6.6 THE POPULATION BIOLOGY OF INFECTIOUS DISEASES

Infectious diseases can be classified into two broad categories: those caused by viruses and bacteria are *microparasitic* diseases, and those due to worms (more commonly found in third-world countries) are *macroparasitic*. Other than the relative sizes of the infecting agents, the main distinction is that microparasites reproduce within their host and are transmitted directly from one host to another. Most macroparasites, on the other hand, have somewhat more complicated life cycles, often with a secondary host or carrier implicated. (Examples of these include malaria and schistosomiasis; see Anderson, 1982 for a review.)

This section briefly summarizes some of the classical models for microparasitic infections. The mathematical techniques required for analyzing the models parallel the techniques applied in Sections 6.2 and 6.3. However, as a general remark, it should be said that the flavor of the models differs somewhat from the species-interactions models introduced in this chapter.

With no a priori knowledge, suppose we are asked to model the process of infection of a viral disease such as measles or smallpox. In keeping with the style of population models for predation or competition, it would be tempting to start by defining variables for population densities of the host $x$ and infecting agent $y$. Here is how such a model might proceed:

---

**Primitive Model for a Viral Infection**

This model is for illustrative purposes only. Let

\[
\begin{align*}
x &= \text{population of human hosts}, \\
y &= \text{viral population}.
\end{align*}
\]

The assumptions are that

1. There is a constant human birth rate $\alpha$.
2. Viral infection causes an increased mortality due to disease, so $g(y) > 0$.
4. In the absence of human hosts, virus particles "die" or become nonviable at rate $\gamma$.

The equations then read:

\[
\begin{align*}
\frac{dx}{dt} &= [\alpha - g(y)]x, \\
\frac{dy}{dt} &= \beta xy - \gamma y.
\end{align*}
\]
The approach leads us to a modified Lotka-Volterra predation model. This view, to put it simply, is that viruses $y$ are predatory organisms searching for human prey $x$ to consume. The conclusions given in Section 6.2 follow with minor modification.

The philosophical view of disease as a process of predation is an unfortunate and somewhat misleading analogy on several counts. First, no one can reasonably suppose it possible to measure or even estimate total viral population, which may range over several orders of magnitude in individual hosts. Second, a knowledge of this number is at best uninteresting and trivial since it is the distribution of viruses over hosts that determines what percentage of people will actually suffer from the disease. To put it another way, some hosts will harbor the infecting agent while others will not. Finally, in the “primitive” model an underlying hidden assumption is that viruses roam freely in the environment, randomly encountering new hosts. This is rarely true of microparasitic diseases. Rather, diseases are spread by contact or close proximity between infected and healthy individuals. How the disease is spread in the population is an interesting question. This crucial point is omitted and is thus a serious criticism of the model.

A new approach is necessary. At the very least it seems sensible to make a distinction between sick individuals who harbor the disease and those who are as yet healthy. This forms the basis of all microparasitic epidemiological models, which, as we see presently, virtually omit the population of parasites from direct consideration.

Instead, the host population is subdivided into distinct classes according to the health of its members. A typical subdivision consists of susceptibles $S$, infectives $I$, and a third, removed class $R$ of individuals who can no longer contract the disease because they have recovered with immunity, have been placed in isolation, or have died. If the disease confers a temporary immunity on its victims, individuals can also move from the third class to the first.

Time scales of epidemics can vary greatly from weeks to years. Vital dynamics of a population (the normal rates of birth and mortalities in the absence of disease) can have a large influence on the course of an outbreak. Whether or not immunity is conferred on individuals can also have an important impact. Many models using the general approach with variations on the assumptions have been studied. An excellent summary of several is given by Hethcote (1976) and Anderson and May (1979), although different terminology is unfortunately used in each source.

Some of the earliest classic work on the theory of epidemics is due to Kermack and McKendrick (1927). One of the special cases they studied is shown in Figure 6.12(a). The diagram summarizes transition rates between the three classes with the parameter $\beta$, the rate of transmission of the disease, and the rate of removal $\nu$. It is assumed that each compartment consists of identically healthy or sick individuals and that no births or deaths occur in the population. (In more current terminology, the situation shown in Figure 6.12(a) would be called an SIR model without vital dynamics because the transitions are from class $S$ to $I$ and then to $R$; see for example, Hethcote, 1976.)
Figure 6.12 A number of epidemic models that have been studied. The total population N is subdivided into susceptible (S), infective (I) and removed (R) classes. Transitions between compartments depict the course of transmission, recovery, and loss of immunity with rate constants β, ν, and γ. A population with vital dynamics is assumed to be producing new susceptibles at rate δ which is identical to the mortality rate. (a) SIR model; (b, c) SIRS models; and (d) SIS model.

Figure 6.12(a) and those following it are somewhat reminiscent of models we have already studied for the physical flows between well-mixed compartments (for example, the chemostat). A subtle distinction must be made though, since the passage of individuals from the susceptible to the infective class generally occurs as a result of close proximity or contact between healthy and infective individuals. Thus the rate of exchange between S and I has a special character summarized by the following assumption:

**Assumption**
The rate of transmission of a microparasitic disease is proportional to the rate of encounter of susceptible and infective individuals modelled by the product (βSI).
The equations due to Kermack and MacKendrick for the disease shown in Figure 6.12(a) are thus

\[
\frac{dS}{dt} = -\beta SI, \quad (27a)
\]
\[
\frac{dl}{dt} = \beta SI - \nu l, \quad (27b)
\]
\[
\frac{dR}{dt} = \nu l. \quad (27c)
\]

It is easily verified that the total population \(N = S + I + R\) does not change. Though these equations are nonlinear, Kermack and MacKendrick derived an approximate expression for the rate of removal \(dR/dt\) (in their paper called \(dz/dt\)) as a function of time. The result is a rather messy expression involving hyperbolic secants; when plotted with the appropriate values given to the parameters it compares rather well with data for death by plague in Bombay during an epidemic in 1906 (see Figure 6.13).

A more instructive approach is to treat the problem by qualitative methods. Now we shall carry out this procedure on a slightly more general case, allowing for a loss of immunity that causes recovered individuals to become susceptible again [Figure 6.12(b)]. It will be assumed that this takes place at a rate proportional to the population in class \(R\), with proportionality constant \(\gamma\). Thus the equations become

\[
\frac{dS}{dt} = -\beta SI + \gamma R, \quad (28a)
\]
\[
\frac{dl}{dt} = \beta SI - \nu l, \quad (28b)
\]
\[
\frac{dR}{dt} = \nu l - \gamma R. \quad (28c)
\]

This model is called an SIRS model since removed individuals can return to class \(S(\gamma = 0\) is the special case studied by Kermack and McKendrick). It is readily shown that these equations have two steady states:

\[
\bar{S}_1 = N, \quad \bar{I}_1 = 0, \quad \bar{R}_1 = 0; \quad (29a)
\]

\[
\bar{S}_2 = \frac{\nu}{\beta}, \quad \bar{I}_2 = \gamma \frac{N - \bar{S}_2}{\nu + \gamma}, \quad \bar{R}_2 = \frac{\nu \bar{I}_2}{\gamma}. \quad (29b)
\]

In (29a) the whole population is healthy (but susceptible) and disease is eradicated. In (29b) the community consists of some constant proportions of each type provided \((\bar{S}_2, \bar{I}_2, \bar{R}_2)\) are all positive quantities. For \(\bar{I}_2\) to be positive, \(N\) must be larger than \(\bar{S}_2\). Since \(\bar{S}_2 = \nu/\beta\), this leads to the following conclusion:
The disease will be established in the population provided the total population \( N \) exceeds the level \( \nu / \beta \), that is,

\[
\frac{N \beta}{\nu} > 1.
\]

This important threshold effect was discovered by Kermack and McKendrick; the population must be "large enough" for a disease to become endemic.

Also for the rate at which cases are removed by death or recovery which is the form in which many statistics are given:

\[
\frac{dx}{dt} = \frac{\beta}{\text{Area}^3} \sqrt{-\phi \text{ sech}^4 \left( \frac{\sqrt{-\phi}}{2} u - \psi \right)}.
\]

(trial-one)

The accompanying chart is based upon figures of deaths from plague in the island of Bombay over the period December 17, 1906, to July 23, 1906. The ordinate represents the number of deaths per week, and the abscissa denotes the time in weeks. As at least 80 to 90 per cent. of the cases reported terminate fatally, the ordinate may be taken as approximately representing deaths as a function of \( t \). The calculated curve is drawn from the formula:

\[
\frac{dx}{dt} = 500 \text{ sech}^4 \left( 0.5t - 7.4 \right).
\]

Figure 6.13 On a page from their original article, Kermack and McKendrick compare predictions of the model given by equations (27a,b,c) with data for the rate of removal by death. Note: \( dx/dt \) is equivalent to \( dR/dt \) in equations (27). (Kermack, W. O., and McKendrick, A. G. (1927). A contribution to mathematical theory of epidemics. Roy Stat. Soc. J., 115, 714.)
The ratio of parameters $\beta/\nu$ has a rather meaningful interpretation. Since removal rate from the infective class is $\nu$ (in units of 1/time), the average period of infectivity is $1/\nu$. Thus $\beta/\nu$ is the fraction of the population that comes into contact with an infective individual during the period of infectiousness. The quantity $R_0 = N\beta/\nu$ has been called the infectious contact number, $\sigma$ (Hethcote, 1976) and the intrinsic reproductive rate of the disease (May, 1983). $R_0$ represents the average number of secondary infections caused by introducing a single infected individual into a host population of $N$ susceptibles. (In papers by May and Anderson, the threshold result is usually written $R_0 > 1$.)

In further analyzing the model we can take into account the particularly convenient fact that the total population

$$N = S + I + R$$

does not change (see problem 25 for verification). This means that one variable, say $R$, can always be eliminated so that the model can be given in terms of two equations in two unknowns. In the following analysis this fact is exploited in applying phase-plane methods to the problem.

---

**Qualitative Analysis of a SIRS Model: Epidemic with Temporary Immunity and No Vital Dynamics**

Since the total population is constant, we eliminate $R$ from equations (28) by substituting

$$R = N - S - I.$$  \hspace{1cm} (30)

The equations for $S$ and $I$ are then

$$\frac{dS}{dt} = -\beta SI + \gamma(N - S - I) = F(S, I),$$  \hspace{1cm} (31a)

$$\frac{dI}{dt} = \beta SI - \nu I = G(S, I).$$  \hspace{1cm} (31b)

**Nullclines**

- $I' = 0$ for $I = 0$ and $S = \nu/\beta$,
- $S' = 0$ for $\beta SI = \gamma(N - S - I)$.

After rearranging,

$$I = \frac{\gamma(N - S)}{(\beta S + \gamma)}.$$  \hspace{1cm}

This curve intersects the axes at $(N, 0)$ and $(0, N)$. 

---

Continuous Processes and Ordinary Differential Equations

Steady states

$$(S_1, I_1) = (N, 0); \ (S_2, I_2) = \left( N - \frac{\nu}{\beta}, \frac{N - (\nu/\beta)}{\nu + \gamma} \right).$$

Jacobian

$$J = \begin{pmatrix} F_S & F_I \\ G_S & G_I \end{pmatrix} = \begin{pmatrix} -(\beta I + \gamma) & -(\beta S + \gamma) \\ \beta l & \beta S - \nu \end{pmatrix}.$$ 

Stability

For $(S_2, I_2)$,

$$\text{Tr} \ J = -(\beta I_2 + \gamma) \text{ is always negative},$$

$$\det \ J = \beta I_2 (\nu + \gamma) \text{ is always positive}.$$ 

Thus this steady state is always stable when it exists, namely when the threshold condition is satisfied. It is evident from Figures 6.14 and 6.15(b) and from further analysis that the approach to this steady state can be oscillatory.

Figure 6.14 Nullclines, steady states, and several trajectories for the SIRS model given by equations $(31a,b)$, which are equivalent to $(28a,b,c)$. 

[Diagram showing nullclines and trajectories for SIRS model]
Figure 6.15 Epidemic models are characterized by the magnitude of an infectious contact number $\sigma$. (a) When $\sigma < 1$, the infective class will disappear. (b) When $\sigma > 1$, there is some stable steady state in which both susceptibles and infectives are present. Shown here is an SIRS model with vital dynamics. [Reprinted by permission of the publisher from Hethcote, H.W. (1976). Qualitative analyses of communicable disease models. Math. Biosci., 28, 344 and 345. Copyright 1976 by Elsevier Science Publishing Co., Inc.]
Mortality from a variety of afflictions, only some of which were caused by disease, were systematically recorded as early as the 1600s in the Bills of Mortality published in London. Reproduced here is the title page of the London Bills of Mortality for 1665, the year of the great plague. The people of the city followed with anxiety the rise and fall in the number of deaths from the plague, hoping always to see the sharp decline which they knew from past experience indicated that the epidemic was nearing its end. When the decline came the refugees, mostly from the nobility and wealthy merchants, returned to the city, and then for a time the mortality rose again as the disease attacked these new arrivals. The plague of 1665 started in June; its peak came in September and its decline in October. The secondary rise occurred in November and cases of the disease were reported as late as March of the following year. [From H. W. Haggard (1957), Devils, Drugs, Doctors, Harper & Row, New York.]

The Diseases, and Casualties this year being 1632.

A
Bortive, and Stillborn ........................................... 445
Afrighted .......................................................... 1
Aged .............................................................. 628
Ague .............................................................. 43
Apoplexy, and Meagrom ............................................ 17
Bit with a mad dog .................................................. 1
Bleeding ............................................................ 3
Bloody flux, scowring, and flux .................................... 348
Brused, Issues, sores, and ulcers ................................ 28
Burnt, and Scalded .................................................. 6
Burst, and Rupture ................................................... 9
Cancer, and Wolf .................................................... 10
Canker .............................................................. 1
Childbed ........................................................... 171
Chrisones, and Infants .............................................. 2288
Cold, and Cough .................................................... 55
Colick, Stone, and Strangury ...................................... 56
Consumption ......................................................... 1797
Convulsion .......................................................... 241
Cut of the Stone ..................................................... 5
Dead in the street, and starved ................................... 6
Drop, and Swelling .................................................. 267
Drowned ............................................................ 34
Executed, and prest to death ...................................... 18
Falling Sickness .................................................... 7
Fever ............................................................... 1108
Fistula .............................................................. 13
Flocks, and small Pox .............................................. 631
French Pox .......................................................... 12
Gangrene ............................................................ 6
Gout ................................................................. 4

Grief ................................................................. 11
Jaundice ............................................................. 43
Jaw-sain ............................................................. 9
Impostume ........................................................... 74
Killed by several accidents ......................................... 48
King's Evil .......................................................... 38
Lethargy ............................................................ 2
Livergrown .......................................................... 87
Lunatique ........................................................... 5
Made away themselves .............................................. 15
Measles ............................................................. 80
Murdered ............................................................ 7
Over-laid, and starved at nurse ................................... 7
Palisa ............................................................... 25
Pleas ............................................................... 1
Plague .............................................................. 8
Planet ............................................................... 13
Pleurisy, and Spleen ................................................. 38
Purple, and spotted Fever ......................................... 38
Quinsie .............................................................. 7
Rising of the Lights ................................................ 98
Sciatica ............................................................. 1
Scurvy, and Itch ..................................................... 9
Scudden ............................................................ 62
Surfeit .............................................................. 86
Swine Pox .......................................................... 6
Teeth ............................................................... 470
Thrush, and Sore mouth ............................................. 40
Tympany ............................................................ 13
Tiasick .............................................................. 34
Vomiting ............................................................ 1
Worms .............................................................. 27

Males ............................................................... 4994
Christened Males ....................................................
In all .............................................................. 9084

Females ............................................................ 4690
Christened Females .................................................
In all .............................................................. 9535

Buried .............................................................. 4932
Whereof, Males .....................................................
In all .............................................................. 9538

Plague .............................................................. 8
Increased in the Burials in the 122 Parishes, and at the Pest-
house this year ...................................................... 903
Decreased of the Plague in the 122 Parishes, and at the Pest-
house this year .................................................... 260 [10]
Numerous other cases have been analyzed in detail. Perhaps the best summary is given by Hethcote (1976), in which theoretical results are followed by biocorollaries that spell out the biological predictions. His paper was used in drawing up Table 6.1, a composite that describes a number of cases.

One point worth mentioning is the essential difference between models in which the susceptible class is renewed (by recovery or loss of immunity) and those in which it is not. [The SIRS and SIS examples shown in Figure 6.12(b−d) belong to the former category.] These distinct types behave differently when the normal turnover of births and deaths is superimposed on the dynamics of the disease. In the SIR type without births, the continual decrease of the susceptible class results in a decline in the effective reproductive rate of the disease. The epidemic stops for want of infectives, not, as it might seem, for want of susceptibles (Hethcote, 1976). On the other hand, if the susceptible class is replenished by births or recoveries, the subpopulation that participates in the disease is maintained, and the disease can persist.

From Table 6.1 we see that SIR models are subdivided into those with and without births and deaths. In other models the chief effect of normal birth and mortality at rates δ is to decrease the infectious contact number σ. This means that a smaller population can sustain an endemic disease. Note that the total population N is taken to be constant in all of these models since the number of deaths from all classes is assumed to exactly balance the births of new susceptibles. Among other things, this permits all such models to be analyzed by methods similar to the method used here since one variable can always be eliminated.

A somewhat different philosophical approach was taken by Anderson and May (1979), who were less interested in the dynamics of the disease itself. By analyzing a model in which a disease-free population grows exponentially, rather than being maintained at a constant level, they demonstrated that epidemics increasing host mortality have the potential to regulate population levels (see problem 30). This adds yet another interesting possibility to the list of causes of decelerating growth rates in natural populations. Aside from inter- and intraspecies competition and predation, disease-causing agents (much like parasites) can control the population dynamics of their hosts.

The theory of epidemics has numerous ramifications, some of which are mathematical and some practical. In recent years more advanced mathematical models have been studied to determine the effects of delay factors (such as a waiting time in the infectious class), age structure, migration, and spatial distributions. Many of these models require sophisticated mathematical methods of analysis (see, for example, Busenberg and Cooke, 1978). An excellent survey with detailed references is given by Hethcote et al. (1981).

One theoretical question such papers often address is whether models with particular structures lead to stable (limit-cycle) oscillations. This question is of interest since some diseases are associated with periodic outbreaks with very low endemic periods followed by peak epidemic cycles. In some cases the forces driving such cyclic behavior are related to seasonality and to changes in contact rates. (A good example is childhood diseases, which invariably peak during the school year when contact between their potential hosts is greatest.) However, even in the absence of externally imposed periodicity, models similar to SIRS can have an inherent ten-
Table 6.1 A Summary of Several Epidemic Models

<table>
<thead>
<tr>
<th>Type</th>
<th>Immunity</th>
<th>Birth/Death</th>
<th>Significant quantity</th>
<th>Results</th>
<th>Figures</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIS</td>
<td>None</td>
<td>Rate $= \delta$</td>
<td>$\sigma = \frac{\beta}{\gamma + \delta}$</td>
<td>(1) $\sigma &gt; 1$: constant endemic infection</td>
<td>6.9(d)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$\sigma$ as above, and $\epsilon = \frac{\eta}{\gamma + \delta}$</td>
<td>(2) $\sigma &lt; 1$: infection disappears</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Disease always eventually disappears leaving some susceptibles.</td>
<td></td>
</tr>
<tr>
<td>SIR</td>
<td>Yes, recovery gives immunity.</td>
<td>None</td>
<td>$\sigma = \frac{S_0 \beta}{\gamma}$ ($S_0$ = initial $S$)</td>
<td>(1) $\sigma &gt; 1$: infection peaks and then disappears</td>
<td>6.9(a)</td>
</tr>
<tr>
<td></td>
<td>Yes, rate $= \delta$</td>
<td>$\sigma = \frac{\beta}{\nu + \delta}$</td>
<td>(2) $\sigma &lt; 1$: infection disappears</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(SIR with carriers)</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
<td>(1) $\sigma &lt; 1$: susceptibles and infectives approach constant levels</td>
<td>6.9(c)</td>
</tr>
<tr>
<td></td>
<td>Temporary, lost at rate $\gamma$</td>
<td></td>
<td>(2) $\sigma &lt; 1$: infectives disappear; only $S$ remains</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIRS</td>
<td>Temporary, lost at rate $\gamma$</td>
<td></td>
<td>$\sigma = \frac{\beta}{\nu + \delta}$</td>
<td>(1) $\sigma &gt; 1$: same as SIR (1) but higher levels of infectives</td>
<td>6.9(c)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(2) $\sigma &lt; 1$: same as SIR (2)</td>
<td></td>
</tr>
</tbody>
</table>
dency to give rise to oscillations. This is particularly true of models with long periods of immunity or some other delaying factor. Hethcote notes that a sequence of at least three removed classes will also achieve the result (for example, $SIR; R_2, R_3, S$).

The implications of many aspects of applying mathematical theory to natural populations are eloquently described in numerous papers by May and Anderson. Some questions are of a basic scientific nature. For example, the extent to which diseases and hosts have coevolved is a fascinating topic; a second controversial question is whether or not diseases are in fact a predominant factor in controlling natural populations. Other questions have more immediate medical ramifications. Anderson and May suggest that theory has an important place in illuminating the impact of disease on human populations and the ability to eradicate or control disease. Two applications of the theory to vaccination programs are briefly highlighted in the following section.

6.7 FOR FURTHER STUDY: VACCINATION POLICIES

Models for infectious diseases lead to a better understanding of how vaccination programs affect the control or eradication of the disease. Several popular articles by Anderson and May (1982) and a more detailed mathematical version (1983) are thought-provoking and informative. The full theory that takes into account age structure of the population uses a partial differential equation model (which would be understood more fully after covering Chapter 11). However, a number of rather interesting consequences of the theory can be understood with no further preparation.

Eradicating a Disease

Immunization can reduce or eliminate the incidence of infection, even when only part of the population receives the treatment. Those individuals who have been vaccinated will be protected from acquiring infection (this is the obvious direct effect). A secondary effect is that since vaccinated individuals are essentially removed from participating in transmission of the disease, there will be fewer infectious individuals and thus a decreased likelihood that an unvaccinated susceptible will come in contact with the disease. This indirect effect is known as herd immunity.

Administering vaccinations to an entire population can be costly. Some vaccines (for example, some measles and whooping cough vaccines) also carry the risk, though rare, of causing various reactions or neurological damage. Thus, if disease eradication can be achieved by partially vaccinating some fraction $p$ of the population, an advantage is gained.

The fraction to be immunized must be such that the remaining population, $(1 - p)N$, will no longer exceed the threshold level necessary to perpetuate the disease. In the terminology of Anderson and May, the reproductive factor $R_0$ of the infection is to be reduced below 1. Since $R_0 = N\beta/\nu$, for a given disease this factor can be estimated from epidemiological and population records. Table 6.2 lists several common diseases with their corresponding $R_0$ factors.
models with long periods, that a sequence of minimal, SIR, R, S, R, S).

cital theory to natural

May and Anderson, the extent to which disease transmissions to control natural

ifications. Anderson suggests the impact of disease. Two articles in the following

ow vaccination popular articles by Anderson (1983) are to account age structure, which would be another of rather different preparation.

1, even when only who have been vac-ious direct effect), mainly removed from infectious individuals ill come in contact

 costly. Some vac-also carry the risk, thus, if disease p of the populai-ning population, perpetuate the disease factor R, of the disease this factor Table 6.2 lists sev-

<table>
<thead>
<tr>
<th>Infection</th>
<th>Location and Time</th>
<th>R₀</th>
<th>Approximate Value of p (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smallpox</td>
<td>Developing countries, before global campaign</td>
<td>3–5</td>
<td>70–80</td>
</tr>
<tr>
<td>Measles</td>
<td>England and Wales, 1956–68; U.S., various places, 1910–30</td>
<td>13</td>
<td>92</td>
</tr>
<tr>
<td>Whooping cough</td>
<td>England and Wales, 1942–50; Maryland, U.S., 1908–17</td>
<td>17</td>
<td>94</td>
</tr>
<tr>
<td>German measles</td>
<td>England and Wales, 1979; West Germany, 1972</td>
<td>6</td>
<td>83</td>
</tr>
<tr>
<td>Chicken pox</td>
<td>U.S., various places, 1913–21 and 1943</td>
<td>9–10</td>
<td>90</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>U.S., various places, 1910–47</td>
<td>4–6</td>
<td>~80</td>
</tr>
<tr>
<td>Scarlet fever</td>
<td>U.S., various places, 1910–20</td>
<td>5–7</td>
<td>~80</td>
</tr>
<tr>
<td>Mumps</td>
<td>U.S., various places, 1912–16 and 1943</td>
<td>4–7</td>
<td>~80</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>Holland, 1966; U.S., 1955</td>
<td>6</td>
<td>83</td>
</tr>
</tbody>
</table>

The fraction p to be immunized is then deduced from the following simple calculation:


Thus

R₀' < 1 \Rightarrow (1 – p)R₀ < 1 \Rightarrow p > 1 – \frac{1}{R₀}
The percentage of the population to be vaccinated thus depends strongly on the infectiousness of the disease. It is noteworthy that smallpox, a disease essentially eradicated by vaccination, has one of the lowest $R_0$ values and a correspondingly low required vaccination fraction. By contrast, measles and whooping cough require a much higher percentage of immunization and would be harder to eradicate.

**Average Age of Acquiring a Disease**

Is it always wise to vaccinate at least some people, even if the disease will not be eradicated? When a disease has different impacts on individuals of different ages, vaccination at a young age can have a somewhat surprising deleterious effect. A case in point is German measles (Rubella). Normally a mild short-lasting infection, Rubella can be particularly devastating when contracted by a pregnant woman, as it results in birth defects to the fetus during the first trimester of pregnancy. Vaccinating *against* Rubella raises the average age at which the disease is first acquired (see box). Thus, rather than incurring the disease on average at age 12, it may be more prevalent at ages 20 to 30, precisely the most dangerous period for women of childbearing ages.

---

**How Vaccinations Raise the Age of First Acquiring a Disease**

Define $\lambda = \beta I$. Called the *per capita force of infection*, $\lambda$ has units of $1$/time and is the rate of acquiring the disease given a population containing $I$ infectives and a transmission constant $\beta$.

Let $A = 1/\lambda$. $A$ is the *average age of first infection*, or average waiting time in the susceptible compartment before acquiring the disease. $A$ has units of time.

Now note that a vaccination program tends to reduce the number of infectives $I$, thus reducing $\lambda$ and *raising* $A$.

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For other aspects of the topic of vaccinations, epidemiology, and population dynamics, the many excellent sources quoted in the references are highly recommended.