

Mathematical Modeling of Tick-Borne Encephalitis

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Abstract

Tick-Borne Encephalitis is a virus that affects one's nervous system and is transmitted from tick to human through tick bite. In recent years, the number of cases of tick-borne encephalitis in Europe has been increasing. This mathematical biological model of Tick-Borne Encephalitis was created in order to further our understanding of such phenomenon, as well as study the relationship between vectors and their hosts. Specifically, we will investigate the population model of ticks in certain regions and its correlation to tick-borne encephalitis infections in the region.

Introduction

How far should a government go to prevent a disease? Tick-borne encephalitis (TBE) is a neurological disease that is transmitted to humans through a vector or host. Ticks receive the infection by interacting with a host such as a rodent or mouse and then pass it on to a human host and infecting that human. Ticks are not affected by TBE and they show no signs of being infected when they have the disease. However, when humans have the disease they can suffer lasting effects and in some cases death (Chapter 4 – Malaria - Yellow Book.)

Since humans can die from this disease, it should be of interest to the general public and it was one of the reasons this topic was chosen to model. This is also an interesting topic because of the need to consider how to create a model for a disease that is transmitted through a vector. Transmission through a vector means that the disease must be passed indirectly through a carrier such as a tick or mosquito instead of being transmitted through human to human contact as is the case with most diseases.

For European countries, Austria at one point had the highest number of deaths occur due to TBE (Kunz, 1.) For many places there is limited to no data found about TBE but a lot of information about TBE can be found from Austria because Austria has implemented a 26-year vaccination program. Since Austria provides good data, parameters similar to that will be used in this model; it is how the data and parameters were decided. If this model can correctly match with the data that is shown in Austria then the model will be a useful model for other regions. This model used specific parameters (which will be explained later) but the overall equations and model used can be assumed relatively accurate for the parameters of any region. This model will help in understanding the effectiveness of a country implementing a vaccination program because it will be a good estimate to predicting the number of cases of TBE.

Objectives

- Create a tick-borne encephalitis disease model for human and tick populations.
- Experiment with controls such as vaccination, no vaccination and tick density control.

Assumptions

For mathematical models assumptions are made to simplify the model. These assumptions may or may not be true but if they are assumed true, they should not

severely change the outcome of the model. For our model we had four basic assumptions.

- There is no vertical transmission of the disease between humans and ticks which means that a person infected with TBE cannot pass it on to their offspring.
- There is no re-immunization needed after full immunity is reached for humans.
- There is no tick immunity because ticks do not get treated for the disease and their lifespan is short enough where there is not time to consider immunity.
- There are equal birth and death rates for ticks and so the population of ticks is constant.

Description of the Mathematical Model

Many diseases are modeled through what is called an S.I.R. (Susceptible, Infected, and Recovered) Model. An S.I.R. model is a very basic disease model for regular human to human transmitted disease. For our vector borne disease we altered the standard S.I.R. model to fit the demands of our model. Our model is a modified version of an S.I.R. model which shows how TBE acts in both humans and ticks.

This model consists of a total of six compartments of population densities. Two are used to represent tick densities and four are used to represent human population densities. Human compartments include: susceptible (S), infected (N), partially immune (P), and completely immune (M). Tick compartments include susceptible (K) and infected (I). Movement from compartment to compartment is restricted to respective species. This means that humans cannot move in the model from human compartment to the tick compartment or vice versa. An example of this would be a member of the “susceptible tick” population entering into the “infected tick” population which does not occur in real life.

The diagram (diagram 1) below was created to serve as a visual for understanding our model. The arrows show what compartments interact with each other. Notice that there is only one arrow that goes from a tick compartment to a human compartment. This is because the disease travels through infected ticks to susceptible humans.

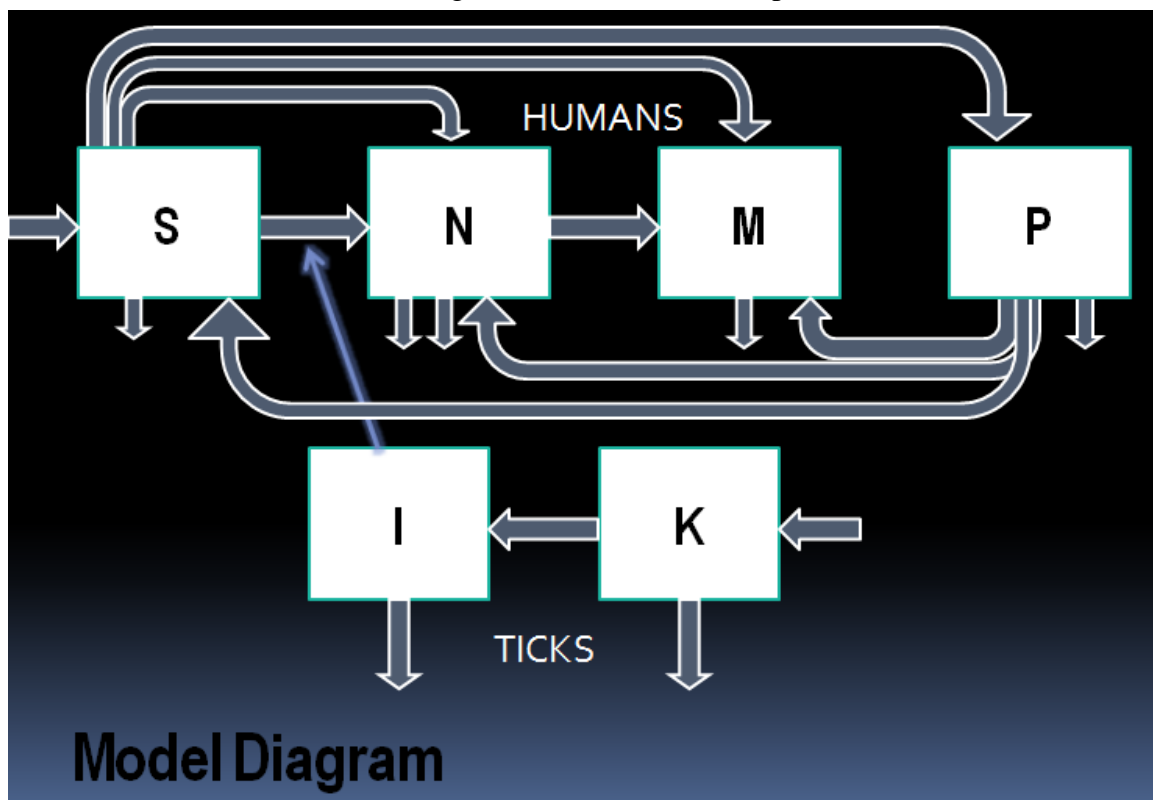


Diagram 1

Table 1 (illustrated below) shows the differential equations that were created and used for this model. These differential equations were created using the rapid prototype or model diagram as a basis. Further understanding of the origin of these equations requires background in mathematical modeling and differential equations.

Human Equations	
$\frac{dS}{dt} = b*(S+N+M+P) + o*P - \frac{a*S*I}{(S+M+N+P)} - v*S - d*S$	
$\frac{dN}{dt} = \frac{a*S*I}{(S+M+N+P)} + h*P - f*N - N*(d+r)$	
$\frac{dP}{dt} = v*S - P*(o + h + d + q)$	
$\frac{dM}{dt} = f*N + q*P - d*M$	
Ticks	
$\frac{dI}{dt} = K*I - I*e$	
$\frac{dI}{dt} = c*(K + I) - K*(e + I)$	

Key	
Susceptible Humans	S
Infected Humans	N
Partially Immune Humans	P
Completely Immune Humans	M
Susceptible Ticks	K
Infected Ticks	I

Table 1

As Table 1 shows the only representation of an interaction between ticks and humans occurs at $\frac{a*S*I}{(S+M+N+P)}$. This represents infected tick density and susceptible human density combining at the rate of infection to determine the number of infected humans for a particular time stop.

Parameters

Table 2 (below) shows the parameters that were chosen.

Table 2

Rate	Figure Used
Human Birth Rate (b)	0.012
Human Death Rate (d)	0.009
Human Infection Rate (a)	0.00003
Vaccination Rate	0.22
Rate of Humans who become Partially Immune (o)	0.02
Rate of Partially Immune who become Infected (h)	0
TBE Death Rate (r)	0.011
TBE Recovery Rate (r)	0.98
Rate of Partially Immune reaching full immunity (q)	0.85
Tick Birth Rate (c)	0.33
Tick Death Rate (d)	0.33
Tick Rate of Infection	0.01
Starting Population Densities	Figure Used

Susceptible Human Population	7,600
Susceptible Tick Population	100,000

Due to the lack of certain data, some parameters were not able to be set with much precision. Parameters were set as close to the data retrieved from Austria's 26-year vaccination program as possible. Actual figures and statistics for Austria's program vary slightly from source to source but the most commonly came across values from the more credible sources are the assumed actual figures. However, it should be noted that the actual figures are taken estimates from a variety of sources which can all be found in the resources portion of this document. The birth rate is represented by (b) and the death rate is represented by (d). The chosen values for these rates are indeed variable in a true model of Austria's population growth, but these figures were very close to actual figures. The end result of the model retrieved a density growth that was accurate over a period of 26 years so the estimation of the growth rates seems reasonable. Two very critical parameters that had to be estimated were tick infection rate (a) and vaccination rate (v). In the case of tick infection rate, the parameter was chosen because it retrieved the most realistic output, given the density of ticks that was chosen for this experiment. To match Austria's current data, the vaccination rate had to be set at a number that would achieve roughly 88% immunity (both partial and complete) over 26 time periods. After humans are vaccinated, some do not complete the three-stage vaccination. To represent those humans in the model, (o) was used and the parameter chosen was the best estimate for this group. Also, partially immune people can still be infected, and (h) was set up as a parameter to track that. There have, however, been no cases of partially immune people becoming infected. Thus, (h) was left at 0 for all experiments. Also, the death rate for infected humans due to encephalitis is rather low, and once recovered, humans are considered completely immune. This recovery rate was tracked with (f). The death rate due to infection was represented by (r). The final human parameter is (q) and it is the rate of partially immune humans completing their immunization.

Tick population density was considered to be constant, and as such, the birth rate (c) and the death rate (e) were set at equal values. Rate of infection within the tick community was a difficult parameter to set. A low number was used that, together with (a) and infected-tick density, would retrieve desired results. Starting population densities were as follows. For the chosen parameters of the starting susceptible human and tick densities, human density was set at 1/1000 of the population density of Austria in 1981, at the introduction of its national vaccination program. The mean Tick/Human ratio was 13.16, which is much lower than many forested and grassland regions in the considered area but it is much higher than many urban or rural areas.

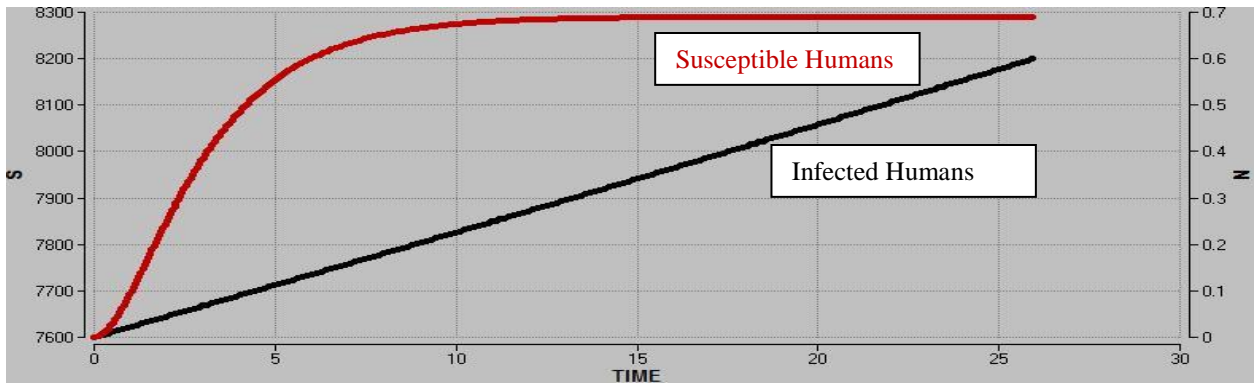


Figure 1

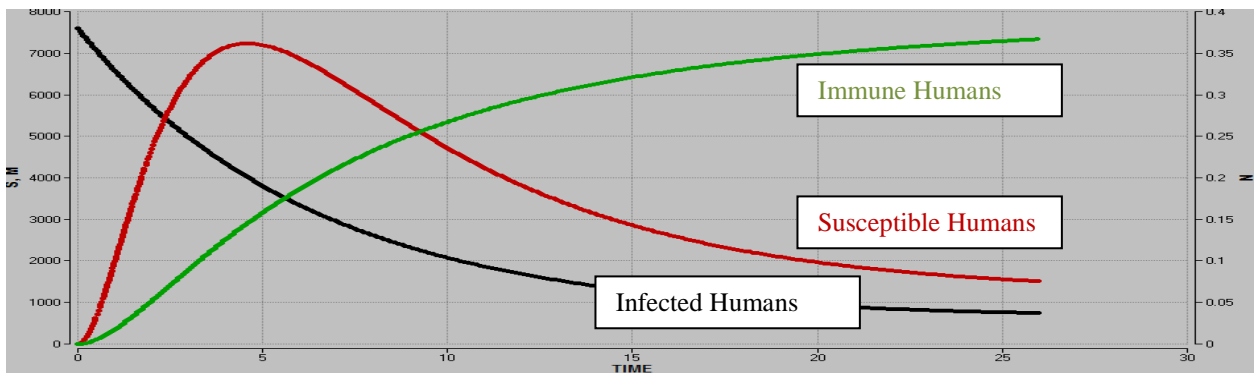


Figure 2

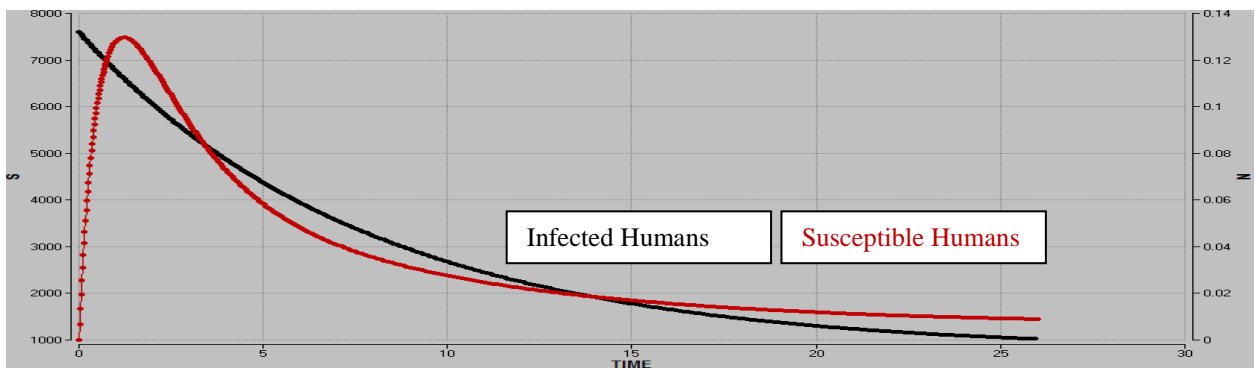


Figure 3

$$\frac{dU}{dt} = g \cdot U \cdot (1 - (U/20000))$$

$$\frac{dS}{dt} = a \cdot S \cdot (U \cdot 1) / (S + M + N + P)$$

Figure 4

Results

Figure 1 shows the results of the experiment with said parameters, with the exception of the vaccination rate (v) at 0. This was a control experiment to make an attempt at emulating the status quo of infection in Austria until 1981. The results were very close, as infected humans reaches an endemic, meaning that it is found often in this

area, level at around 0.7 (this translates to roughly 700 cases per 7.6 million people; Austria, by contrast, had 677 reported TBE cases in 1981). Figure 2 shows the result of the second experiment which introduces a vaccination. The results suggest a close to endemic level of infection that matched Austria's reported results rather closely (the model suggests about 40 cases of TBE, Austria reported 45 in 2007). Finally, figure 3 shows the third experiment which looks at a tick-density control. It should be noted that for this, a logistic growth model was used for tick population which is a standard model that creates a maximum value for the tick population. A constant rate of infected ticks (0.1) was used. The starting population of ticks was still set to 100,000, but the population was reduced negatively until it reached a population of 20,000 which models a death in ticks because the tick density control is in place for this experiment. The growth rate (g) was set to 0.33. The results of this experiment yielded a somewhat similar but faster and more effective result at decreasing the number of humans with TBE than the vaccination experiment. Infected humans drop to almost 0 and susceptible humans to below 2,000.

Sensitivity Analysis

It is appropriate to consider the sensitivity of parameters and initial conditions that is either more important or less known in the system of equations to be paramount to others. Hence, the sensitivity of some parameters is not considered. The most sensitive parameter in our model is the infection rate (a), and it is also the least known parameter. If we change this parameter from 0.00003 to 0.00004, the endemic level of infected humans over 26 time periods goes from 0.07 to 0.09 (with vaccination rate held at 0). This is an increase of 200 cases. The next most sensitive parameter is the vaccination rate (v). Raising the vaccination rate from 0.22 to 0.32 changes the number of TBE cases to about 30 and the number of completely immune humans to about 7,900. Another unknown is the population of ticks. Our model uses a constant population of 100,000. If we change that population to 200,000, we see that infected human cases levels off at about 1,400, or roughly double the amount of cases.

Conclusion

Thousands of people each year are infected with tick-borne encephalitis, with the majority of those recovering (Kunz, 1.) However, not everyone infected with the disease fully recovers and a small number of cases lead to death. There are vaccinations that are very effective in preventing tick-borne encephalitis; in some studies almost 99% effective (Kunz, 1.) This model focused a lot of attention on the country of Austria. Austria has shown what an aggressive vaccination program can do to reduce the number of cases of tick-borne encephalitis.

The number of cases of tick-borne encephalitis in the endemic regions of Europe and Asia has been on the rise. The nature of the disease makes it difficult to eliminate. Eliminating the original host or reducing the population of ticks is not realistic, possible, or even something that would be considered.

One conjecture is that vaccination will yield the best results for fighting this disease, along with good education programs for people who live in or visit the endemic regions and for people who will be visiting the endemic regions. This model projects that without vaccination the only result will be a larger number of people infected with TBE.

Resources

"Chapter 4 - Malaria - Yellow Book | CDC Travelers' Health." Centers for Disease

Control and Prevention. Apr.-May 2009

<<http://wwwn.cdc.gov/travel/yellowbook/ch4/malaria.aspx>>.

Deelman, Ewa, Thomas Caraco, Boleslaw K. Szymanski, and Teri Klein. "Parallel Discrete Event Simulation of Lyme Disease." Ed. Lawrence Hunter. (1996).

Electronic Proceedings for the 1996 Pacific Symposium on Biocomputing. Jan.

1996. World Scientific Publishing Co. Apr.-May 2009 <<http://helix-web.stanford.edu/psb96/deelman.pdf>>.

Donoso Mantke, O., R. Schädler, and M. Niedrig. "A survey on cases of tick-borne encephalitis in European countries." Eurosurveillance 13 (2008).

Eurosurveillance. 24 Apr. 2008. Eurosurveillance. Apr.-May 2009

<<http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=18848>>.

International Press Breakfast. Professor Dr. Christian Kunz. "Professor Dr. Christian Kunz Appointed First Honorary Member of the ISW-TBE." Press release. 30 Oct.

2007. ISW-TBE. Apr.-May 2009 <[http://www.tick-](http://www.tick-victims.info/iddb/archiv7320/110_archiv7320_76761.pdf)

[victims.info/iddb/archiv7320/110_archiv7320_76761.pdf](http://www.tick-victims.info/iddb/archiv7320/110_archiv7320_76761.pdf)>.

Koella, JC, and R. Antia. "Epidemiological models for the spread of anti-malarial resistance." Malaria Journal (2003): 2-3. Malaria Journal. 19 Feb. 2003. BioMed

Central Ltd. Apr.-May 2009 <<http://www.malariajournal.com/content/2/1/3>>.

Kunz, C. "TBE vaccination and the Austrian experience." (2003): 1-21. Pub Med. Apr.

2003. NCBI. Apr.-May 2009

<<http://www.ncbi.nlm.nih.gov/pubmed/12628814?ordinalpos=1&itool=EntrezSys>

tem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DiscoveryPanel.Pubmed_Discovery_RA&linkpos=2&log\$=relatedreviews&logdbfrom=pubmed>.

Mwambi, H G, J. Baumgärtner, and K P Hadeler. "Ticks and tick-borne diseases: a vector-host interaction model for the brown ear tick." Statistical Methods in Medical Research 9 (2000): 279-301. Statistical Methods in Medical Research. 2000. SAGE. Apr.-May 2009 <<http://smm.sagepub.com/cgi/reprint/9/3/279>>.

Tumwiine, J., J.Y.T. Mugisha, and L.S. Luboobi. "A mathematical model for the dynamics of malaria in a human host and mosquito vector with temporary immunity." Applied Mathematics and Computation 189 (2007): 1953-967. Science Direct. 15 Jan. 2007. Apr.-May 2009 <http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6TY8-4MVN0WP-3&_user=1822432&_rdoc=1&_fmt=&_orig=search&_sort=d&_docanchor=&view=c&_searchStrId=942961058&_rerunOrigin=google&_acct=C000054570&_version=1&_urlVersion=0&_userid=1822432&md5=1ddaaa01c674b72913655b1906951c2a>.