CHAPTER 8: ERADICATING INFECTIOUS DISEASES

The toll from infectious diseases in the U.S. was huge not long ago. Vaccines and drugs have been profoundly successful in reducing this scourge. Yet we have been successful in eradicating only one disease, smallpox. Simple mathematical models explain why it is difficult to eradicate a disease and why some diseases are more difficult than others to eradicate.

SECTION 1

Introduction

Our society has had many scares recently from new infectious diseases:

- HIV
- Ebola
- SARS
- West Nile
- Bird Flu

There are two different bases to our fears. One is how likely we are to get it. The other is how bad it will be if we do get it. In the above list, only HIV and West Nile have become permanent (endemic) infections in the human population, but we are or have been worried that the others might invade and start spreading. All but West Nile have high mortality rates.

No matter how bad a disease is, if we can prevent it from spreading in the population, it will die out. And even if we can't make it die out, reducing its spread means that fewer people will be hurt by it. Some very simple math models underlie the principles used to control infectious diseases.

SECTION 2

Basic Reproductive Number, R_0

In epidemiology, the most fundamental property of a disease is its basic reproductive number R_0, or the average number of new infections started by the first infection in a population. When an infection first enters the population, its spread is like a chain reaction: 1 infection becomes R_0 new infections, those each start new infections to make R_0^2, then those become R_0^4, and so on. If R_0 >1, the disease spreads in what is called an epidemic, and the larger the value of R_0, the faster the spread. The table below gives some estimates of R0 for some common infectious diseases.

DISEASE	R_0
Measles	5 - 18
Chicken Pox	7 - 12
Polio	5 - 7
Smallpox	1.5 - 20
HIV	2 - 12
SARS (crowded)	2.2 - 3.6
SARS (community)	1.2

We can see that the estimates have a lot of variation. In part, this is because R_0 is a limited model – it is not the same across all environments. This point was important in the SARS outbreak. SARS showed moderately good trans missions in high-density apartment buildings and hospitals, but (fortunately) it was poorly transmitted in normal com-munity settings.

From this epidemiological perspective, the goal is to reduce R_0 to be <1. When this happens, the infection will die out, perhaps gradually. Intuition suggests two ways we might reduce R_0. One is to block transmission, as by clean ing up the environment, wearing masks or gloves, etc. The other is to use a vaccine to reduce the number of people who can get infected.

Epidemiological Models

Some simple but elegant math underlies disease eradication. The main result uses an equation for the rate at which the number of infected individuals (I) changes over time:

change in number of infected individuals = new infections – loss of old infections from death & recovery

$$\mathbf{delta-I} \;=\; \mathbf{BSI} \;-\; \mathbf{I(r+d)}$$

SYMBOL	VALUE
I	number of infected individuals
delta-I	change in number of infected individuals
S	number of susceptible individuals
B	the infection rate parameter (disease-dependent)
r	the rate at which infected individuals recover
d	the rate at which infected individuals die

The goal is to make delta-I < 0, and with 2 steps of algebra, this condition becomes:

$$R_0 = BS/(r+d) < 1$$

We haven't shown that BS/(r+d) is R_0, but it is when all individuals are susceptible (I = 0).

Let's now consider how to use this result. The parameters b, r, and d are all properties of the infection. S is a property of the population (the number of susceptibles). If we wore masks and cleaned up the environment, we would reduce B. A drug that hastened recovery would increase r. Vaccination would reduce S, because as more people are vaccinated, there are fewer susceptibles about.

Suppose now that R_0 was 3 in an unvaccinated population. This formula would say we needed to reduce S to 1/3 (or vaccinated 2/3) to cause extinction. But if R0 was 30, we would need to vaccinate 29/30 = 97% of the population. If a vaccine was only 90% effective (which is pretty good), we could never reduce S to the 3% and achieve the extinction threshold with just the vaccine.

SECTION 4

Model Strengths and Weaknesses

Foremost, the mathematical model allows us to identify the properties of the infection and population that are important to control. No matter how much hands-on work we did with an epidemic and a vaccine, we might never understand why eradication did or did not work without some kind of model of the epidemic process. Furthermore, we can work through the model quickly, without having to watch thousands get sick and die year after year.

The model also gives us an idea of what to change to reduce infection rates: shorten the term of infection (increase r), reduce b, reduce S. The latter two are obvious, but the first is not necessarily. Nor would we have a quantitative appreciation for what to do without the model.

The model has many limitations. It does not fit sexually-transmitted diseases even approximately. It assumes a constant b, which clearly varies from place to place. It assumes "mass action" (by counting the number of new infections as bSI), which means that a susceptible person in New York has the same chance of getting the infection as a person in Langtry, TX, regardless of where most of the infections are found. We know this isn't right. Indeed, when smallpox was finally eliminated, it was achieved by tracking down the last few infected individuals and ensuring that their contacts were vaccinated. Poliovirus still exists in part of Africa and Asia despite high levels of vaccination in the rest of the world.

SECTION 5

Flu

The latest infectious disease to cause significant worry is bird flu. Bird flu is caused by a virus designated influenza A. Bird flu virus is the same general type of influenza virus that circulates in the human population every year, for which we have vaccines. Flu is generally a respiratory infection, causing fever and aches, but one rare type of flu infects the membranes of the eye. In typical years, influenza kills an average of 36,000 Americans, mostly old ones.

Influenza poses several types of problems:

- First, we have influenza vaccines, but we need to be re-vaccinated every year. Why? The reason is that influenza viruses keep evolving to escape our immune system, so that old immunity becomes progressively less effective. It's not that our immunity wanes, rather the viral targets of that immunity keep changing. But this change in the virus is slow and gradual. The situation is similar to a car manufacturer making slight changes to a model every year, to keep pace with changing consumer preferences. The newer vaccines keep pace with newly-evolved viral structures.

- There are several types of influenza strains. These have very different properties from each other with respect to our immune system (much greater than the differences that evolve within a type). They are designated with letters and numbers, such as H3N1. This system refers to 2 of the types of proteins in the virus (hemagglutinin and neuraminidase) that are important to immune recognition. Currently, the human population has H3N1 and H1N1 circulating. Birds have several types (up through H9) that are not found in humans. There are also influenza strains found in other animals (pigs, horses, ...) Occasionally, a strain from a species with another H-type or N-type successfully humans and starts an epidemic referred to as a "pandemic." Pandemics are problems because they kill more than the usual numbers of people.

Three pandemics from the 1900s are recognized:

i. 1918 – the first H1N1 (Spanish flu), killing 20,000,000-40,000,000 people worldwide (500,000 in the U.S.)

ii. 1957 – the first H2N2 (Asian flu)

iii. 1968 – the first H3N2 (Hong Kong flu)

H1N1 died out but was re-introduced by a botched vaccine in Russia. H2N2 is gone now, and we have H1N1 and H3N1 in our population.

- The bird flu we hear lots about is H5N1. So far it spreads rapidly in birds, but dies out whenever it jumps into humans (thus R0<1 for humans so far). Our population has no prior exposure to it, which may explain why the mortality rate is about 50%, but lack of immunity is probably not the sole cause of this high death rate. The big worry is that, if we don't monitor it carefully, the virus will jump into humans, spread among a few people with close contact, and evolve to the point that R0 >1. When this happens, we are in trouble, unless there is a vaccine. Although we have known about H5 infecting humans for nearly a decade, making a vaccine has been difficult because other influenza viruses for vaccines are grown in chicken embryos. H5N1 kills the embryos, so we can't get enough virus for a vaccine. This problem has been overcome, but initial vaccine results have been discouraging because the vaccine did not elicit high antibody levels.

External Links

Eradicating Polio

Bill Gates on Eradicating Polio

D.A. Henderson, Leader in Global Smallpox Eradication

D.A. Henderson, MD, Chronicles the 10-year fight to eliminate smallpox

Eradicating Rinderpest