OPTIMAL ANALYSIS OF THE EFFECT OF D1 AND D2 VACCINES ON MEASLES VIRUS

Adama, Patience Woye [1], Aliyu, Abdullahi Hassan [1] , Ogunniran, Matthew Ayodeji [2] , Evans, Patience Ogheneofejiro [3] and Somma, Samue[1] Abu4

[1]Mathematics Department, The Federal Polytechnic Bida, Nigeria
[2]Department of Mathematics, University of Ilorin, Nigeria
[3]Department of Mathematics, Anchor University Lagos, Nigeria
[4]Department of Mathematics, Federal University of Technology, Minna, Nigeria

May 28, 2024

OUTLINE

Abstract

Measles, an acute viral infectious disease caused by the measles morbillivirus, belongs to the paramyxovirus family. It spreads through direct contact and airborne transmission, primarily infecting the respiratory tract through coughs, sneezes, and nasal secretions. The prevalence of measles is a concern in African and developing countries where overpopulation and limited birth control measures exist. Outbreaks in such regions pose significant risks. In this study, a mathematical model was developed to analyze measles transmission, considering various immunization strategies, and the effectiveness of the Two-Dose vaccination $D_1(t)$ and $D_2(t)$. A control model was formulated, and the Disease-Free Equilibrium (DFE) state was determined. The basic reproduction number, denoted as R_0, was computed to assess the potential spread of the virus. Local stability analysis of the DFE was conducted using Jacobian Matrix Techniques, revealing that the DFE is locally asymptotically stable when R_0 is less than 1. The findings suggest that global eradication of measles is feasible if R_0 remains below one.
Key words: Basic Reproduction Number R_0, D_1 and D_2 Vaccination, Jacobian Matrix, Measles, Optimal Control, Stability

Introduction I

Measles outbreak remains a recurring episode and continues to be responsible for millions of deaths globally every year. Measles is an acute respiratory illness caused by an extremely contagious virus called *Morbillivirus*. It is transmitted mainly through coughing and sneezing, and therefore unvaccinated individuals living nearby could be more likely to get infected [1, 2, 3]. People infected by measles develop symptoms such as high fever, cough, runny nose (coryza), red and watery eyes (conjunctivitis), and rash [4, 5]. This virus could be serious in all age groups; however, children younger than 5 years of age are more likely to suffer from measles complications. Common complications include ear infections, diarrhea, pneumonia, and encephalitis (swelling of the brain). Moreover, if acquired earlier in life, the virus could result in long-term complications of a fatal disease called subacute sclerosing panencephalitis (SSPE) [6, 7, 8]. Although a safe and effective vaccine has been available since the early 1960s, measles remains an important cause of mortality and morbidity among young children globally. In 2019, about 207,500 people died and about 869,770 were infected with measles worldwide, and most of them were children [9]. The African region, high in measles prevalence, is a key player in the global fight against measles [10, 11]. The strategy called Periodic Supplementary Immunization Activities (SIAs), also known as vaccination campaigns, has enhanced vaccination coverage and interrupted measles transmission in Africa [12, 13, 14].

Introduction II

The first dose of the measles-containing vaccine should be given to infants as early as 9 months of age in nations where the disease is still spreading, and the second dose should be given as late as 15–18 months [2].

Immunization for Measles Prevention

Immunization is the most successful public health measure to date [1, 2] enabling prevention of disease at the population level. Approximately two to three million deaths are prevented globally each year through immunization [2, 3]. About 23.2 million deaths were prevented by the measles vaccine between 2000 and 2018, resulting in a 73% drop in measles cases globally within that period [4]. Despite these advances, developing countries continue to suffer from several endemic diseases, some of which are vaccine-preventable diseases (VPD). Immunization, therefore, remains a key intervention towards the achievement of the third Sustainable Development Goal (SDG 3) of the United Nations. Among several infectious diseases, measles has received prominent attention internationally due to its high infectivity rate [5, 6] and its attendant morbidity and mortality.

Progress Towards Measles Elimination in Nigeria I

To determine whether a country or a WHO Region has achieved elimination, the regional verification commission considers 5 lines of evidence, including the population immunity, quality of surveillance, sustainability of the programme, genotyping evidence, and the disease epidemiology [1]. All six WHO regions have set measles elimination objectives for 2020. The Americas eliminated the disease in 2016, but the high number of measles cases in Venezuela and Brazil in 2017 led the region to lose its measles elimination status in 2018 [2, 3]. In the WHO African Region (AFR), accelerated measles control activities began in 2001 and in 2011, the region adopted the 2020 measles elimination target [4]. To complement routine immunization coverage and reduce immunity gaps, AFR Member States conducted periodic supplemental immunization activities (SIAs) to reach unimmunized children missed by routine vaccination services, improving measles-case management, and established a case-based measles surveillance [5]. Since 2001, significant progress has been achieved: the number of reported cases decreased by 86% from 520,102 in 2000 to 72,603 in 2017, and the percentage of children who received the 1st dose of Measles-containing vaccine (MCV1) as recommended in the region increased from 53.0% to 70.0% during the same period [6]. Nigeria is the most populous nation in Africa and the seventh most populous in the world. The country occupies an area of 923,768 square kilometers. In terms of land mass and population size, the northern part of the country is larger than the southern part. Nigeria is affected by four climate types (e.g., Tropical rainforest, Savannah, tropical dry/Sahel, and Highland climate). These

Progress Towards Measles Elimination in Nigeria II

climate types are different from the southern part to the northern part of Nigeria through the country's middle belt. The tropical rainforest climate can be found in the south of Nigeria, while the dry climate can mostly be seen in the north of the country [7]. In Nigeria, the peak season for measles transmission begins in January and runs through May; the transmission peak is generally attained in the dry season in Sub-Saharan Africa. Nigeria introduced measles vaccination into the routine immunization program in 1978 for children aged 9 months [8]. Also during the early measles control period, case-based measles surveillance was initiated in 2006 [9]. In 2011, the country endorsed the 2020 elimination goal of reduction of measles incidence to less than 1 case per 10^6 population per year, and achievement of at least 95% MCV1 coverage in routine immunization and during campaigns at both national and district levels. Measles surveillance performance indicator targets should be maintained and include obtaining a blood specimen from 1 suspected measles case in at least 80% of districts annually, and investigating 2 or more cases of non-measles febrile rash illness per 100,000 population annually [4]. During the early stages of implementing measles control activities, Nigeria conducted an initial "catch-up" campaign (target age: 9 months to 15 years; Administrative coverage: 96.0% in late 2005, and a "follow-up" campaign (target age: 9 months to 4 years; Administrative coverage: 112.0% in 2008. With routine MCV1 coverage of less than 50.0%, high incidence rate and the persistence of measles outbreaks, the country has been conducting nationwide mass vaccination campaigns every 2 years. The National

Progress Towards Measles Elimination in Nigeria III

MCV1 coverage was 33% in 2000, 44% in 2006, and 41% in 2007; the country saw its measles vaccination coverage slightly increase from 53% in 2008 to 56% in 2010 [8]. The incidence of confirmed measles was 2 cases per million in 2006 and increased to 16 cases per million in 2007 and 68 cases per million in 2008 as more cases were captured by the recently introduced system [10]. Previous studies have described progress toward measles elimination in Nigeria during 2005–2008 and 2012–2016 [9, 11].

SECOND-DOSE IMMUNIZATION FOR PREVENTION I

The World Health Organization (WHO) recommends that two doses of the measles-containing vaccine (MCV) be included in all national immunization regimens. An estimated 169 million children worldwide are believed to have missed out on receiving the first dose of the measles vaccine between 2010 and 2017 and an additional 19.2 million in 2018 [?, ?]. Furthermore, measles led to a loss of 140,000 lives worldwide in 2018, according to estimates from the United States Centers for Disease Control and Prevention and WHO [?]. Countries in all the six WHO regions have adopted measles elimination goals [?]. The elimination of measles is confirmed by the absence of endemic measles transmission in a region or other defined geographical area for a minimum of 1 year within the framework of an efficient surveillance system. Between 2000 and 2015, there was a 70% decline in the global number of recorded cases of measles, from 853,479 to 254,928, and a 75% fall in the incidence of measles cases per million people, from 146 to 36. These patterns show progress toward both regional and global measles elimination targets as well as milestones for measles control [?, ?]. Moreover, WHO, UNICEF, and other partners created the Global Measles and Rubella Strategic Plan 2012–2020 [?]. This strategy plan's primary goal was to provide the measles-containing second-dose vaccine (MCV2) to every child [?]. However, none of the 2020 milestones or elimination goals (less than one case per 100,000 population per year) were met [?]. Some nations still experience repeated outbreaks of measles despite the UNICEF and WHO's comprehensive measles reduction strategy, as well as the cooperation of international

organizations for reducing mortality due to measles [?]. The vaccination of at least 95% of the population with two doses of the measles vaccine effectively prevents the incidence and transmission of the disease within that community, ensuring herd immunity and the protection of all individuals, including those who are not vaccinated [?]. MCV2 coverage in the WHO European Region was just 90% [?]. Although MCV2 has recently been introduced in Africa, most nations still have minimal coverage. Of the 26 nations that implemented MCV2, only eight achieved a coverage rate of above 80% in 2015 [?]. In seven nations, the coverage ranged from $60 to 80\%$, while in eight countries, it was less than 60% [?]. Nonetheless, a great number of people die due to the highly contagious measles every year [?]. An estimated 207,500 measles deaths were reported worldwide in 2019, with 147,900 (more than 70%) of those deaths occurring in African nations [?]. Over the past 10 years, there has been a decrease in the death rate due to measles in Africa [?]; however, the disease remains an issue in the region [?, ?]. Although some studies have reported the determinants of second-dose measles vaccination coverage in East Africa, none of them have systematically reviewed the second-dose measles vaccination coverage, which varies and is not uniform throughout the nation. Public health stakeholders must choose the optimal vaccination schedules based on their nation's epidemiology, the features of its health system, and the best available data regarding the second-dose measles vaccination coverage at measles elimination in order to control the disease. The reported determinants include antenatal care (ANC),

mother's education, place of delivery, birth order, receiving pentavalent 3, age of the child, information about MCV2, distance of the vaccination site, knowledge about immunization, attitude, maternal age, complete immunization, postnatal check, waiting time, residence near the health facilities, family size, household wealth status, maternal occupation, and mother's marital status [?, ?, ?].

The World Health Organization (WHO) and United Nations International Children's Emergency Fund (UNICEF) recommended measles-containing vaccine dose 1 (MCV1) at 9 months of age, and a second dose (MCV2) of measles vaccine at age 15–18 months through routine services strategies [?, ?]. The timing for the first dose and second dose differs across countries, hence in a nation with low levels of measles transmission the first dose may be administered at 12 months and MCV2 based on programmatic considerations. However, the vaccination should not be limited to the mentioned times and every opportunity should be taken to vaccinate, particularly those less than 15 years of age [?, ?]. Studies showed that the relative efficacy of two-dose (MCV1 and MCV2) is high in preventing the disease compared to only the one-dose group [?, ?, ?]. All countries have been recommended to include routine MCV2 in their national vaccination schedule regardless of the level of coverage with a routine dose of MCV1 [?]. Many countries have eradicated the virus successfully by advancing the coverage of two routine doses of the measles vaccine [?]. However, measles elimination has not been achieved due to different determinants and measles continues to be a leading cause of childhood

death in developing countries [?, ?, ?]. Many factors could contribute to the routine dose of MCV2 coverage remaining far below targets in many countries of Sub-Saharan Africa. Research revealed that the socio-demographic characteristics of families as well as the communities were significant variables. In addition, knowledge, perceptions, and attitudes towards vaccination (both at the community level and individual level) had been obstacles to meeting the target of eliminating the disease.

Model Formation I

In this model, we consider a population of humans within a community, dividing them into seven compartments. The total population is categorized into the following classes: Susceptible class, $S_1(t)$, first Dose class $D_1(t)$, 7% of the population after the first dose lose immunity and go to the susceptible class after the first dose $S_2(t)$. The second Dose class $D_2(t)$, Exposed class $E(t)$, Infected class, $I(t)$, and Recovered class, $R(t)$. The susceptible human population increases by recruitment at rate α. Individuals in the susceptible class receive the first vaccination dose at a rate ρ, they move to the susceptible class after losing immunity at a vaccine wane rate τ and then take the second vaccination dose at a rate ϵ. The susceptible humans ($S_1(t)$ and $S_2(t)$) get in contact with the release of the infected person at rate β to get exposed to the measles virus. The exposed individuals will be infected by the virus at rate θ which makes them move to the infected class. Those who were attended to immediately after being infected by giving them supportive care, good nutrition, adequate fluid, and treatment of dehydration with Oral Rehydration Solution move to the recovered class at rate σ. While 93% of individuals that successfully take the two doses of the vaccine at rate γ and were not exposed within the period recover at rate ω. We assume that the recovered individuals gain immunity to the disease and do not ever get affected again. Natural mortality occurs in all the classes at a rate μ and mortality caused by measles is denoted as δ.

Model Formation II

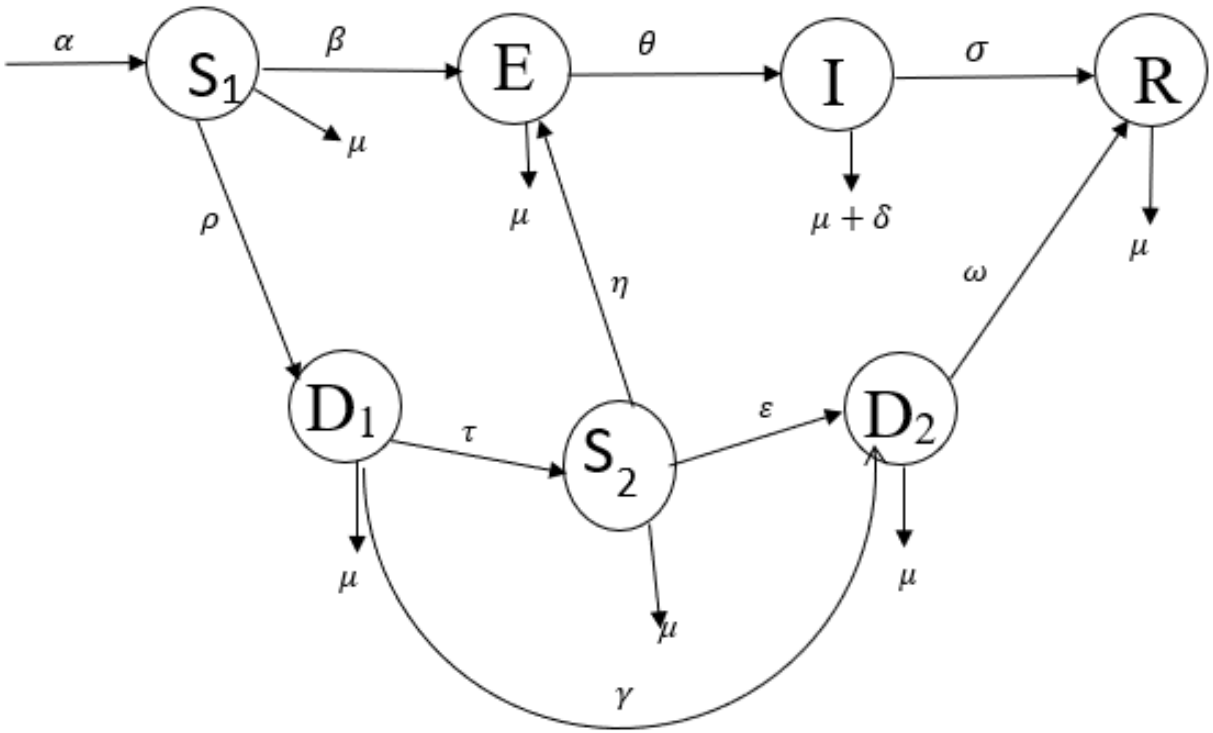

Figure: measles-model chart

Model Formation III

The equations of the model are formulated in the form of a system of ordinary differential equations as shown below:

$$\frac{dS_1}{dt} = \alpha - \beta S_1 I - \mu S_1 - \rho S_1 \tag{3.1}$$

$$\frac{dD_1}{dt} = \rho S_1 - \tau D_1 - \mu D_1 - \gamma D_1 \tag{3.2}$$

$$\frac{dS_2}{dt} = \tau D_1 - \eta S_2 - \epsilon S_2 - \mu S_2 \tag{3.3}$$

$$\frac{dD_2}{dt} = \epsilon S_2 + \gamma D_1 - \mu D_2 - \omega D_2 \tag{3.4}$$

$$\frac{dE}{dt} = \beta S_1 I + \eta S_2 - \theta E - \mu E \tag{3.5}$$

$$\frac{dI}{dt} = \theta E - \sigma I - \mu I - \phi I \tag{3.6}$$

$$\frac{dR}{dt} = \sigma I + \omega D_2 - \mu R \tag{3.7}$$

Boundedness of the Solution

Let the total population be $N = S_1(t) + D_1(t) + S_2(t) + D_2(t) + E(t) + I(t) + R(t)$, then

$$\frac{dN}{dt} = \frac{dS_1}{dt} + \frac{dD_1}{dt} + \frac{dS_2}{dt} + \frac{dD_2}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = \alpha - (S_1 + D_1 + S_2 + D_2 + E + I + \tag{3.8}$$

This implies that

$$\frac{dN}{dt} \leq \alpha - \mu N \tag{3.9}$$

Integrating both sides of (3.9) we have

$$\int_0^t \frac{dN}{\alpha - \mu N} \leq \int_0^t dt \tag{3.10}$$

$$-\frac{1}{\mu} \ln(\alpha - \mu N)\Big|_0^t \leq t \tag{3.11}$$

Analysis of the Model II

Hence (3.10) gives

$$N_t \leq \frac{\alpha}{\mu} - \left[\frac{\alpha - \mu N_0}{\mu}\right] e^{-\mu t} \tag{3.12}$$

By taking $t \to \infty$, we obtain $N_t = \frac{\alpha}{\mu}$. This implies that the model in (3.1) to (3.7) can be studied in the feasible region.

Equilibrium State of the Model I

At equilibrium, the time derivatives are equal to zero, i.e.,

$$\frac{dN}{dt} = \frac{dS_1}{dt} = \frac{dD_1}{dt} = \frac{dS_2}{dt} = \frac{dD_2}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0 \tag{3.13}$$

Disease Free Equilibrium (DFE) State
Let

$$E^0 = (S_1^0, D_1^0, S_2^0, D_2^0, E^0, I^0, R^0) \tag{3.14}$$

To find the Disease Free Equilibrium (DFE) state of the given system of differential equations, we set the rates of change (the derivatives) to zero and solve for the equilibrium values of the state variables when there is no infection. At the DFE, there should be no infected individuals, meaning $I = 0$ and $E = 0$.
substituting $I = 0$ and $E = 0$ into equations (3.1) to (3.7) gives:

$$(S_1, D_1, S_2, D_2, E, I, R) = \left(\frac{\alpha}{\mu + \rho}, 0, 0, 0, 0, 0, 0\right) \tag{3.15}$$

Equation (3.15) is the Disease-Free Equilibrium (DFE) point of the model.
Endemic Equilibrium State:

Equilibrium State of the Model II

$$S_1 = \frac{\alpha}{\beta I + \mu + \rho} \tag{3.16}$$

$$D_1 = \frac{\rho\alpha}{(\beta I + \mu + \rho)(\tau + \mu + \gamma)} \tag{3.17}$$

$$S_2 = \frac{\tau\rho\alpha}{(\beta I + \mu + \rho)(\tau + \mu + \gamma)(\eta + \epsilon + \mu)} \tag{3.18}$$

$$D_2 = \frac{\rho\alpha(\epsilon\tau(\eta + \epsilon + \mu) + \gamma)}{(\beta I + \mu + \rho)(\tau + \mu + \gamma)(\mu + \omega)} \tag{3.19}$$

$$E = \frac{(\sigma + \mu + \varphi)I}{\theta} \tag{3.20}$$

$$R = \frac{\sigma I}{\mu} + \frac{\omega\rho\alpha(\epsilon\tau(\eta + \epsilon + \mu) + \gamma)}{\mu(\beta I + \mu + \rho)(\tau + \mu + \gamma)(\mu + \omega)} \tag{3.21}$$

The Basic Reproduction Number (R_0) I

In this model, the next generation matrix method as described by Driessche (2002) is used to get the basic reproduction number R_0. The basic reproduction number of an infected person is a threshold that indicates the total number of potential diseases that have developed in a completely susceptible population during its transmission period. It is given by $R_0 = \rho(FV^{-1})$. F and V are the matrices created for the new infection and transmission, respectively.
The infection components are $E(t)$ and $I(t)$ in equations (3.5) and (3.6) above, given by

$$\left.\begin{aligned} \frac{dE}{dt} &= \beta S_1 I + \eta S_2 - (\theta + \mu)E \\ \frac{dI}{dt} &= \theta E - (\sigma + \mu + \phi)I \end{aligned}\right\} \tag{3.22}$$

We can define the vectors $X = [E, I]$ and the matrices F and V as follows:

$$F = \begin{bmatrix} 0 & \beta S_1 \\ 0 & 0 \end{bmatrix} \quad \text{and} \quad V = \begin{bmatrix} \theta + \mu & 0 \\ \theta & \sigma + \mu + \phi \end{bmatrix}$$

Then, the next-generation matrix FV^{-1} can be calculated as:

$$FV^{-1} = \begin{bmatrix} 0 & \beta S_1 \\ 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{\theta+\mu} & \frac{-\theta}{(\theta+\mu)(\sigma+\mu+\phi)} \\ 0 & \frac{1}{\sigma+\mu+\phi} \end{bmatrix}$$

The Basic Reproduction Number (R_0) II

And this simplifies to:

$$FV^{-1} = \begin{bmatrix} 0 & \frac{-\beta S_1}{(\sigma+\mu+\phi)} \\ 0 & 0 \end{bmatrix}$$

The basic reproduction number (R_0) for this system is given by:

$$R_0 = \frac{\beta S_1}{\sigma + \mu + \phi} \tag{3.23}$$

Local Stability of the Disease Free Equilibrium I

In analyzing the local stability for the disease free equilibrium, we obtain the Jacobian matrix for the system of our model (3.1) – (3.7). The Jacobian matrix of our model equations is given as:
In analyzing the local stability for the disease free equilibrium, we obtain the Jacobian matrix for the system of our model (3.1) – (3.7). The Jacobian matrix of our model equations is given as:

$$J_E = \begin{pmatrix} -(\beta I + \mu + \rho) & 0 & 0 & 0 & 0 & -\beta S_1 & 0 \\ \rho & -(\tau + \mu + \gamma) & 0 & 0 & 0 & 0 & 0 \\ 0 & \tau & -(\eta + \epsilon + \mu) & 0 & 0 & 0 & 0 \\ 0 & \gamma & \epsilon & -(\mu + \omega) & 0 & 0 & 0 \\ \beta I & 0 & \eta & 0 & -(\theta + \mu) & \beta S_1 & 0 \\ 0 & 0 & 0 & 0 & \theta & -(\sigma + \mu + \theta) & 0 \\ 0 & 0 & 0 & \omega & 0 & \sigma & -\mu \end{pmatrix} \quad (3.24)$$

At Disease Free Equilibrium (DFE), equation (3.24) above will become

$$J_E = \begin{pmatrix} -(\mu + \rho) & 0 & 0 & 0 & 0 & -\frac{\beta\alpha}{(\mu+\rho)} & 0 \\ \rho & -(\tau + \mu + \gamma) & 0 & 0 & 0 & 0 & 0 \\ 0 & \tau & -(\eta + \epsilon + \mu) & 0 & 0 & 0 & 0 \\ 0 & \gamma & \epsilon & -(\mu + \omega) & 0 & 0 & 0 \\ 0 & 0 & \eta & 0 & -(\theta + \mu) & \frac{\beta\alpha}{(\mu+\rho)} & 0 \\ 0 & 0 & 0 & 0 & \theta & -(\sigma + \mu + \theta) & 0 \\ 0 & 0 & 0 & \omega & 0 & \sigma & -\mu \end{pmatrix} \quad (3.25)$$

where:

$$A = (\mu + \rho)$$

Local Stability of the Disease Free Equilibrium II

$$B = (\tau + \mu + \gamma)$$

$$C = (\eta + \epsilon + \mu)$$

$$D = (\mu + \omega)$$

$$E = (\theta + \mu)$$

$$F = (\sigma + \mu + \phi)$$

substituting into equation (3.24)above gives:

$$J_E = \begin{pmatrix} -A & 0 & 0 & 0 & 0 & -\frac{\beta\alpha}{A} & 0 \\ \rho & -B & 0 & 0 & 0 & 0 & 0 \\ 0 & \tau & -C & 0 & 0 & 0 & 0 \\ 0 & \gamma & \epsilon & -D & 0 & 0 & 0 \\ 0 & 0 & \eta & 0 & -F & \frac{\beta\alpha}{A} & 0 \\ 0 & 0 & 0 & 0 & \theta & -G & 0 \\ 0 & 0 & 0 & \omega & 0 & \sigma & -\mu \end{pmatrix} \tag{3.26}$$

Applying elementary row operation on equation (3.27), we have;

$$R_2 = R_2 - \frac{\rho}{(-A)} R_2$$

Local Stability of the Disease Free Equilibrium III

$$J_E = \begin{pmatrix} -A & 0 & 0 & 0 & 0 & -\frac{\rho\beta\alpha}{A} & 0 \\ 0 & -B & 0 & 0 & 0 & 0 & 0 \\ 0 & \tau & -C & 0 & 0 & 0 & 0 \\ 0 & \gamma & \epsilon & -D & 0 & 0 & 0 \\ 0 & 0 & \eta & 0 & -F & \frac{\beta\alpha}{A} & 0 \\ 0 & 0 & 0 & 0 & \theta & -G & 0 \\ 0 & 0 & 0 & \omega & 0 & \sigma & -\mu \end{pmatrix} \tag{3.27}$$

$$R_3 = R_3 - \frac{\tau}{(-B)} R_2$$

and

$$R_4 = R_4 - \frac{\gamma}{(-B)} R_2$$

$$J_E = \begin{pmatrix} -A & 0 & 0 & 0 & 0 & -\frac{\beta\alpha}{A} & 0 \\ 0 & -B & 0 & 0 & 0 & -\frac{\rho\beta\alpha}{A^2} & 0 \\ 0 & \tau & -C & 0 & 0 & -\frac{\tau\rho\beta\alpha}{BA^2} & 0 \\ 0 & \gamma & \epsilon & -D & 0 & -\frac{\rho\beta\alpha}{BA^2} & 0 \\ 0 & 0 & \eta & 0 & -F & \frac{\beta\alpha}{A} & 0 \\ 0 & 0 & 0 & 0 & \theta & -G & 0 \\ 0 & 0 & 0 & 0 & 0 & \sigma & -\mu \end{pmatrix} \tag{3.28}$$

Local Stability of the Disease Free Equilibrium IV

$$R_4 = R_4 - \frac{\epsilon}{(-C)} R_3$$

and

$$R_5 = R_5 - \frac{\eta}{(-C)} R_3$$

$$J_E = \begin{pmatrix} -A & 0 & 0 & 0 & 0 & -\frac{\beta\alpha}{A} & 0 \\ 0 & -B & 0 & 0 & 0 & -\frac{\rho\beta\alpha}{A} & 0 \\ 0 & \tau & -C & 0 & 0 & -\frac{\tau\rho\beta\alpha}{A^2} & 0 \\ 0 & \gamma & \epsilon & -D & 0 & -\frac{\epsilon\rho\beta\alpha}{CBA^2} & 0 \\ 0 & 0 & \eta & 0 & -F & \frac{\beta\alpha}{A} - \frac{\gamma\beta\alpha}{BA^2} & 0 \\ 0 & 0 & 0 & 0 & \theta & -G & 0 \\ 0 & 0 & 0 & 0 & 0 & \sigma & -\mu \end{pmatrix} \tag{3.29}$$

$$R_6 = R_6 - (\frac{\theta}{-F}) R_5$$

and

$$R_7 = R_7 - (\frac{\omega}{-D}) R_4$$

Local Stability of the Disease Free Equilibrium V

$$J_E = \begin{pmatrix} -A & 0 & 0 & 0 & 0 & -\frac{\beta\alpha}{A} & 0 \\ 0 & -B & 0 & 0 & 0 & -\frac{\rho\beta\alpha}{A} & 0 \\ 0 & \tau & -C & 0 & 0 & -\frac{\tau\rho\beta\alpha}{A^2} & 0 \\ 0 & \gamma & \epsilon & -D & 0 & -\frac{\epsilon\rho\beta\alpha}{CBA^2} & 0 \\ 0 & 0 & \eta & 0 & -F & \frac{\beta\alpha}{A} - \frac{\gamma\beta\alpha}{BA^2} & 0 \\ 0 & 0 & 0 & 0 & \theta & -(G+H) & 0 \\ 0 & 0 & 0 & 0 & 0 & \sigma + (\frac{\omega}{D})(\frac{\epsilon\rho\beta\alpha}{CBA^2}) & -\mu \end{pmatrix} \tag{3.30}$$

where

$$H = (\frac{\theta}{F})(\frac{\beta\alpha}{A} - \frac{\tau\rho\beta\alpha}{BA^2})$$

and

$$K = \sigma + (\frac{\omega}{D})(\frac{\epsilon\rho\beta\alpha}{CBA^2})$$

now

$$R_7 = R_7 - (\frac{K}{-(G+H)})R_4$$

$$J_E = \begin{pmatrix} -A & 0 & 0 & 0 & 0 & -\frac{\beta\alpha}{A} & 0 \\ 0 & -B & 0 & 0 & 0 & -\frac{\rho\beta\alpha}{A} & 0 \\ 0 & \tau & -C & 0 & 0 & -\frac{\tau\rho\beta\alpha}{A^2} & 0 \\ 0 & \gamma & \epsilon & -D & 0 & -\frac{\epsilon\rho\beta\alpha}{CBA^2} & 0 \\ 0 & 0 & \eta & 0 & -F & \frac{\beta\alpha}{A} - \frac{\gamma\beta\alpha}{BA^2} & 0 \\ 0 & 0 & 0 & 0 & \theta & -(G+H) & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -\mu \end{pmatrix} \tag{3.31}$$

Local Stability of the Disease Free Equilibrium VI

Equation (3.31) is an upper triangular matrix

Theorem

:(Local Stability of DFE)
The disease-free equilibrium state is locally asymptotically stable if all the eigenvalues of the Jacobian matrix (3.18) are negative, otherwise unstable.

Proof.
We calculate the eigenvalues λ_i where $i = 1, 2, \ldots, n$ of the Jacobian matrix to determine the nature of the eigenvalues using the characteristic equation. From the upper triangular Jacobian matrix in (3.18), we get the characteristic equation as

$$J_E = \begin{pmatrix} -A-\lambda & 0 & 0 & 0 & 0 & -\frac{\beta\alpha}{A} & 0 \\ 0 & -B-\lambda & 0 & 0 & 0 & -\frac{\rho\beta\alpha}{A} & 0 \\ 0 & \tau & -C-\lambda & 0 & 0 & -\frac{\tau\rho\beta\alpha}{A^2} & 0 \\ 0 & \gamma & \epsilon & -D-\lambda & 0 & -\frac{\epsilon\rho\beta\alpha}{CBA^2} & 0 \\ 0 & 0 & \eta & 0 & -F-\lambda & \frac{\beta\alpha}{A} - \frac{\gamma\beta\alpha}{BA^2} & 0 \\ 0 & 0 & 0 & 0 & \theta & -(G+H)-\lambda & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -\mu-\lambda \end{pmatrix} \tag{3.32}$$

Equation (3.32) yield

$$(-A-\lambda)(-B-\lambda)(-C-\lambda)(-D-\lambda)(-F-\lambda)(-(G+H)-\lambda)(-\mu-\lambda) = 0 \tag{3.33}$$

Hence equation (3.33) implies,

$$\lambda_1 = -A < 0 \tag{3.34}$$

Local Stability of the Disease Free Equilibrium VII

$$\lambda_2 = -B < 0 \tag{3.35}$$

$$\lambda_3 = -C < 0 \tag{3.36}$$

$$\lambda_4 = -D < 0 \tag{3.37}$$

$$\lambda_5 = -F < 0 \tag{3.38}$$

$$\lambda_1 = -(G + H) < 0 \tag{3.39}$$

$$\lambda_1 = -\mu < 0 \tag{3.40}$$

Hence, the Disease Free Equilibrium (DFE) is locally asymptotically stable if (3.34) – (3.40) hold, otherwise unstable.

References I

- Abbas, Moustafa, et al. "Seroprevalence of Measles, Mumps, Rubella and Varicella among Staff of a Hospital in Riyadh, Saudi Arabia." PubMed, vol. 82, 1 Jan. 2007, p. 283. Accessed 28 May 2024.
- Balcha Masresha, et al. "Measles Mortality Reduction and Pre-Elimination in the African Region, 2001–2009." The Journal of Infectious Diseases, vol. 204, no. $suppl_1$, 1 July 2011, pp. S198–S204, https://doi.org/10.1093/infdis/jir116. Accessed 2 May 2023.
- Dabbagh, Alya, et al. "Progress toward Regional Measles Elimination — Worldwide, 2000–2017." MMWR. Morbidity and Mortality Weekly Report, vol. 67, no. 47, 30 Nov. 2018, pp. 1323–1329, https://doi.org/10.15585/mmwr.mm6747a6. Accessed 6 Apr. 2019.
- Estofolete, Cassia Fernanda, et al. "Prevalence of Measles Antibodies in São José Do Rio Preto, São Paulo, Brazil: A Serological Survey Model." Scientific Reports, vol. 10, no. 1, 20 Mar. 2020, p. 5179, www.nature.com/articles/s41598-020-62151-3, https://doi.org/10.1038/s41598-020-62151-3. Accessed 11 Feb. 2021.

References II


Griffin, Diane. "The Immune Response in Measles: Virus Control, Clearance and Protective Immunity." Viruses, vol. 8, no. 10, 12 Oct. 2016, p. 282, www.ncbi.nlm.nih.gov/pmc/articles/PMC5086614/, https://doi.org/10.3390/v8100282. Accessed 25 Mar. 2019.


Gupta, Satish Kumar, et al. "Introduction Strategy of a Second Dose Measles Containing Vaccine in India." Indian Pediatrics, vol. 48, no. 5, May 2011, pp. 379–382, https://doi.org/10.1007/s13312-011-0066-1. Accessed 16 Apr. 2021.


Janse, Marga, et al. "Identifying Cross-Utilization of RSV Vaccine Inventions across the Human and Veterinary Field." Pathogens, vol. 12, no. 1, 27 Dec. 2022, p. 46, https://doi.org/10.3390/pathogens12010046. Accessed 1 Jan. 2023.


Loharikar, Anagha, et al. "Status of New Vaccine Introduction — Worldwide, September 2016." MMWR. Morbidity and Mortality Weekly Report, vol. 65, no. 41, 21 Oct. 2016, pp. 1136–1140, www.cdc.gov/mmwr/volumes/65/wr/mm6541a3.htm, https://doi.org/10.15585/mmwr.mm6541a3. Accessed 27 Nov. 2019.

References III

- Masresha, Balcha, et al. "Introduction of the Second Dose of Measles Containing Vaccine in the Childhood Vaccination Programs within the WHO Africa Region -Lessons Learnt." Journal of Immunological Sciences, vol. 2, no. SI1, 1 Sept. 2018, pp. 113–121, https://doi.org/10.29245/2578-3009/2018/si.1117. Accessed 14 Jan. 2023.
- Mina, Michael J., et al. "Measles Virus Infection Diminishes Preexisting Antibodies That Offer Protection from Other Pathogens." Science, vol. 366, no. 6465, 31 Oct. 2019, pp. 599–606, https://doi.org/10.1126/science.aay6485. Accessed 5 Dec. 2019.
- Moss, William J., and Peter Strebel. "Biological Feasibility of Measles Eradication." The Journal of Infectious Diseases, vol. 204, no. $suppl_1$, July 2011, pp. S47–S53, academic.oup.com/jid/article/204/$suppl_1$/S47/2192303 , https://doi.org/10.1093/infdis/jir065. Accessed 18 May 2019.
- Otten, M, et al. "Public-Health Impact of Accelerated Measles Control in the WHO African Region 2000–03." The Lancet, vol. 366, no. 9488, 3 Sept. 2005, pp. 832–839, www.sciencedirect.com/science/article/abs/pii/S0140673605672169, https://doi.org/10.1016/S0140-6736(05)67216-9. Accessed 21 Nov. 2020.

References IV

- Poland, Gregory A. "Variability in Immune Response to Pathogens: Using Measles Vaccine to Probe Immunogenetic Determinants of Response." American Journal of Human Genetics, vol. 62, no. 2, 1 Feb. 1998, pp. 215–220, https://doi.org/10.1086/301736. Accessed 25 Apr. 2023.
- Takahashi, Saki, et al. "The Geography of Measles Vaccination in the African Great Lakes Region." Nature Communications, vol. 8, no. 1, 25 May 2017, https://doi.org/10.1038/ncomms15585.
- Wallace, Aaron S., et al. "Assessment of Vaccine Wastage Rates, Missed Opportunities, and Related Knowledge, Attitudes and Practices during Introduction of a Second Dose of Measles-Containing Vaccine into Cambodia's National Immunization Program." Vaccine, vol. 36, no. 30, July 2018, pp. 4517–4524, https://doi.org/10.1016/j.vaccine.2018.06.009. Accessed 15 Apr. 2020.
- World Health Organization. "Measles Vaccines: WHO Position Paper, April 2017 – Recommendations." Vaccine, vol. 37, no. 2, Jan. 2019, pp. 219–222, https://doi.org/10.1016/j.vaccine.2017.07.066. Accessed 20 June 2019.
- "World Health Organization." Who.int, World Health Organization, 2022, www.who.int/.

References V


Yanagi, Y. "Measles Virus: Cellular Receptors, Tropism and Pathogenesis." Journal of General Virology, vol. 87, no. 10, 1 Oct. 2006, pp. 2767–2779, https://doi.org/10.1099/vir.0.82221-0. Accessed 20 Apr. 2020.

May 28, 2024

Thank You