only the infective classes.

3.2 The Next Generation Matrix

Define X_s to be the set of all Disease Free states, that is

$$X_s = \{x \geq 0 \mid x_i = 0, i = 1, 2, 3, \dots\}$$

In order to compute R_0 , it is important to distinguish new infections from all other changes in the population.

Let $F_i(x)$ be the rate of appearance of new infections in compartments i ,

V_i^+ be the rate of transfer of individuals into compartment i by all other means.

V_i^- be the rate of transfer of individuals out of compartment i :

It is assumed that each function $(F_i(x), V_i^+, V_i^-)$ is continuously differentiable at least twice with respect to each variable.

The transmission model consists of the non negative initial conditions together with the following system of equations

$$\dot{x}_i = f_i(x) = F_i(x) - V_i(x), \quad i = 1, 2, 3, \dots, n$$

where $V_i(x) = V_i^- - V_i^+$ and the functions satisfy the following conditions:

- If $x \geq 0$, then $F_i(x), V_i^-(x), V_i^+(x) \geq 0$ for $i = 1, 2, 3, \dots, n$. That is, if the compartment is empty, there will be no transfer of individuals out of the compartment by death, infection nor other means
- If $x_i = 0$, then $V_i^- = 0$ (that is, nobody leaves the compartment). In particular if $x \in X_s$, then $V_i^- = 0$ for $i = 1, 2, 3, \dots, m$
- $F_i = 0$, for $i > m$ (m is the number of infective classes)
- If $x \in X_s$, then $F_i = 0$ and $V_i^- = 0 \quad \forall i = 1, 2, 3, \dots, m$
- If $F_i(x)$ is set to zero, then all the eigenvalues of $DF(x_0)$ have negative real parts.

Lemma 1.1

If x_0 is a disease free equilibrium (DFE) of (3.3.) and $F_i(x)$ satisfies conditions (a) – (e), then the derivatives $DF(x_0)$ and $DV(x_0)$ are partitioned as

$$DF(x_0) = \begin{pmatrix} f_{11} & \cdots & f_{1j} \\ \vdots & \ddots & \vdots \\ f_{i1} & \cdots & f_{ij} \end{pmatrix}, \quad i = 1, 2, 3, \dots, m; \quad j = 1, 2, 3, \dots, m$$

$$DV(x_0) = \begin{pmatrix} v_{11} & \cdots & v_{1j} \\ \vdots & \ddots & \vdots \\ v_{i1} & \cdots & v_{ij} \end{pmatrix}, \quad i = 1, 2, 3, \dots, m; \quad j = 1, 2, 3, \dots, m$$

where F and V are the $m \times m$ matrix defined by:

$$F = \frac{\partial F(x_0)}{\partial x_j} \text{ and } V = \frac{\partial V(x_0)}{\partial x_j}$$

F is non-negative and V is a non-singular matrix.

Following Diekmann et al. (2000), the product of the matrix FV^{-1} is called the next generation matrix for the model and we shall set the reproduction number (R_0) as equal to the spectral radius $\rho(FV^{-1})$, i.e, $R_0 = \rho(FV^{-1})$.

We shall now apply the method to find the reproduction number of the model

$$\frac{dS}{dt} = A - \mu S - \beta SI_1$$

$$\frac{dE}{dt} = \beta SI_1 - (\mu + \omega)E$$

$$\frac{dI_1}{dt} = \omega E - (\mu + \delta)I_1 - \theta \beta I_1 I_2$$

$$\frac{dI_2}{dt} = \theta \beta I_1 I_2 - (\mu + \delta)I_2$$

$$\frac{dR}{dt} = \delta I_2 + \delta I_1 - \mu R$$

Re-arranging the equation such that we start with the infective classes;

$$\frac{dE}{dt} = \beta SI_1 - (\mu + \omega)E$$

$$\frac{dI_1}{dt} = \omega E - (\mu + \delta)I_1 - \theta \beta I_1 I_2$$

$$\frac{dI_2}{dt} = \theta \beta I_1 I_2 - (\mu + \delta)I_2$$

$$\frac{dR}{dt} = \delta I_2 + \delta I_1 - \mu R$$

$$\frac{dS}{dt} = A - \mu S - \beta SI_1$$

There are three infected classes in this model, the exposed class E , the infected classes I_1 and I_2 respectively, hence our $m = 3$.

$$F = \begin{pmatrix} \beta SI_1 \\ -\partial \beta I_1 I_2 \\ \partial \beta I_1 I_2 \end{pmatrix}, \quad V = \begin{pmatrix} (\mu + \omega)E \\ (\mu + \delta)I_1 - \omega E \\ (\mu + \delta)I_2 \end{pmatrix}$$

The disease free equilibrium point of the system of equations has coordinates:

$$(S_0, E_0, I_1, I_2, R_0) = \left(\frac{A}{\mu}, 0, 0, 0, 0 \right)$$

According to lemma 1.1, we have

$$F = \frac{\partial F(x_0)}{\partial x_j} \text{ and } V = \frac{\partial V(x_0)}{\partial x_j}, \quad j = 1, 2, 3.$$

$$F = \begin{pmatrix} 0 & \beta S_0 & 0 \\ 0 & -\partial \beta I_1 & -\partial \beta I_2 \\ 0 & \partial \beta I_1 & \partial \beta I_2 \end{pmatrix}, \quad V = \begin{pmatrix} (\mu + \omega) & 0 & 0 \\ -\omega & (\mu + \delta) & 0 \\ 0 & 0 & (\mu + \delta) \end{pmatrix}$$

The inverse of the matrix V is given as:

$$V^{-1} = \frac{1}{(\mu + \omega)(\mu + \delta)(\mu + \delta)} \begin{pmatrix} (\mu + \delta)(\mu + \delta) & 0 & 0 \\ \omega(\mu + \delta) & (\mu + \delta)(\mu + \omega) & 0 \\ 0 & 0 & (\mu + \omega)(\mu + \delta) \end{pmatrix}$$

$$V^{-1} = \begin{pmatrix} \frac{1}{(\mu + \omega)} & 0 & 0 \\ \frac{\omega}{(\mu + \omega)(\mu + \delta)} & \frac{1}{(\mu + \delta)} & 0 \\ 0 & 0 & \frac{1}{(\mu + \delta)} \end{pmatrix}$$

Computing the matrix multiplication of the next generation matrices F and V^{-1} , we obtained:

$$FV^{-1} = \begin{pmatrix} 0 & \beta \frac{A}{\mu} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{(\mu + \omega)} & 0 & 0 \\ \frac{\omega}{(\mu + \omega)(\mu + \delta)} & \frac{1}{(\mu + \delta)} & 0 \\ 0 & 0 & \frac{1}{(\mu + \delta)} \end{pmatrix}$$

$$\frac{dR}{dt} = \delta I_2 + \delta I_1 - \mu R$$

$$\frac{dS}{dt} = A - \mu S - \beta S I_1$$

There are three infected classes in this model, the exposed class E , the infected classes I_1 and I_2 respectively, hence our $m = 3$.

$$F = \begin{pmatrix} \beta S I_1 \\ -\partial \beta I_1 I_2 \\ \partial \beta I_1 I_2 \end{pmatrix}, \quad V = \begin{pmatrix} (\mu + \omega)E \\ (\mu + \delta)I_1 - \omega E \\ (\mu + \delta)I_2 \end{pmatrix}$$

The disease free equilibrium point of the system of equations has coordinates:

$$(S_0, E_0, I_1, I_2, R_0) = \left(\frac{A}{\mu}, 0, 0, 0, 0 \right)$$

According to lemma 1.1, we have

$$F = \frac{\partial F(x_0)}{\partial x_j} \text{ and } V = \frac{\partial V(x_0)}{\partial x_j}, \quad j = 1, 2, 3.$$

$$F = \begin{pmatrix} 0 & \beta S_0 & 0 \\ 0 & -\partial \beta I_{1_0} & -\partial \beta I_{1_0} \\ 0 & \partial \beta I_{1_0} & \partial \beta I_{1_0} \end{pmatrix}, \quad V = \begin{pmatrix} (\mu + \omega) & 0 & 0 \\ -\omega & (\mu + \delta) & 0 \\ 0 & 0 & (\mu + \delta) \end{pmatrix}$$

The inverse of the matrix V is given as:

$$V^{-1} = \frac{1}{(\mu + \omega)(\mu + \delta)(\mu + \delta)} \begin{pmatrix} (\mu + \delta)(\mu + \delta) & 0 & 0 \\ \omega(\mu + \delta) & (\mu + \delta)(\mu + \omega) & 0 \\ 0 & 0 & (\mu + \omega)(\mu + \delta) \end{pmatrix}$$

$$V^{-1} = \begin{pmatrix} \frac{1}{(\mu + \omega)} & 0 & 0 \\ \frac{\omega}{(\mu + \omega)(\mu + \delta)} & \frac{1}{(\mu + \delta)} & 0 \\ 0 & 0 & \frac{1}{(\mu + \delta)} \end{pmatrix}$$

Computing the matrix multiplication of the next generation matrices F and V^{-1} , we obtained:

$$FV^{-1} = \begin{pmatrix} 0 & \beta \frac{A}{\mu} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{(\mu + \omega)} & 0 & 0 \\ \frac{\omega}{(\mu + \omega)(\mu + \delta)} & \frac{1}{(\mu + \delta)} & 0 \\ 0 & 0 & \frac{1}{(\mu + \delta)} \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} \frac{\beta A \omega}{\mu(\mu+\omega)(\mu+\delta)} & \frac{\beta A}{\mu(\mu+\delta)} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

The spectral radius of a matrix is the largest eigenvalues of the matrix; hence we look for the eigenvalues of the above matrix.

$$|FV^{-1} - \lambda I| = \begin{vmatrix} \frac{\beta A \omega}{\mu(\mu+\omega)(\mu+\delta)} - \lambda & \frac{\beta A}{\mu(\mu+\delta)} & 0 \\ 0 & -\lambda & 0 \\ 0 & 0 & -\lambda \end{vmatrix} = 0$$

The eigenvalues of the above matrix is given as:

$$\lambda_1 = 0$$

$$\lambda_2 = 0$$

$$\lambda_3 = \frac{\beta A \omega}{\mu(\mu+\omega)(\mu+\delta)}$$

Therefore the reproduction number of the given system of equations denoted as R_0 is:

$$R_0 = \rho(FV^{-1}) = \frac{\beta A \omega}{\mu(\mu+\omega)(\mu+\delta)}$$

For the endemic equilibrium state, the reproduction number is calculated as before using the endemic states:

$$S^* = \frac{A\theta}{\theta\mu + \mu + \delta}$$

$$E^* = \frac{A(\mu + \delta)}{\beta(\omega + \mu)(\mu + \delta)}$$

$$I_1^* = \frac{\mu + \delta}{\theta\beta}$$

$$I_2^* = \frac{A\omega}{\beta(\omega + \mu)(\theta\mu + \mu + \delta)} - \frac{\mu + \delta}{\theta\beta}$$

$$R^* = \frac{A\omega\delta}{\mu\beta(\omega + \mu)(\theta\mu + \mu + \delta)}$$

We recall that:

$$F = \begin{pmatrix} 0 & \beta S^{**} & 0 \\ 0 & -\beta I_2^{**} & -\beta I_1^{**} \\ 0 & \beta I_2^{**} & \beta I_1^{**} \end{pmatrix}, \quad V = \begin{pmatrix} (\mu + \omega) & 0 & 0 \\ -\omega & (\mu + \delta) & 0 \\ 0 & 0 & (\mu + \delta) \end{pmatrix}$$

$$V^{-1} = \begin{pmatrix} \frac{1}{(\mu + \omega)} & 0 & 0 \\ \frac{\omega}{(\mu + \omega)(\mu + \delta)} & \frac{1}{(\mu + \delta)} & 0 \\ 0 & 0 & \frac{1}{(\mu + \delta)} \end{pmatrix}.$$

Inserting the values of the endemic state into the next generation matrix, we obtain:

$$F = \begin{pmatrix} 0 & \beta \frac{A\omega}{\partial\mu + \mu + \delta} & 0 \\ 0 & -\beta \left(\frac{A\omega}{\beta(\omega + \mu)(\partial\mu + \mu + \delta)} - \frac{\mu + \delta}{\partial\beta} \right) & \beta \left(\frac{\mu + \delta}{\partial\beta} \right) \\ 0 & \beta \left(\frac{A\omega}{\beta(\omega + \mu)(\partial\mu + \mu + \delta)} - \frac{\mu + \delta}{\partial\beta} \right) & \beta \left(\frac{\mu + \delta}{\partial\beta} \right) \end{pmatrix}$$

$$F = \begin{pmatrix} 0 & \frac{\beta A\omega}{\partial\mu + \mu + \delta} & 0 \\ 0 & \frac{-\partial A\omega}{(\omega + \mu)(\partial\mu + \mu + \delta)} - \mu + \delta & \mu + \delta \\ 0 & \frac{\partial A\omega}{(\omega + \mu)(\partial\mu + \mu + \delta)} - \mu + \delta & \mu + \delta \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} \frac{\beta A\omega}{(\partial\mu + \mu + \delta)(\mu + \omega)(\mu + \delta)} & \frac{\beta A\omega}{(\partial\mu + \mu + \delta)(\mu + \delta)} & 0 \\ \frac{-\partial A\omega^2}{(\mu + \delta)(\omega + \mu)^2(\partial\mu + \mu + \delta)} - \frac{\omega}{(\mu + \omega)} & \frac{-\partial A\omega}{(\mu + \delta)(\omega + \mu)(\partial\mu + \mu + \delta)} - 1 & 1 \\ 0 & 0 & 1 \end{pmatrix}$$

The three eigenvalues of the above matrix was computed and the spectral radius was found to be

$$R_0 = \rho(FV^{-1}) = 1 + \frac{\partial A\omega}{(\mu + \delta)(\omega + \mu)(\partial\mu + \mu + \delta)} (\beta + 1) > 1$$

Hence, the endemic equilibrium is stable.

4 Discussion

The next generation matrix gives the case of what happens at long run if the epidemic persists. The reproduction numbers for the two cases of disease free and endemic equilibrium were calculated as above. The result for the endemic case show that if the nursing mothers have successfully completed their vaccine and get immunity to the disease, there is a higher percentage that their infants will remain immune due to strong antibody obtained from their mothers. The case of the disease free show that the population will remain without the disease break out for a long time.

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