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A Mathematical Model of Cerebrospinal Meningitis Epidemic: A Case Study for Jirapa District, Ghana

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Abstract

We develop a mathematical model that governs the epidemiology of cerebrospinal meningitis (CSM) in Jirapa, Ghana. For proper control to be instituted, however, the cerebrospinal meningitis and their dynamics must be known. This paper reports on the dynamics of cerebrospinal meningitis caused by bacterial infection and gives suggestions as how they can be controlled. We study the existence of a solution, the stability of equilibria, and investigate bifurcations of the system. We perform numerical simulation on the model for Jirapa District in Upper West Region of Ghana.

Keywords: Mathematical Model, Cerebrospinal meningitis (CSM), Stability Analysis, Bifurcation, Respiratory Tract, Simulation**.**

1. Introduction

In the Gold Coast (Ghana), an epidemic of Cerebrospinal Meningitis (CSM) was reported for the first time in 1906; it seems probable that this was caused by meningococcus. Infection with meningococcus can cause a variety of diseases, but the most common ones are meningitis (the swelling of the membranes and fluid that cover the brain and spinal cord) and/or septicaemia (blood poisoning). The epidemic started in the north-west of the Gold Coast and spread widely throughout the area during the following dry season [1]. During the dry season, the presence of dust in the air and upper respiratory tract infections due to cold nights, the local immunity of the pharynx are diminished increasing the risk of meningitis. The organism causing the disease is transmitted through direct contact via respiratory droplets from an infected person to an uninfected person in a homogeneous population. For instance due to overcrowding situations in boarding schools and in various household in the community, a person is easily infected with the disease since the probability of walking within the range of the respiratory droplet of an infective person is very high. The bacteria can then manoeuvre their way into the bloodstream where they may invade and multiply in the cerebrospinal fluid. In most people, antibodies kill the bacteria before they can cause the disease [2], however it is possible to carry the meningococci and be infectious while not showing any symptoms of infection. We have included the recorded trend of spread of cerebrospinal meningitis for the past four years, with data from District Health Management Team (DHMT), as shown in Figure 1.

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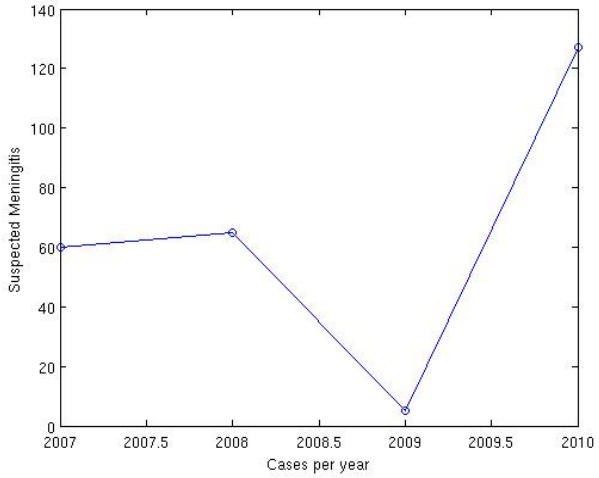

Figure 1 Cerebrospinal Meningitis data reported by the District Health Management Team (DHMT) of Jirapa from 2007 – 2010

According to the Director General of Ghana Health Service at least 20 people have died and several others hospitalized in the Upper West, Upper East and Northern Regions of Ghana following an outbreak of cerebrospinal meningitis (CSM). Medical experts confirmed that cases reported in Jirapa district (worst affected) were beyond the epidemic threshold following the death of 8 out of 52 initial reported cases. Meningitis control activities currently rely on the early identification of epidemics followed by a rapid deployment of polysaccharide vaccines [3]. Although much debate has been dedicated to the efficacy of these interventions [4, 5], it is widely recognised that there is only a short lead-time for vaccination once an epidemic is underway. This constraint is because current vaccines lack immunological memory and confer no significant herd immunity [6]. Bacterial meningitis should always be viewed as a medical emergency since it is potentially fatal and treatment must be initiated as quickly as possible. In trying to reduce the number of carriers in the community, a range of drugs available currently includes penicillin G, ampicillin, chloramphenicol and ceftriaxone. Oily chloramphenicol is the drug of choice in areas with limited health facilities and during epidemics since it is less expensive and given intramuscularly as a single dose injection [7]. Hence a mathematical model based on the Susceptible-Carrier-Infectives-Vaccination-Recovered (SCIVR) model perfectly applies in this situation.

2. Mathematical Modeling

We divide the population (N) into five sub-populations, according to their disease status: the populations who are susceptible to infection (S), those who are carrying the infection and are infectious, but show no sign of the disease (C), those who have the disease and are still infected (I), those who have been immune following vaccination (V), and those who are recovered (R). The susceptible population is increased by recruitment of individuals (either by birth or immigration), and by the loss of immunity, acquired through previous vaccination or natural infection. This population is reduced through vaccination (moving to class V), infection (moving to class I) and by natural death or emigration. The population of vaccinated individuals is increased by

vaccination of susceptible individuals. Since the vaccine does not confer immunity to all vaccine recipients, vaccinated individuals may become infected, but at a lower rate than unvaccinated. The vaccinated class is thus diminished by this infection (moving to class I) by waning of vaccine-based immunity (moving to class S) and by natural death. The population of carrier individuals is increased by those carrying of infection of susceptibles, including those who remain susceptible despite being vaccinated. It is diminished by natural death, death due to disease and by recovery from the disease (moving to class R). The population of infected individuals is increased by infection of susceptibles, including those who remain susceptible despite being vaccinated. It is diminished by natural death, death due to disease and by recovery from the disease (moving to class R). The recovered class is increased by individuals recovering from their infection and is decreased as individuals succumb to natural death. The interactions between the five categories of the population are shown in Figure 2.

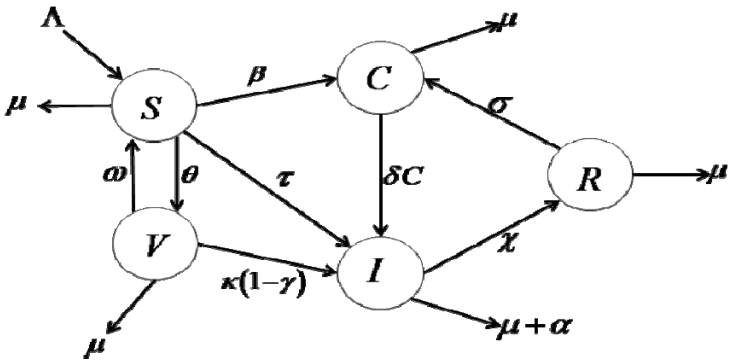

Figure 2 A compartmental model for the cerebrospinal meningitis.

2.1 Assumptions

Six assumptions were assumed as follows:

(1) A constant population with the birth and death rate being equal.
(2) Recovered individuals cannot be vaccinated.
(3) A vaccinated individual who gets infected and then recovers will return to the susceptible class with no vaccine protection.
(4) People cannot recover from the carriage state or infected state and return to the susceptible population – i.e. once infected you cannot be re-infected.
(5) You cannot die directly from the disease.
(6) There is a natural death rate from each compartment.

$$\left.\begin{aligned}
\frac{dS}{dt} &= \Lambda + \omega V - (\theta + \mu + \beta + \tau) S \\
\frac{dC}{dt} &= \beta S + \sigma R - (\delta + \mu) C \\
\frac{dI}{dt} &= \tau S + \delta C + \kappa(1-\gamma) V - (\alpha + \mu + \chi) I \\
\frac{dV}{dt} &= \theta S - (\mu + \omega) V - \kappa(1-\gamma) V \\
\frac{dR}{dt} &= \chi I - (\sigma + \mu) R
\end{aligned}\right\} \qquad 1$$

We have a five-dimensional nonlinear system with the form:

$$\left.\begin{aligned}
S' &= f_1(S,C,I,V,R) \\
C' &= f_2(S,C,I,V,R) \\
I' &= f_3(S,C,I,V,R) \\
V' &= f_4(S,C,I,V,R) \\
R' &= f_5(S,C,I,V,R)
\end{aligned}\right\} \qquad 2$$

where $\Lambda, \omega, \theta, \mu, \beta, \delta, \sigma, \alpha, \chi, \tau, \kappa$ and γ are non- negative parameters. The model parameters and their respective description are given in Table 1.

Table 1 Model parameters and their interpretations

Parameter	Description
Λ	Recruitment rate
μ	Natural death rate
γ	Vaccine efficacy
β	Carrier infection rate
δ	Rate moving from carrier to infected
σ	Recovery rate of carriers
θ	Vaccine uptake rate
χ	Recovery rate of infection
ω	Rate at which vaccine wanes
α	Death rate due to infection
τ	Infection rate
κ	Proportion of infected people who are vaccinated

2.2 Equilibrium points and local stability analysis

We find the equilibrium solution of Equation 2 by calculating $f_1\left(\hat{S},\hat{C},\hat{I},\hat{V},\hat{R}\right)=0$, $f_2\left(\hat{S},\hat{C},\hat{I},\hat{V},\hat{R}\right)=0$, $f_3\left(\hat{S},\hat{C},\hat{I},\hat{V},\hat{R}\right)=0$, $f_4\left(\hat{S},\hat{C},\hat{I},\hat{V},\hat{R}\right)=0$ and $f_5\left(\hat{S},\hat{C},\hat{I},\hat{V},\hat{R}\right)=0$ simultaneously which has a disease – free equilibrium $E_0=\left(S_0,0,0,V_0,0\right)$, where

$$S_0=\frac{\Lambda\left(\kappa-\kappa\gamma+\mu+\omega\right)}{\left(\tau+\beta+\theta+\mu+\omega\right)},\quad \textit{and}\quad V_0=\frac{\Lambda\theta}{\left(\tau+\beta+\theta+\mu+\omega\right)}$$

There is an endemic equilibrium $\hat{E}=\left(\hat{S},\hat{C},\hat{I},\hat{V},\hat{R}\right)$ if $R_0>1$ where

$$\hat{S}=\frac{\Lambda+\omega\hat{V}}{\left(\theta+\mu+\beta+\tau\right)},$$

$$\hat{C}=\frac{\beta\hat{S}+\sigma\hat{R}}{\left(\delta+\mu\right)},$$

$$\hat{I}=\frac{\tau\hat{S}+\delta\hat{C}+\kappa\left(1-\gamma\right)\hat{V}}{\left(\alpha+\mu+\chi\right)},$$

$$\hat{V}=\frac{\theta\hat{S}}{\left(\mu+\omega\right)-\kappa\left(1-\gamma\right)},$$

$$\hat{R}=\frac{\chi\hat{I}}{\sigma+\mu}.$$

Regarding the stability of the disease – free equilibrium E_0, we have the following result.

Definition: The basic reproduction number R_0 is the average number of secondary infections produced when one infected individual is introduced into a host virgin population.

Theorem 1. *If* $R_0<1$ *the* E_0 *is stable; if* $R_0>1$ *then* E_0 *is unstable.*

Proof. The Jacobian matrix at E_0 is

$$J\left(E_0\right)=\begin{pmatrix}-\left(\theta+\mu+\beta+\tau\right) & 0 & 0 & \omega & 0\\ \beta & -\left(\delta+\mu\right) & 0 & 0 & \sigma\\ \tau & \delta & -\left(\alpha+\mu+\chi\right) & \kappa\left(1-\gamma\right) & 0\\ \theta & 0 & 0 & -\left(\mu+\omega\right)-\kappa\left(1-\gamma\right) & 0\\ 0 & 0 & \chi & 0 & -\left(\sigma+\mu\right)\end{pmatrix}$$

The eigenvalues of the matrix J, can be determined by roots of the characteristic equation $\left|J-\lambda I\right|=0$ where, I is the Identity matrix

$$\begin{vmatrix} -(\theta+\mu+\beta+\tau)-\lambda & 0 & 0 & \omega & 0 \\ \beta & -(\delta+\mu)-\lambda & 0 & 0 & \sigma \\ \tau & \delta & -(\alpha+\mu+\chi)-\lambda & \kappa(1-\gamma) & 0 \\ \theta & 0 & 0 & \left[-(\mu+\omega)-\kappa(1-\gamma)\right]-\lambda & 0 \\ 0 & 0 & \lambda & 0 & -(\sigma+\mu)-\lambda \end{vmatrix} = 0$$

$$-\sigma-\mu-\lambda \begin{vmatrix} -\theta-\mu-\beta-\tau-\lambda & \theta & 0 & \omega \\ \beta & -\delta-\mu-\lambda & 0 & 0 \\ \tau & \delta & -\alpha-\mu-\chi-\lambda & \kappa(1-\gamma) \\ \theta & 0 & 0 & -\mu-\omega-\kappa-\kappa\gamma-\lambda \end{vmatrix} = 0$$

$$(\sigma+\mu+\lambda)(\alpha+\mu+\chi+\lambda) \begin{vmatrix} -\theta-\mu-\beta-\tau-\lambda & 0 & \omega \\ \beta & -\delta-\mu-\lambda & 0 \\ \theta & 0 & -\mu-\omega-\kappa-\kappa\gamma-\lambda \end{vmatrix} = 0$$

$$(\sigma+\mu+\lambda)(\alpha+\mu+\chi+\lambda)(-\delta-\mu-\lambda) \begin{vmatrix} -\theta-\mu-\beta-\tau-\lambda & \omega \\ \theta & -\mu-\omega-\kappa-\kappa\gamma-\lambda \end{vmatrix} = 0$$

Let

$$A = \begin{pmatrix} -(\theta+\mu+\beta+\tau) & \omega \\ \theta & -(\mu+\omega+\kappa+\kappa\gamma) \end{pmatrix}$$

Then all eigenvalues of matrix $J(E_0)$, λ, are negative if

(i) $det(A) > 0$

(ii) $Trace(A) < 0$

Now

$$det(A) = (\theta+\mu+\beta+\tau)(\mu+\omega+\kappa+\kappa\gamma) - \omega\theta$$

and

$$Trace(A) = -(\theta+\mu+\beta+\tau) - (\mu+\omega+\kappa+\kappa\gamma)$$

Clearly $Trace(A) < 0$ since all coefficients $\theta, \mu, \beta, \tau, \omega, \kappa$ and γ are positive. The implication of the negativity of all the eigenvalues of the Jacobian is that disease – free equilibrium is stable. To discuss the properties of the endemic equilibrium $\hat{E} = (\hat{S}, \hat{C}, \hat{I}, \hat{V}, \hat{R})$ we form an associated Jacobian matrix J^* and obtaining the eigenvalues as usual from $|J^* - \lambda I| = 0$. Results in characteristics polynomial of the form $a^5 + b_1 a^4 + b_2 a^3 + b_3 a^2 + b_4 a + b_5 = 0$ where, $b_1, b_2, \cdots\cdots, b_5$, are values depending on the various combination of the model parameter. In this case the five eigenvalues could be negative, positive, zeros, or any combination of the three alternatives. Thus, the endemic equilibrium could be stable, unstable, or saddle.

3. Numerical Simulations

The system is solved using a fourth order Runge - Kutta scheme. The parameter values that we use for numerical simulations are shown in Table 2 with initial conditions: $S(0) = 100$, $C(0) = 0$, $I(0) = 0$, $V(0) = 20$, and $R(0) = 0$. The dynamics of cerebrospinal meningitis diseases with and without carriers have already been carried out in previous studies, but these models do not account for the vaccination. Therefore, we illustrate some numerical results for the model with vaccination (Figures 3-7).

Table 2 Parameters values used in numerical simulations

Parameter	Description	Values	References
Λ	Recruitment rate	0.125	Estimated
μ	Natural death rate	0.05	DHMT
γ	Vaccine efficacy	0.5	Estimated
β	Carrier infection rate	0.01	Estimated
δ	Rate moving from carrier to infected	0.8	[10]
σ	Recovery rate of carriers	0.3	[10]
θ	Vaccine uptake rate	0.7	Estimated
χ	Recovery rate of infection	0.1	[10]
ω	Rate at which vaccine wanes	0.05	Assumed
α	Death rate due to infection	0.1	DHMT
τ	Infection rate	0.02	Estimated
κ	Proportion of infected people who are vaccinated	0.1	Assumed

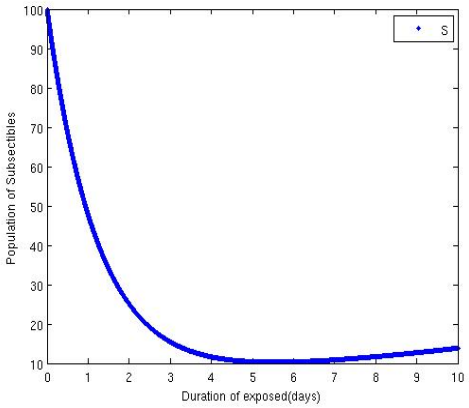

Figure 3 Evolution of the susceptible population per day in Jirapa.

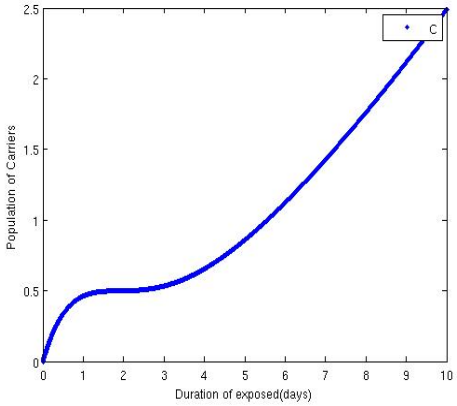

Figure 4 Evolution of the carrier population per day in Jirapa.

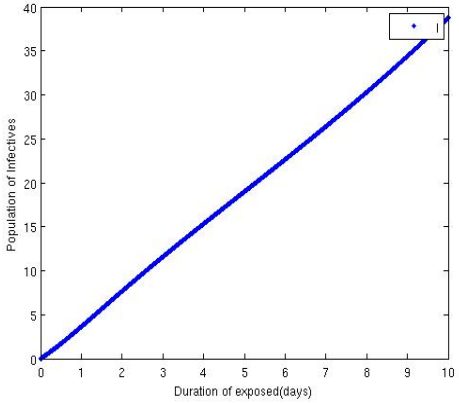

Figure 5 Evolution of the susceptible population per day in Jirapa.

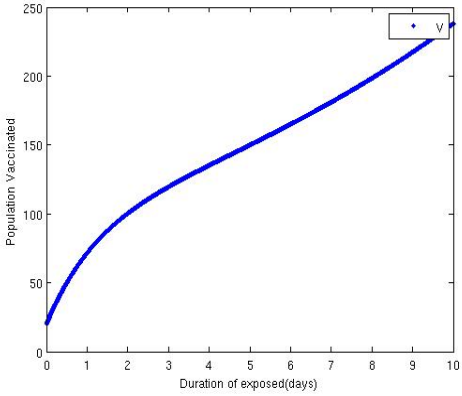

Figure 6 Evolution of the carrier population per day in Jirapa .

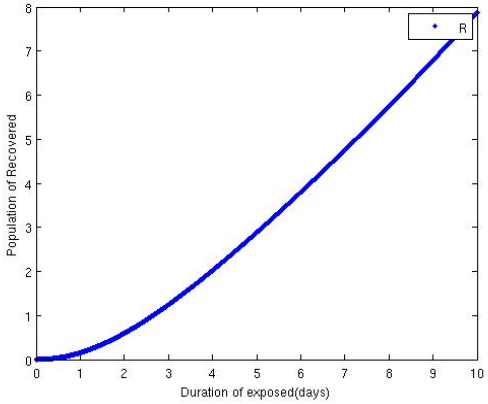

Figure 7 Evolution of the recovered population per day in Jirapa.

From Figure 3 we note that, during the initial days, there is a very sharp drop in the population of subsectible individuals, while other populations increase. The slight rise and fall after the initial 2 days in the population of carriers could be attributed to complacency on the part of some individuals or may be due to oscillations in the system independent of external factors (Figure 4). However in Figure 5, there is an exponential increment of the population of infectives. We find that people tend to relax after the initial shock of the disease threat. However, we note that this is not for long, and this could be attributed to the fact that vaccination levels continue to rise, so as people continue to receive vaccination, infection is controlled (Figure 6). After some time, we note a slight increase in the vaccination levels. However, these numbers remain very low. This could be due to the fact that, as infection rises, a few will risk getting vaccinated in the hope of being cured.

4. Discussion

A typical epidemic starts in the dry season and abates with the onset of the rains. However, the lack of an early warning system in the prediction of meningococcal epidemics makes vaccination almost start shortly before the onset of the rains, which abate meningococcal epidemics even without the vaccine. Vaccination during epidemics arrests only about half of the cases [8] before the onset of the rains.

We have shown that the epidemic of meningococcal disease was already on the decline when nationwide vaccination campaign was launched. However, the introduction of the vaccine reduced the incidence of infection to a predicted low of five cases per year, compared with 40 per year with no vaccination.

For controlling meningitis, especially in Jirapa, the anthropologist can make a considerable contribution in order to understand the local beliefs and find a way to explain the importance of early action and creating adaptation of the population to insure quick treatment of the sick, protection of the other members of the family or community. Cooperation with the traditional healers and investigation and understanding of their methods could contribute to an early intervention on the process of the illness and the spreading of the disease.

We assumed that vaccination gives complete protection against infection and carriage, whereas Trotter *et al.* [9] showed a small chance that there could be carriage or infection after vaccination.

5. Conclusions

The epidemiology of meningococal meningitis was investigated in the Jirapa district in Upper West Ghana. Conventional epidemiological tools were used to determine patients and carrier characteristics. Several molecular typing and phylogenetic analysis techniques were applied to characterize the bacterial isolates, and to compare them to other meningococcal strains isolated in different regions of the world. We showed how stability analysis using linear perturbation equations can determine the stability of steady states of the system. These equilibria can change their stabilities or appear and disappear as a result of changing parameter values. We finish the project by considering numerical solutions of differential equations. We use Matlab to numerically solve both the ordinary differential equation model and simulate the result.

APPENDIX

Data reported by the District Health Management Team (DHMT) Jirapa from 2007-2010 (Tables 3 and 4)

Table 3 Trend of cases from 2007 to 2010

Disease Condition	Cases per year				Remarks
	2007	2008	2009	2010	
Suspected Meningitis	60	65	5	127	Cases from 2007-2009 were all Gram negative. Details of 2010 are shown in Table 4

Table 4 Break down of 2010

Cases	Deaths	General CFR (%)	LP Performance Rate	LPs Done	Nm A	Nm C	Nmw 135	Deaths Due to W135	W135 CFR (%)	S. Pneum	Hib	Others
112	15	13	83	93	1	0	22	4	18	1	0	1

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