Considering the decline in maternal measles antibody titres

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Introduction

Global measles vaccination has led to a 74% drop in mortality between 2000 and 2007. However, this increase in coverage has implications for maternal antibodies passed on through placental transfer. Greatly reduced levels of infection as a result of vaccination have led to a reduction in natural boosting within the population, and consequently the immunity of the population at large may be influenced. In addition, in the UK, the average age of pregnancy is increasing and by extension, so is the time between vaccination and maternity. Therefore waning of immunity through vaccination is an important factor to consider in modeling the impact of mass vaccination and its implication for vaccination schedules. Determining the optimal age at which vaccination is administered is based on a delicate balancing act between the age at which the largest proportion of infants will respond to the vaccine and the dynamics of measles within the population. The main factor causing infants to fail to respond to vaccination is maternal antibodies, which serve as protection against measles in early infancy but prevent successful vaccination as they bind to both killed or live-attenuated virus in the vaccine, and thus prevent the induction of new immune responses.

Currently vaccination against measles in the UK is administered at 13 months. We can investigate the implications of shorter duration of immunity through models based on the distribution of maternal immunity, to attempt to answer the following question: should vaccination schedules be altered to account for the increased window of susceptibility in infants?

Tasks

There is quite a large body of literature containing information about antibody titres in both infants and mothers over time which considers vaccinated and non-vaccinated women. Investigate the various methods used to assess antibody titre and how the immune response descreases over time. How do you think we can then use this information to relate antibody titres in the mother to the proportion of infants susceptible as a function of their age?

Here are some initial tasks to help answer this question:

1. First explore the data currently available (examples include [3, 5, 8–11, 13]). Splitting into the major methods used to assess antibody titre, plot the proportion of infants immune as a function of their age. Use `glmfit` in MATLAB with the suitable link function to fit the data. Can you see any general trends?

2. Consider some distribution of antibodies for the mother, a gamma distribution seems sensible, and relate this to cord titre via a linear relationship (see e.g. [2]).

3. Assume exponential decay of antibody titre distribution in infants. Suppose that below a threshold T, infants become susceptible. Determine the proportion of infants susceptible at age a (assuming cord titre is equivalent to age 0).

4. Varying the mean antibody titre whilst fixing a sensible T and decay constant, plot the resulting immunity functions (proportion of infant immune as a function of time). Do the curves qualitatively resemble data found in the literature?

5. Now parameterise, fit the gamma distribution to data from 1979 [14] and 1986 [7] using MATLAB (I will provide a table of the data contained in the scatterplots in each of these papers) and estimate parameters for the decay rate and threshold based on data available in the literature. Do the results you obtain for the immunity function make sense?

A potential extension to this project could be to consider approaching the problem using a simple differential equation model. As a starting point, imagine that infants can be split into two categories: high immunity and low immunity based on whether their mothers contracted measles, moving into the susceptible class. Assume some age of vaccination, and that vaccinated individuals cannot

be infected, yet those susceptible can undergo standard SIR dynamics. Once in the vaccinated or recovered class, individuals can then bear children into the high or low immunity classes respectively. Construct a differential equation model which incorporates all of this information.

Code up your equations in MATLAB. You will be unable to do this simply using `ode45` and the like so will have to investigate methods of numerical integration and code up a numerical solver yourself. After starting the equations at equilibrium in the absence of vaccination, what are the long term implications in the various classes after vaccination is introduced?

Two papers which provide an excellent starting point for this project are [1, 8].

References

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