Dynamics of Rubella Virus in Populations with Different Vaccination Policies

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Abstract

Rubella is a contagious disease that affects individuals around the world. This mild disease becomes critical when a susceptible pregnant woman is infected. The fetus has a high risk of developing congenital rubella syndrome that leads to malformations and stillbirths. Interaction between countries with different vaccination policies can lead to an increase of rubella cases in either country. In this study we use mathematical models of differential equations to analyze how the interaction between Mexico and the United States affects the dynamics of Rubella. We show that the United States and Mexico must develop a dual policy to succeed in eradicating the rubella virus.

1 Introduction

Rubella, also known as German measles, is a viral disease caused by a togavirus of the genus Rubivirus. It was first identified by George Maton in 1814 and named by Henry Veale in 1866. This highly contagious disease is transmitted when a person inhales air particles, which have been exhaled by infected individuals. The general symptoms of this mild illness include

a rash and adenopathy. In some adult cases, rubella may cause serious symptoms such as low-grade fever, headaches, and swollen glands. Newborns, as well as adults, suffer from serious symptoms. Norman Gregg was the first to observe that rubella infection can cause miscarriages, stillbirths, and malformation of the fetus. If a pregnant woman is infected by the rubella virus during her first trimester of pregnancy, the fetus will be more likely to develop Congenital Rubella Syndrome, CRS (Hethcote 1989, 215). Furthermore, CRS can cause infants to be born with cataracts, heart disease, mental retardation, blindness and deafness (Coronado 1997, 1). The virus' effect on the fetus is a serious public health issue, since "[more] than 20,000 babies were born with birth defects during an outbreak of rubella in 1964-1965. The same outbreak also resulted in at least 10,000 miscarriages and stillbirths" (March of Dimes, 1997). Such outbreaks led scientists and researchers to examine the spread of rubella and to develop a vaccine, introduced to the public in 1969, against the disease. Immunization is achieved through an MMR (Measles, Mumps, Rubella) vaccination. Once an individual contracts the disease, he or she develops antibodies and becomes immune to the virus.

Different countries, such as Mexico and the United States, have their own vaccination policies to control the spread of rubella. In the United States, state laws require that a child receive an MMR vaccination before enrolling in kindergarten, while Mexico prefers to keep their policy of no-vaccination. Mexico's Public Health Center has reported that even though doctors recommend child vaccination, the vaccine increases the age of first infection. Therefore, the vaccine would benefit the children, but the incidences of rubella would then be translated to adults (Hethcote 1997, 215). Consequently, there is a higher probability of pregnant women becoming infected, which leads to an increase in cases of CRS. Marco V. Jose and Mexico's Public Health Center analyzed Mexico's theoretical estimates of rubella cases and found that it was best to keep the policy of no-vaccination. On the other hand, the United States has studied the dynamics of rubella and has concluded that its policy of vaccination is effective. Statistics in the United States show that the number of reported rubella cases has declined by more than 99% since the vaccination policy was enforced. Yet, recently, there has been a moderate increase of rubella and a dramatic increase of CRS cases (Medaccess, 1997). The majority of these cases occur among people in the work place and children born to Hispanic mothers (Coronado 1997, 1). These different views of Mexico and the United States regarding vaccination can lead to a change in the dynamics of rubella in both countries.

In this study, we model how the interaction between bordering countries with different vaccination policies, such as Mexico and the United States, affects the dynamics of rubella. This is critical because each country neglects the possibility of "[reintroducing the infection] from neighboring countries"(Center for Disease Control, 1997). Such an oversight can lead to

unrealistic expectations of eradication.

1.1 Introduction to the model

In our study, we model the interaction between Mexico and United States by combining two $S \rightarrow I \rightarrow R$ models in which each population is divided into epidemiological subgroups of susceptibles (S), infected (I) and recovered (R) individuals as the Figure 1 shows.

Our model considers a close population of Mexicans and Americans, such that $M + G$ is our total population, where M is our Mexican population, and G is our American population. We assume that the effective contact rate of the Mexican population amongst themselves and the American population amongst themselves is the same, β. Citizens in one country are just as likely to interact with each other as those in another country. Considering that the populations are not isolated, we let β' be the interaction rate between Mexicans and Americans. We suppose that $\beta > \beta'$ where the probability of contact between individuals of the same country is greater than the probability of contact between individuals of a different country. We take the duration of rubella, γ, to be an average of ten days in both countries since the difference between the rates in each country is very small. $1/\mu_m$ is the average life span of a Mexican and $1/\mu_g$ is the average life span of an American. In addition, we let p and q equal the percentage of the population that is vaccinated in Mexico and the United States, respectively. For the case where there is no vaccination, p and q are equal zero. Note that we assume that the disease is spread only by infected individuals.

From the SIR model we can construct the following system of equations for our two populations:

$$\frac{dS_m}{dt} = (1-p)\mu_m M - (\beta I_m + \beta' I_g)\frac{S_m}{M+G} - \mu_m S_m, \tag{1}$$

$$\frac{dI_m}{dt} = (\beta I_m + \beta' I_g)\frac{S_m}{M+G} - (\mu_m + \gamma) I_m, \tag{2}$$

$$\frac{dR_m}{dt} = p\mu_m M + \gamma I_m - \mu_m R_m, \tag{3}$$

$$\frac{dS_g}{dt} = (1-q)\mu_g G - (\beta I_g + \beta' I_m)\frac{S_g}{M+G} - \mu_g S_g, \tag{4}$$

$$\frac{dI_g}{dt} = (\beta I_g + \beta' I_m)\frac{S_g}{M+G} - (\mu_g + \gamma) I_g, \tag{5}$$

$$\frac{dR_g}{dt} = p\mu_g G + \gamma I_g - \mu_g R_g, \tag{6}$$

where $M = S_m + I_m + R_m$ and $G = S_g + I_g + R_g$.

Considering Theime's theorem and a constant population for Mexico and the Unuted States, this model can be reduced to the system of four equations

$$\frac{dI_m}{dt} = (\beta I_m + \beta' I_g)\frac{M - I_m - R_m}{M + G} - (\mu_m + \gamma)I_m, \tag{7}$$

$$\frac{dR_m}{dt} = p\mu_m M + \gamma I_m - \mu_m R_m, \tag{8}$$

$$\frac{dI_g}{dt} = (\beta I_g + \beta' I_m)\frac{G - I_g - R_g}{M + G} - (\mu_g + \gamma)I_g, \tag{9}$$

$$\frac{dR_g}{dt} = p\mu_g G + \gamma I_g - \mu_g R_g. \tag{10}$$

In the following part of our report, we will use these modified equations to calculate our equilibrium points, to study general and individual cases of our R_0, and to run simulations from a program created in Matlab. Finally, we draw conclusions based on the results obtained from our model, and we suggest improvements for future models.

2 Methodology

To evaluate our system of equations, we analyze the basic reproductive number, R_0, which is dependent on our parameters. R_0 represents the average number of secondary infections caused by introducing a single infected individual into a host population of N susceptibles (Edelstein-Keshet. 1988, 247). The R_0 of our differential equations will determine whether the disease will be eradicated. As the values of our parameters increase or decrease, our R_0 increases or decreases as well. We specifically want to observe when the vaccination rates decrease R_0 to be less than 1. If $R_0 < 1$, the disease-free equilibrium will be stable. This implies that with time the disease will die out. If $R_0 > 1$, the disease-free equilibrium is unstable and the disease will persist.

To calculate the basic reproductive number (R_0), we consider the disease-free equilibrium. To find all the equilibrium points, we set the differential equations equal to zero and solve for the different variables. A detailed explanation of these two processes is found in the appendix. We will calculate the R_0's for each of the two populations, as well as the general R_0 for the whole system. We represent the general R_0 in terms of the R_0^m and R_0^g so that we can to see the relationship between the two populations and to further explore the effects of interaction between the two populations.

Our R_0^g and R_0^m for Americans and Mexicans, respectively, are:

$$R_0^g = \frac{\beta(1-q)G}{(\gamma+\mu_g)(M+G)} \qquad \text{and} \qquad R_0^m = \frac{\beta(1-p)M}{(\gamma+\mu_m)(M+G)}.$$

Both R_0's represent the number of susceptibles who will be infected by an infectious individual. When at least one of the particular populations' R_0's are less than 1, the general R_0 is $\max(R_0^m, R_0^g)$, (Castillo-Chavez, 1996.)

Our basic reproductive number is

$$R_0 = \frac{(R_0^g + R_0^m) + \sqrt{(R_0^g + R_0^m)^2 + 4(1-z)R_0^g R_0^m}}{2}$$

where $z = \beta'/\beta$ and $0 < z \leq 1$.

We break down the analysis of the system of equations into four cases:

Case 1: $R_0^g < 1$ and $R_0^m < 1$. Since the R_0 equals $\max(R_0^m, R_0^g)$, it can be concluded that $R_0 < 1$; therefore, with time, the disease will be eradicated in both countries. This is a trivial solution, and hence, we will not analyze or discuss this case any further.

Case 2: $R_0^m < 1$ and $R_0^g > 1$. Since $R_0^m < 1$, the disease will be eradicated in Mexico, but in the U.S. the disease will persist. Taking into consideration that R_0 is $\max(R_0^m, R_0^g)$, we need to calculate R_0^g; thus we only need to look at the system for the American population. Note that we do not ignore the Mexican population because there is still interaction between the two populations for which our system of equations accounts. To find the R_0^g, we consider the disease free-equilibrium; thus $I_g = 0$. We solve $\frac{dR_g}{dt} = 0$ for R_m and find that the disease free-equilibrium is $(0, qG)$. If $R_0^g < 1$, then the disease free equilibrium is stable; thus with time, the disease will die out. If $R_0^g > 1$, the equilibrium

$$\left(\mu_m\left(\frac{M}{\mu_m+\gamma_m} - \frac{M+G}{\beta}\right), \gamma_m\left(\frac{M}{\mu_m+\gamma_m} - \frac{M+G}{\beta}\right)\right)$$

is stable; thus the disease will never be eradicated in the U. S.

Case 3: $R_0^g < 1$ and $R_0^m > 1$. Here, the disease is eradicated in the U. S. and persists in Mexico; therefore, we calculate R_0^m. Thus, we only need to look at the system for the Mexican population. Note that we do not ignore the American population; our system of equations accounts for the interaction between the two populations. Again we consider the disease-free equilibrium for this system $I_m = 0$ and $R_m = pM$. If $R_0^m < 1$, $(0, pM)$ will be stable; therefore

the disease will be eradicated. If $R_0^m > 1$, the equilibrium point

$$\left(\mu_g\left(\frac{G}{\mu_g+\gamma_g}-\frac{M+G}{\beta'}\right),\gamma_g\left(\frac{G}{\mu_g+\gamma_g}-\frac{M+G}{\beta'}\right)\right)$$

is stable; hence the disease will never be eradicated.

Case 4: $R_0^g > 1$ and $R_0^m > 1$. The disease coexists in both countries. When the R_0 is greater than one, then the endemic equilibrium is stable, and the disease will never be eradicated in either of the countries. To calculate the R_0, we consider the disease-free equilibrium for the whole system: $I_m = 0$, $R_m = pM$, $I_g = 0$, and $R_g = qG$. If $R_0 < 1$, the disease-free equilibrium is stable and with time, the disease will be eradicated in both countries. If $R_0 > 1$, the disease-free equilibrium is unstable, which implies that the disease will exist in both countries. Finding the endemic equilibrium is complicated and the results are difficult to translate into biological meaning. Thus, we did not explicitly find the point; instead we prove that the point exists (see the appendix). Furthermore, since the endemic point was not explicitly found, we cannot determine its stability, but some numerical analysis implies that the equilibria is stable. It is here that we want to observe how R_0 changes with different values of p and q, the vaccination percentages. If $R_0 < 1$, the disease free equilibrium is stable. This tells us that the disease will be eradicated in both countries. (It is important to note that in the analysis, it was found that this case was divided into two cases. This finding will be discussed in the next section.)

The analysis of our four cases is necessary to understand the dynamics of the populations' interactions and the percentage of vaccination. The second and third cases assume that each country, when attempting to eradicate rubella, does not consider the neighboring immunization and infection rate of the neighboring countries, but each does account for the interaction rate.

3 Analysis

Our system of equations incorporates a number of parameters that will each affect the basic reproductive number. Often, if the number of parameters is large, it is very difficult or nearly impossible to analyze the system. In order to analyze the system, four cases were considered based on R_0. Thus, it is logical to have a numerical analysis based on R_0. This simplifies our analysis and allows us to draw some conclusions. Recall that if at least one of R_0^m or R_0^g are less than one, then $R_0 = \max(R_0^m, R_0^g)$. Finally, if R_0^m and R_0^g are both greater than one, then

$$R_0 = \frac{1}{2}\left((R_0^m + R_0^g) + \sqrt{(R_0^m + R_0^g)^2 + 4(1-z)R_0^m R_0^g}\right).$$

Moreover, our R_0 can be rewritten in terms of R_0^m and R_0^g and z, where z is the contact ratio (β'/β and $\beta' < \beta$, so $z < 1$. These simplifications allow us to plot R_0 as a function of R_0^m and R_0^g, therefore our only parameter becomes z. Figure 2 shows the general plot of R_0 as a function of R_0^m and R_0^g. Five sections appear:

1. Section I includes all values of R_0^m and R_0^g less than one. If R_0 is found in section I, the disease will be eradicated in both countries.

2. Section II includes the cases where $R_0^g > 1$ and $R_0^m < 1$. In this case the disease would die out in Mexico, but it would persist in the United States. Although the disease is eradicated in Mexico, the Mexican government still has to take an active role in the fight against Rubella because the contact rate of Mexicans with Americans has an effect on R_0^g.

3. Section III is similar to the second; here $R_0^g < 1$ and $R_0^m > 1$. This section predicts that rubella will persist in Mexico and die out in the US. Again, the United States responsibility in the fight against Rubella is not eliminated.

4. Section IV, $R_0^g > 1$ and $R_0^m > 1$; thus the disease will coexist in both countries.

5. Section V, $R_0^g > 1$ and $R_0^m > 1$, but the disease will persist in only one country. For instance, the disease will die out in Mexico but persist in the U.S. and visa-versa.

As the ratio z increases the x-asymptote of the R_0 function is further away from the origin and, more importantly, from the line $x = 1$. This means that as the ratio increases, the area in Section V increases.

Figure 3 shows the function of for various values of z.

Figure 4 displays the change of asymptotes as a function of z. The function plots the distance of the x-asymptote from the origin. This gives an idea of how the section V is growing. The larger the value of z, the larger the area in Section V, the harder it is to draw a conclusion. This part of the analysis implies that while all the parameters affect the value of R_0, it is extremely important to look at the ratio of effective contact rates squared.

We are also interested in observing how vaccination can be used to reduce R_0, such that R_0 is included in Section I of Figure 1. Thus we will see what percentage of Americans and Mexicans needs to be vaccinated to eradicate the disease.

Figure 5 plots R_0 as a function of p and q when $\beta = 0.4$ and $z = 0.5$. If this plot is rotated as in Figure 6, it is easy to see that the vaccination rate for the U. S. has to be greater than 87

% to eradicate the disease. If the plot is rotated as in Figure 7, it is clear that the vaccination rate for Mexico has to be at least 64 % to eradicate the disease.

Figure 8 charts the vaccination rates needed in the U.S. and Mexico to eradicate the disease for various contact rates (β). R_0 is based on z, but the various simulations conducted for each β indicate that z has very little effect on R_0 when considering the different vaccination rates. There was only a difference of 1 or 2 between the different values of z. (See Table 1).

$\beta \backslash z$	0.1	0.2	0.3	0.4	0.5	0.6	0. 7	0.8	0.9
0.1	0/44	0/45	0/46	0/46	0/46	0/46	0/46	0/46	0/46
0.2	26/73	26/74	26/74	26/74	27/74	27/24	27/74	27/74	27/74
0.3	50/83	50/83	50/83	50/83	50/83	50/83	50/83	50/83	51/83
0.4	64/87	64/87	64/87	64/87	64/87	64/87	64/87	65/87	65/87
0.5	70/88	70/88	70/88	70/88	71/89	71/89	71/89	72/89	72/89
0.6	77/91	77/91	77/91	77/91	77/91	77/91	77/91	77/91	77/91
0.7	78/92	78/92	78/92	78/92	79/92	79/92	79/92	79/92	79/92
0.8	83/93	83/93	83/93	83/94	83/94	83/94	83/94	83/94	83/94
0.9	86/95	86/95	86/95	86/95	86/95	86/95	86/95	86/95	86/95

Table 1: Percentage of Americans vaccinated/ Percentage of Mexicans vaccinated (p/q) (z = Contact Ratio (b'/b)2).

Thus if $\beta = 0.4$ and z is any value, then the percentage of Mexicans that need to be vaccinated is at least 65% and the percentage of Americans vaccinated has to be greater than 87%. In this analysis the effective contact rate β, plays a major role in determining the value of R_0. From Figure 8 we can easily conclude that the best way to eradicate the disease is to vaccinate a larger percentage of Americans than Mexicans. The percentage of vaccination needed to eradicate the disease is extremely realistic because for most values of β the U. S. already vaccinates a larger percentage than what the model predicts.

The last set of values that we want to analyze is when the percentage of Mexicans vaccinated equals the percentage of Americans vaccinated, such that $R_0 < 1$. Figure 9 differs from Figure 8 because it incorporates the idea of having one general vaccination policy with equal vaccination rates instead of a system with two different vaccination rates. Figure 9 gives various values of vaccination for different values of β. If we want to vaccinate the same amount in the U. S. as in Mexico the rate has to be greater than 80 %. Again, the vaccination rate needed to eradicate the disease (reduce R_0 to less than one) is highly dependent on the contact rate β. As the effective contact rate increases you have to vaccinate a larger percentage of

the population. Furthermore, vaccination rates are insensitive to changes in z (see Table 2).

$\beta \backslash z$	0.1	0.5	0.9
0.1	0.45	0.55	0.58
0.2	0.71	0.79	0.80
0.3	0.82	0.85	0.86
0.4	0.86	0.88	0.90
0.5	0.88	0.90	0.90
0.6	0.92	0.92	0.92
0.7	0.92	0.92	0.93
0.8	0.94	0.94	0.95
0.9	0.95	0.96	0.96

Table 2: % Mexicans Vaccinated = % Americans Vaccinated ($p = q$).

From Figures 8 and 9, we conclude that the most efficient way to eradicate rubella is to have different vaccination rates in Mexico and the U. S. This would require that they work together; as long as there is interaction between two populations, the two countries have a responsibility to aid each other in the fight against Rubella. It is to their benefit that the neighboring country vaccinates enough of their population.

4 Improvements

After having completed our study of rubella, we propose several additional methods of analysis that would refine further studies of the subject. We would suggest that further analyses take age structure into consideration. For instance, if we were to include age structure in our model our functions would not only be dependent on time, but also on age. This would allow us to analyze more closely the number of infected individuals at a specific age. This is critical for a disease such as rubella, where we find that as one gets older the symptoms become severe, especially for pregnant women. When infected, the fetus is at a high risk of developing Congenital Rubella Syndrome, CRS.

The analysis of the interaction between two countries allows us to consider space. The spatial structure would allow us to find the different number of infected individuals in different areas of space, or in our case, a country. This allows us to take into account demographic conditions. In our model we take into account the effective contact rate between Mexicans

and Americans, β'; yet this rate is different in other areas of the United States and Mexico which are far from border states. The further a state is from the border, the less likely it is for the individuals living there to come in contact with an infected individual from the neighboring country.

Our model can be modified to include more parameters that can account for a more complex model. For example, we can assume that each of the effective contact rates, β' and β, are different in each country. Hence, we would end up with four different effective contact rates instead of two. Another possibility would be to take into account random proportional mixing of contacts which would again add more effective contact rates. Furthermore, the average duration of the disease, γ, can be made different for each country, which would make our model more specific. For example, poverty in border towns might affect the duration of the disease, due to accessibility, quantity, and quality of health facilities; therefore, a specific γ, would be appropriate. The assumptions made in our model were carefully chosen to give a realistic description of the dynamics of the disease.

5 Conclusion

The study of disease using mathematical models allows us to analyze research questions from a different perspective. In our model, the use of differential equations was critical for studying the rubella virus. We found that we could make conclusions about important aspects of the dynamics of this by considering two different populations, such as Mexico and the United States, where the different vaccination policies of these countries can affect the spread of disease. Most importantly, we found that Mexico and the United States must work together to eradicate the rubella virus because of the interaction between Mexicans and Americans. Our model allows us to predict that in order to eradicate the disease, both countries should vaccinate (see Figure 8), which is not the present case.

The versatility of our model allows us not only to analyze the dynamics of rubella infection between Mexico and the United States, but to examine the dynamics of the spread of any disease between neighboring countries. The disease studied, like rubella, must be transmitted by infected individuals who can be modeled using a SIR model of susceptibles, infected and recovered individuals. Examples of such diseases include: the measles, chicken pox, and mumps. The generality of our model permits us to not only model neighboring countries, but any two countries. Hence, we can analyze global issues regarding many diseases.

It is important to realize the significance of making global health policies. Often analyses

of diseases or social dynamics are performed in each country without considering the effects from the rest of the world. Unfortunately, when trying to decide how to eradicate rubella, it is unrealistic to consider only factors inside one's country because infected travelers from other countries can spread the disease as well. Finally, our analysis allows us to propose that countries should begin to think in a global perspective: global health policies would be more effective in eradicating many diseases.

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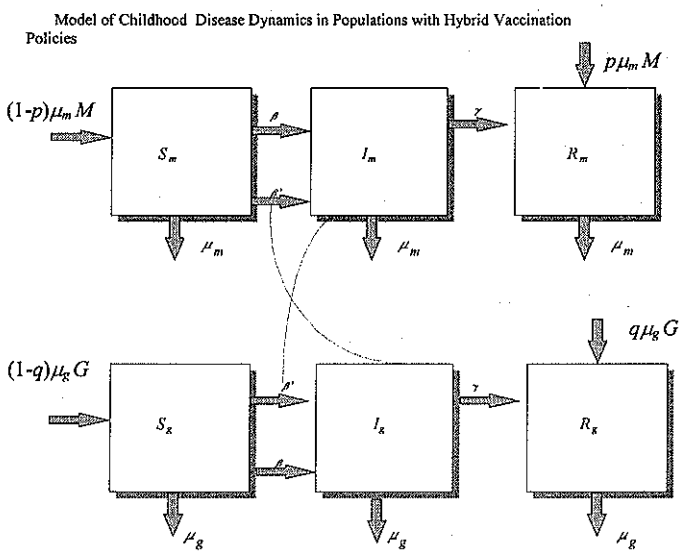

Figure 1: A diagram for the two combined SIR models. All parameters indicated with an M refer to the Mexican population and those with a G refer to the American population. The parameters used include: μ_g = Per-capita American mortality rate; μ_m = Per-capita Mexican mortality rate; β = Effective contact rate amongst Mexicans only; β = Effective contact rate amongst Americans only; β' = Effective contact rate between Mexicans and Americans; $1/\gamma$ = Duration of rubella disease; p = Percentage of Mexicans vaccinated; q = Percentage of Americans vaccinated; G = American population; M = Mexican population.

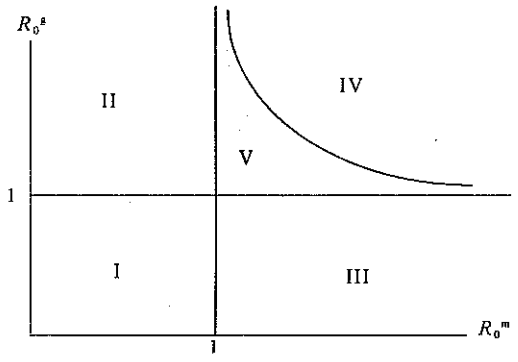

Figure 2: Basic Reproductive Number.

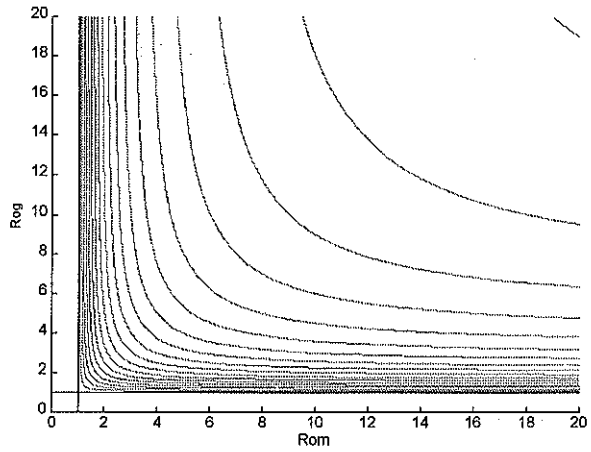

Figure 3: R_0 *vs.* z.

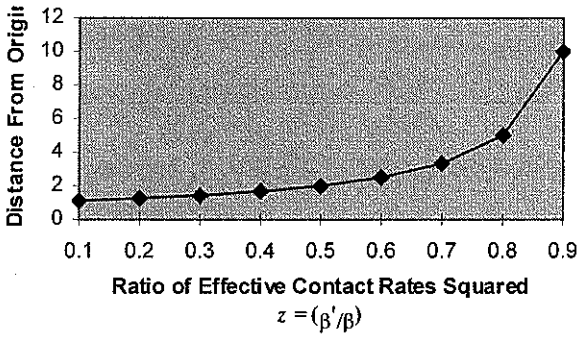

Figure 4: Change in x-asymptote as a function of z.

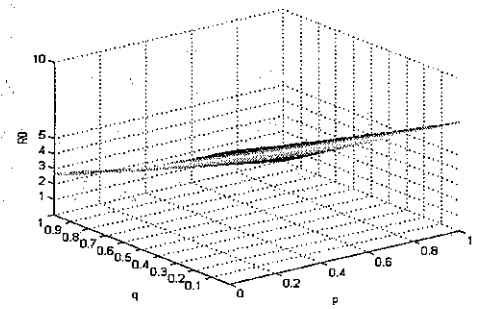

Figure 5: A plot of R_0 as a function of p and q with $\beta = 0.4$ and $z = 0.5$

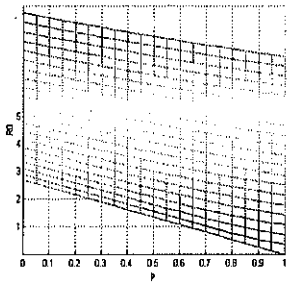

Figure 6: A rotation of Figure 5 shows that the vaccination rate for the U. S. has to be greater than 87 %.

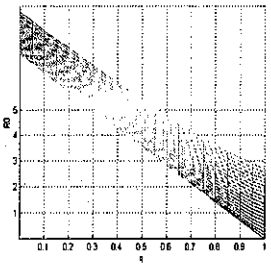

Figure 7: Another rotation of Figure 5 shows that the vaccination rate for the U. S. has to be greater than 64 %.

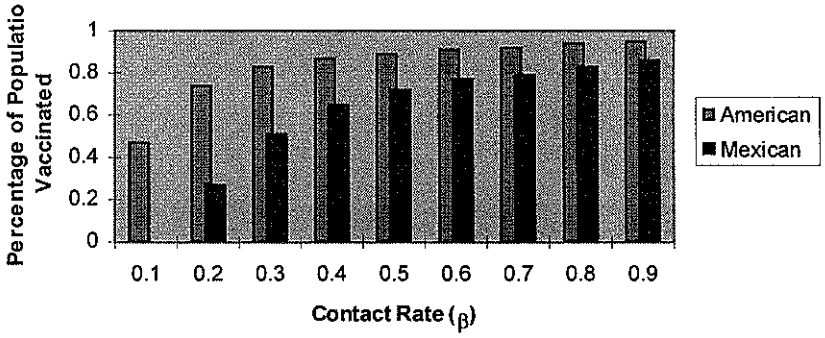

Figure 8: Basic Reproductive Number less than one; disease eradicated in both countries.

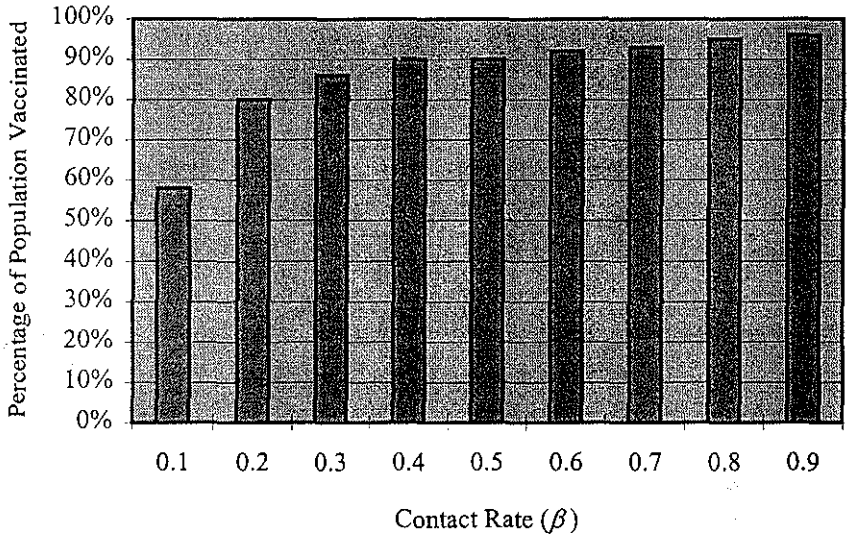

Figure 9: Basic Reproductive Number Less than One (Disease Eradicated); Vaccination Rate the Same in Both Countries.