How sick should a pathogen make its host?

- The evolution of virulence in myxoma virus
The conventional wisdom (CW)

1. “The ideal of parasitism is actually commensalism.” (Hoeprich 1989. *Infectious diseases*)

2. “Given enough time a state of peaceful coexistence eventually becomes established between any host and parasite.” (Dubos 1960 in *Attenuated Infection.*)

3. “For nature, survival of the species is all that counts.” (Brunet & White 1972. *Natural history of infectious disease*)

4. “Attenuated infection represents a state in which the most favorable conditions are provided for the greatest number of individuals over the longest period of time.” (Simon 1960. *Attenuate infection the germ theory in contemporary prespective.*)
More CW

5. “The reasons why Staphylococci are harmless in some individuals and virulent pathogens in others remains a mystery”. (Norden & Ruben 1981)

6. Norden and Ruben recognized that hospital-acquired staph infections were more severe, and suggested that this was the case because people were already sick. They did not consider the possibility that greater virulence evolved in hospitals. (from P. Ewald 1994: Evolution of infectious disease.)
Overthrow of the CW
(begining with May & Anderson)

1. $R_0$ (the number of secondary infections). If we introduce a single infected individual into a susceptible population, how many new infections will we get? That number is $R_0$. Assuming that infection is the only source of mortality,

2. Selection on parasites will tend to maximize $R_0$, not host survival.
Lecture 11.5. Virulence evolution and the spread of infectious disease.

Question: how sick should parasites make their hosts?

Mxyoma virus and rabbits.
(draw in dynamics)
1. **Rabbits evolved resistance.**

   Original 1950 viral strain injected into 1957 Australian rabbits. Rabbits more resistant

2. **Virus evolved to be less virulent.**

   1957 virus from Aussie rabbits infected into European rabbits. Mortality rates were reduced compared to original strain of the virus.
Parasite sterilizes the snail.

And it causes the ants to be eaten.

(It is quite hard on sheep too.)
The famous SIR (Susceptible-Infected-Resistant[ or Removed]) model.

We want to know how the number of infected individuals changes over time. Let $I$ be the number of infected hosts. Let $S$ be the number of susceptible hosts, and let $R$ be the number hosts that are removed from the infected class due to host recovery or mortality.

\[
\frac{dS}{dt} = -\beta IS \tag{1}
\]

\[
\frac{dI}{dt} = \beta IS - rI \tag{2}
\]

\[
\frac{dR}{dt} = rI \tag{3}
\]

where $\beta$ is the probability of contact ($c$) between susceptible and infected individuals times the probability of disease transmission ($a$); and where $r$ is the “removal rate” due to host recovery or host mortality. (see Otto and Day’s Book for more formal definition of Beta).
Now, how do we know if the disease will spread? Thought experiment: what would happen if we introduce a single infected individual into a host population? To find out, set $I = 1$. Assume the whole population is susceptible, thus $S = N$, where $N$ is the total population size ($N = S + I + R$). Doing this, equation (2) becomes:

$$\frac{dI}{dt} = \beta N - r$$

(4)

The spread of the disease requires that the solution to (4) is positive, which only requires that $\beta N > r$. There therefore exists a threshold density $N_T$ for disease spread, where

$$N_T = \frac{r}{\beta}$$

(5)

The disease will spread if the actual host density is greater than the threshold density: $N > N_T$. 
Returning to equation (4), the rate of spread of the disease is $\beta N - r$. Clearly, if the disease is to spread, then $\beta N - r > 0$, or equivalently,

$$\frac{\beta N}{r} > 1$$  \hspace{1cm} (6)

Note that the ratio on the left hand side is not a rate, but rather a unit-less number (as it gives a rate ($\beta$) divided by a rate ($r$) {note that $1/r$ gives the duration of the infection}. This number represents the number of secondary infections resulting from the initial infection, and it is called the “reproductive number” or $R_0$. Thus for the infection to spread, we require that

$$R_0 = \frac{\beta N}{r} > 1$$  \hspace{1cm} (7)

As we will see, $R_0$ is a very important number in epidemiology.
If the disease spreads,

1. Will every single susceptible host become infected, or

2. Will the infection die out before infecting everyone?

Think about it this way. If the disease spreads, at what point will the number of infected individuals begin to decline. Look at equation (2). The number of infected individuals will decline when $\beta S < r$, which is when

$$S < \frac{r}{\beta}.$$  \hspace{1cm} (8)

Remember that we decided that $\beta < r$, so the ratio has to be greater than one.

Finally, let’s say we know the flu is coming. What fraction of the population would we need to vaccinate ($p$) to prevent an epidemic? The disease will not spread if

$$\frac{\beta}{r} N (1 - p) < 1$$ \hspace{1cm} (9)
which is when

\[ p > 1 - \frac{1}{R_0} \]  

(10)

Thus the larger the value for \( R_0 \), the more people that we would need to vaccinate.

Values for \( R_0 \) have been estimated as follows: measles 12-18; polio 5-7; 1918 flu 2-3; HIV 2-5; SARS 2-5; smallpox 6-7; Ebola (1995) 1.7-8.6.

List the assumptions of the SIR model

1. **Mass Action.** Any infected host can contact any uninfected host. No spatial structure.

2. **Resistance, once gained, is not lost during the course of infection.**
3. No births or immigration into the host population. (The disease dynamics are so fast, that there is no time for host reproduction.)

Below is the discrete-time simulation for $\beta = 0.001; \nu = 0.5; N = 1000.$ see file “SIR workbook density.xls”
Now, let’s consider the evolution of virulence. As above, the number of new infections resulting from introducing a single infected host is called $R_0$.

From above, we have

$$R_0 = \frac{\beta N}{r}$$

(11)

where $r$ is the rate of removal from the infected population, where removal can be due to recovery, natural mortality in the host population, and infection-mediated mortality.

Let’s assume for now that hosts do not recover from infection, but they do suffer natural mortality with rate $d$, and infection-mediated mortality at rate $v$, where $v$ stands for virulence ($r = v + d$). Our equation for the number of secondary infections becomes.

$$R_0 = \frac{\beta N}{v + d}$$

(12)
Let’s make the reasonable assumption that the transmission coefficient, Beta, depends on virulence, $v$.

$$R_0 = \frac{\beta(v)N}{v + d} \quad (13)$$

where $\beta(v)$ means beta is a function of $v$.

Borrowing form our “size-number compromise” model, we could make $\beta(v)$ a diminishing returns function of virulence. For example,

$$\beta(v) = c(x - \frac{v_{\text{min}}}{v}) \quad (14)$$

where $c$ gives the contact rate; and $x$ is between zero and one, and gives the maximum frequency of hosts that can be infected. $v_{\text{min}}$ gives the minimum virulence (prob. of host death) required to give some degree of transmission.
As in previous lectures, we can find the ESS for virulence (from the parasite’s point of view) by solving for the conditions for which the first derivative of $R_0 = 0$, provided the second derivative is negative. For our present model, the ESS is at

$$\hat{v} = \frac{v_{\text{min}} + (v_{\text{min}}^2 + dxv_{\text{min}})^{1/2}}{x}$$

(15)

(see: “6. virulence Max R0.nb”)
\[ \beta(v) = c \left( x - \frac{V_{\text{min}}}{v} \right) \]

Infectious period:

\[ \text{Infectious period} = \frac{1}{v + d} \]
Note: this is the corrected version for $v^*$.

Note that anything that shifts the local maximum to the right also increases virulence.

Also: the optimal virulence model turns out to be conceptually very similar to the life-history model of the size-number trade-off.