# 10 The population biology of infectious disease

In 1918 and 1919 a pandemic strain of influenza swept around the globe. It is estimated that 500 million people became infected with this strain of the flu (about a third of the world's population), and perhaps 50 million people died.   That particular strain was particularly virulent and many of the deaths occurred in young and otherwise healthy individuals. Nevertheless, like all epidemics, the incidence of disease declined about as fast as it appeared. By the end of 1920 the flu viruses circulating through the human population were more similar to the regular seasonal influenza.

For example, records from the British Royal Air Force show that one wave of the epidemic increased exponentially over a period of about 6 weeks, but then declined approximately exponentially in a similar time frame (Fig 10.1).

Figure 10.1. Reported cases of the 1918 "Spanish" flu in the British Royal Air Force during one wave of the outbreak, September 1918 to January 1919. The initial spread of the disease is close to exponential, but eventually that wave of the epidemic died out.
(Source: Historical Influenza Database http://influenza.sph.unimelb.edu.au)
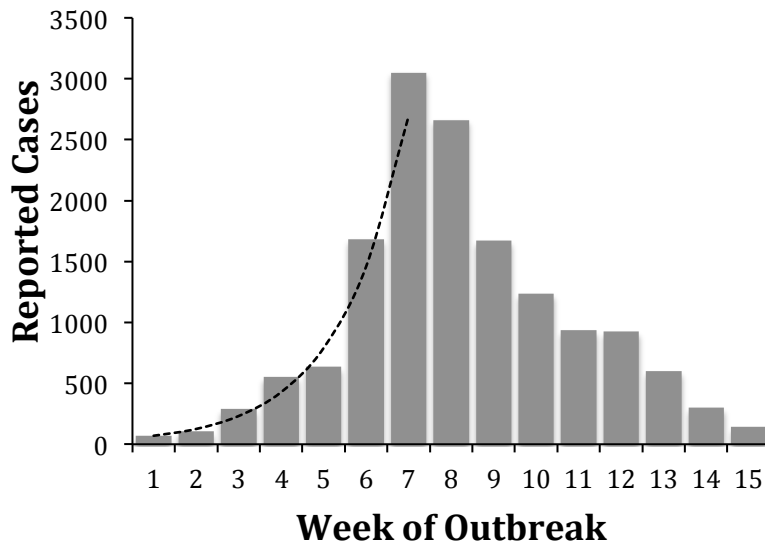
Some diseases spread quickly through a population in what is known as an **epidemic**. Most are not the global "pandemics" such as the 1918 influenza, but rather show rapid growth though a local population.   Epidemics typically have a period of rapid spread, followed by decline to baseline levels. Other diseases are **endemic** in a population, meaning that they are present at low but stable level in the population.

What determines whether a particular disease becomes an epidemic? How can we use that understanding of disease transmission to prevent outbreaks?

10.1 **Modeling Epidemics**

The spread of a disease epidemic is usually fast (on the order of days or weeks) so we can ignore growth of the host population. In that case the total population size is approximately constant so we only need to keep track of the proportion of infected and healthy individuals.

For many diseases, people who recover from the disease are at least partially immune. That means that recovered people will not be immediately re-infected by the same strain of the disease. Sometimes the immunity is long lasting, as in chicken pox or measles, and other times the immunity lasts only a single season, as with influenza.

We will consider three pools of people in a population: Susceptible (S), Infected (I), and Recovered (R).   Over this time period, we will assume the population size is constant so we will just keep track of the *proportions* of individuals in the population who are susceptible, infectious, or recovered. Therefore S+I+R=1.0.

When an individual contracts the disease, they move from the healthy, susceptible, pool and into the infected pool.   Similarly, when infected people are no longer infectious, they move from the infected pool to the recovered pool. We'll assume that recovery is permanent, at least over the time scale of the epidemic. For simplicity, we'll also include any individuals that die in the same "recovered" pool, because they can no longer transmit or contract the disease.

Infectious diseases spread by some form of contact between infected and susceptible individuals. The particular form of contact varies by disease. A contact could just be from being in the same room as someone who is sneezing from a respiratory illness. On the other hand sexually transmitted diseases will require some form of sexual contact, etc. Transmission of the disease will include both the average number of "contacts" per time and the probability of transmission following a contact.   If we assume that individual are mixing randomly, then the probability that a susceptible individual contacts an infected individual is S*I. And we'll let β (beta) be the transmission rate. That will depend on the number of people encountered as well as the probability of transmission from infected to susceptible individuals following contact.

Recovery moves people from the infected pool to the recovered pool at a rate γ (gamma, per individual per time).

$$\text{Susceptible} \quad \rightarrow \quad \text{Infected} \quad \rightarrow \quad \text{Removed or Recovered}$$
$$\beta \qquad\qquad\qquad \gamma$$

where
- β is the transmission rate of the disease following contact between susceptible and infected individual.
- γ is the removal rate of infected individuals (either by death or recovery)

The pool of susceptible individuals will decline over the course of the epidemic as new individuals become infected. Without births or immigration, there is no way to generate additional susceptible individuals in this model. If we assume random encounters among individuals, then meetings of infected and susceptible individuals will be proportional to the product S*I. Therefore, the rate of change of susceptibles is:

$$\frac{dS}{dt} = -\beta IS$$

<div align="right">10.1</div>

The pool of infected individuals will grow as new individuals become infected (at rate $+\beta SI$) and decline as infected individuals recover. Recovery removes individuals from the infected pool at rate γ, so the overall change in the population of infecteds is:

$$\frac{dI}{dt} = \beta IS - \gamma I$$

<div align="right">10.2</div>

Finally, the pool of recovered (or removed) individuals will increase over the epidemic as infected individuals recover:

$$\frac{dR}{dt} = \gamma I$$

<div align="right">10.3</div>

Because S+I+R=1.0, we only really have to keep track of two classes (and then we know what the third must be).

The big questions for an epidemic are
 • under what conditions will disease spread? (when is dI/dt>0).
 • when will the infection stop growing (dI/dt= 0) (the epidemic has reached its peak)
 • What is the total fraction of the population that will contract the disease?

     Using equation 10.2, under what conditions will the disease spread? _____

dI/dt is zero when I is zero (the disease is not present) or when $\beta S = \gamma$. Rearranging the latter we get:

$$\hat{S} = \frac{\gamma}{\beta}$$

<div align="right">10.4</div>

That means that there is a critical proportion of susceptible individuals that are required in order for there to be an epidemic. If S is less than that number, $\frac{dI}{dt} < 0$ and the infection will die out.

     Is it possible to reduce the number of susceptible individuals in the population? How?
     _____

You can also rearrange equation 10.4 say to that *dI/dt* will be zero when β = γ /S. For a given population of susceptible individuals, if the transmission rate (β) is lower than that threshold the epidemic will not spread.

What can health professionals do to reduce the transmission rate of the disease?

_____

Contact number:

The length of time that a person is infectious is approximately 1/ γ. If β is the transmission rate per unit time, and 1/ γ is the total time a person is infectious, then β*1/ γ is the total number of infections produced by an infected individual over the entire time they are infectious.

That is an important epidemiological parameter known as the **contact number**:

$$R_0 = \frac{\beta}{\gamma}$$ 10.5

If the R_0 is greater than 1, then each infectious individual is infecting more than one other person so the disease will spread. If R_0 is less than 1 then the epidemic will die out.

Epidemiologists chose the same symbol (R_0) to describe the spread of infection that we used to describe population growth in chapter 4. Why? _____

Table 10.1 Contact number for various diseases.

Disease	Location	Years	R_0
Measles	Cirencester, England	1947-50	13-14
	England and Wales	1950-68	16-18
	Kansas, USA	1918-21	5-6
	Ghana	1960-68	14-15
Pertussis	England and Wales	1944-78	16-18
	Maryland, USA	1943	16-17
	Ontario, Canada	1912-13	10-11
Chickenpox	Maryland, USA	1913-17	7-8
	Baltimore, USA	1943	10-11
	England and Wales	1944-68	10-12
Diphtheria	New York, USA	1918-19	4-5
	Maryland, USA	1908-17	4-5
Mumps	Baltimore, USA	1943	7-8
	England and Wales	1960-80	11-14
	Netherlands	1970-80	11-14
Rubella	England and Wales	1960-70	6-7
	Czechoslovakia	1970-77	8-9
	Poland	1970-77	11-12
	Gambia	1976	15-16
Poliomyelitis	USA	1955	5-6
	Netherlands	1960	6-7

(source: Anderson and May, Infectious Diseases of Humans as cited in the web page at
*http://www.pitt.edu/%7Esuper1/lecture/lec1181/index.htm)*

The contact rates in Table 10.1 for any particular disease show a lot of variation. If the disease is the same, how can Ro vary so much? _____

(Hint: what are the variables that contribute to Ro and how might they vary in different countries and different times?)

Note: Equation 10.5 is the total number of new infections produced by an infected individual *in a completely susceptible population*. After some individuals become infected and develop immunity the number of new infections produced will decline. That is because only contacts between infected and susceptible individuals can spread the disease. Contact between infected and resistant individuals has no effect on the overall dynamics. At any given time the contact effective contact rate is $R=R_0*S$. The reduction in the pool of susceptible individuals eventually shifts the effective contact number for being greater than 1.0 to being less than 1.0. At that time the epidemic starts to die out.

10.2 Influenza

Let's apply this model to examine the spread of influenza.   The period of maximum infectiousness of influenza lasts about 3 days. So, very roughly, about 1/3 of the infected should be recovering each day. That means that γ is approximately 1/3. Various studies have estimated β for influenza and have determined that it is approximately 0.7. Figure 10.2 shows the time course of an epidemic with those parameters.

Figure 10.2. Numerical results for an epidemic assuming it starts with a single infected person in an initial population of 100,000. In this example B=0.7; γ=0.33.
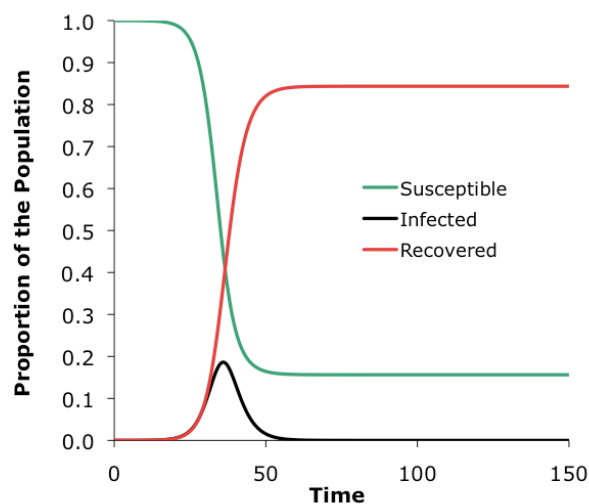
Notice that at the peak of the epidemic, only about 20% of the population is infected. Nevertheless, we can track the cumulative effect of the epidemic by looking at the change in the proportion of susceptible individuals. All of the individuals who leave the susceptible pool do so because they become infected. By the end of the epidemic, the proportion of

susceptibles is less than 20%. That means that over 80% of the population contracted the disease at some point. (The same thing can be seen by the increase in recovered individuals). But also notice that not everyone gets the disease. That is another general feature of epidemics. They can spread through a population but they will typically end before everyone gets sick. Some people will escape the disease.

10.3 Herd immunity

Equation 10.4 implies that there is a critical threshold of susceptible individuals for epidemic to spread. One way to prevent the spread of disease is to vaccinate individuals. If a high-enough proportion of the population is vaccinated, then the epidemic will eventually die out, even in unvaccinated individuals. That is known as "herd immunity". Unvaccinated people can indirectly benefit if enough others in the population receive the vaccination.

> For this model of influenza, what fraction of the population of the population must be susceptible for the disease to spread? _____

> What is the minimum fraction of a susceptible population that would have to receive the vaccine in order to prevent a flu outbreak? _____

(For the most recent swine flu epidemic in the US, the CDC estimated that only about 20% of the US population was vaccinated. But many others probably became resistant after being exposed naturally to the virus.)

That shows the somewhat surprising result that it is possible to completely prevent an epidemic even when far less than 100% of the population receives the vaccine. In general, diseases with high contact rates require a larger proportion of the population to be vaccinated than do diseases with low contact rates.

> Comparing equation 10.4 and 10.5, what is the relationship between the contact rate and the fraction of the population that must be vaccinated to prevent an epidemic? _____

10.4 A case of measles

Measles used to be a disease that affected nearly 100% of the population, usually during childhood. The incidence of measles in the US has declined to essentially zero following the widespread adoption of the measles vaccine.

However, in 2005, an unvaccinated woman traveled to Romania and returned to Indiana unknowingly infected. She attended a church gathering and within two weeks 18 members of the church community with sick with the measles, which then spread to other family members. The 34 people who got measles during that outbreak was the largest measles epidemic in the US in recent years.

Figure 10.3

Measles–United States,1950-2001

Among unvaccinated people in the church community, 89% became infected with measles during that outbreak and 9% were hospitalized. But fortunately, the disease did not continue spreading into the wider community. Why not?
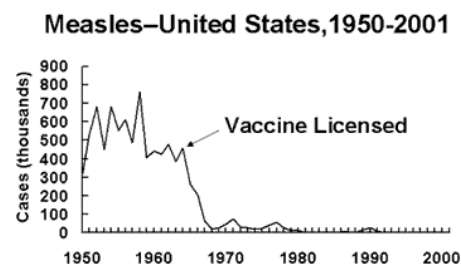
For measles, the contact number for a susceptible population is about R_0=12-16.

> Given that contact number, what fraction of the population would have to be vaccinated in order to prevent the spread of measles? _____

In Indiana, approximately 92% of children are vaccinated against measles soon after birth, and by kindergarten 98% of the population has been vaccinated. That vaccination percentage (as well as intervention by public health officials) was sufficient to contain the spread of that measles outbreak. It only spread in a particular community that had a high percentage of unvaccinated people.
(Source: Parker et al. 2006. Implications of a 2005 Measles Outbreak in Indiana for Sustained Elimination of Measles in the United States. New England Journal of Medicine 355:447-455)\

10.5 Vaccine Effectiveness:

Vaccines are never 100% effective. Let's imagine that the measles vaccine has 95% effectiveness. If we want to have a minimum vaccination rate of at least 92% then we would actually have to vaccinate 92% / 0.95 = 97% of the population to ensure sufficient coverage of the vaccine.

Partial effectiveness is also the reason most people get two doses of the measles vaccine. With two doses the effectiveness increases to nearly 100%.   You can calculate the effectiveness after two doses as 1- (probability that both doses fail) = $1-(0.05^2)$= 0.998
http://cdc.gov/vaccines/vpd-vac/combo-vaccines/mmr/faqs-mmr-hcp.htm).

Vaccination against measles has been effective, but vaccines have been even more successful against poliomyelitis ("polio"). For poliovirus, β is approximately 0.4. The infectious period lasts about 16 days, so γ is approximately 1/16.
s

> Approximately what fraction of the population would have to be vaccinated in order to provide herd immunity against polio? _____

Each dose of the polio vaccine has an effectiveness of about 70%.   Even if 100% of children were vaccinated, approximately 30% of the population would remain susceptible.
> Would that be sufficient to prevent the spread of polio?_____

With 3 doses, however, the polio vaccine has over 95% effectiveness: $1-(0.30^3)$=0.975. Most children in the US receive all three (or four) doses of the vaccine, so it has been relatively easy to reach the herd immunity threshold for the polio virus.   There has not been a natural infection of polio in the US for over a decade and the disease has been very nearly eradicated worldwide.

10.6 **Endemic diseases**

In this introduction to the dynamics of infectious disease we have only considered the short term dynamics within a single wave of an epidemic.   If we are to consider endemic diseases that persist in a population (at least at a low rate) we must also consider births and deaths in the host population.

We will assume that newborns are always susceptible, so all births enter the susceptible pool. Deaths, however, occur in all three classes of people. We'll assume that the death rate for infected individuals is different than the death rate for susceptible and recovered individuals (D > d).

$$\frac{dS}{dt} = m(S + I + R) - \beta IS - dS$$

$$\frac{dI}{dt} = \beta IS - \gamma I - DI$$

$$\frac{dR}{dt} = \gamma I - dR$$

for simplicity assume that the overall birth and death rate is the same (so pop size about constant) therefore m=d

SKIP ALL OF THIS for now at least

10.7 **Answers;**

p 3.   The disease will spread when $dI/dt > 0$, i.e. when $\beta IS > \gamma I$ or $S > \gamma/\beta$

It may be possible to decrease the proportion of susceptible individuals by vaccination.

p 4. Transmission of the disease could be reduced by social distancing (i.e. quarantine, or closing schools) or by hygiene (hand washing or wearing facemasks or gloves).

In both cases, R_0 is the lifetime reproductive success.   For disease, it is the total number of new infections over the entire infectious period of an individual. In chapter 4 it was the total number of offspring over the entire life of an individual.

p 5. R_0 can vary a lot because γ and β can vary. β will be higher or lower depending on how dense the population is, or by whether schools are open or closed. γ may be decreased by effective health care.

p 6. For influenza, $S^* = 0.33/0.7 = 47\%$
That means that at least 53% must be vaccinated in order to reduce S to a low enough percentage.

From 10.4 and 10.5, the critical vaccination proportion $= 1 - (1/R_0)$

p 7. For measles, if $R_0 = 12.6$, then the vaccination proportion must be at least $1-(1/12.6) = 92\%$
For polio, $\gamma=1/16$, $\beta=0.4$ and $S^* = 0.156$
That means at least $1-S^* = 84.4\%$ must be vaccinated

No. One dose of the vaccine could not work. Given that one dose of the vaccine is only 70% effective, that would require $0.84/0.7 = 120\%$ of the population to be vaccinated (which is of course impossible).