A Population-Dynamics Approach to Assess the Threat of Plant Pathogens as Biological Weapons against Annual Crops

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In recent years there has been considerable concern expressed in the scientific and popular literature about the threat of biological terrorism (Simon 1997, Henderson 1998, Abelson 1999, Atlas 1999, Osterholm 1999, Stone 2000, Hardy 2001, Stimson Center 2001). This general interest had been propelled by US executive orders on weapons of mass destruction, White House initiatives on biological and chemical weapons preparedness (White House 1994, 1998a, 1998b, 1998c, 1999a), and the release of information from the former Soviet Union on the extent of biological weapons research conducted during the cold war (Alibek and Handelman 1999, Tucker 1999). Obviously, this concern has intensified since the tragedies of September 11, 2001 (Lawler 2001). Much attention has been directed toward the use of pathogenic microorganisms as biological weapons against humans, but there has been growing awareness of the potential use of microbes as weapons against crops as well (MacKenzie 1999, Rogers et al. 1999, Schaad et al. 1999, Yang and Sanogo 2000), especially in view of information that has come to light concerning Iraq's past efforts to develop biological weapons against crop plants (Whitby and Rogers 1997).

The impact of plant diseases on agriculture is immense. In the United States, for example, annual total losses due to crop diseases are estimated at over $30 billion, with 65% of that amount attributed to introduced (invasive) microbes (Pimentel et al. 2000). Economically important pathogens continue to be accidentally introduced, some with very large economic consequences (Bandyopadhyay et al. 1998, Gottwald et al. 2001). Although, to our knowledge, plant pathogens have never been deliberately introduced into US crops as an act of warfare or terrorism, there is concern that this and many other countries are vulnerable to such acts of aggression (Kadlec 1995, Horn and Breeze 1999, Pearson 1999).

USING A COUPLED DIFFERENTIAL-EQUATION MODEL, WE SHOW THE CONDITIONS NECESSARY FOR LONG-TERM PERSISTENCE OF A PLANT DISEASE AFTER A PATHOGENIC MICROORGANISM IS INTRODUCED INTO A SUSCEPTIBLE ANNUAL CROP

The chances of a given plant pathogen being used successfully as a biological weapon involve, among other things, ease of production, storage, and delivery, and then the fate of the introduced pathogen once it is introduced into a susceptible crop (Schaad et al. 1999). This article is concerned with assessing the risk of the latter, including accidentally introduced plant pathogens (Yang et al. 1991, Ruesink et al. 1995, Schmitz and Simberloff 1997, Enserink 1999), a key component of the Executive Order on Invasive Species (White House 1999b). The Animal and Plant Health Inspection Service (APHIS) of the US Department of Agriculture uses several

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variations of generic risk-assessment methods to determine the risk of certain plant pathogens (and other pests) being nondeliberately introduced, spreading, and causing economic or other consequences (Orr et al. 1993). This approach does not explicitly or formally deal with the population dynamics of potentially introduced organisms in assessing risk, making it difficult to generate general principles of disease development.

Theoretical epidemiology does provide a means, however, based on population dynamics, of predicting the outcome when a pathogen is introduced into a susceptible host population (Mollison 1986, Anderson and May 1990, Diekmann et al. 1990, van den Bosch et al. 1999). This approach has been most extensively used in studying diseases of animals, and especially people; a considerable amount of research with plant epidemics also has been done (Campbell and Madden 1990, Swinton and Gilligan 1996, Gilligan and Kleczkowski 1997, Gilligan et al. 1997). In fact, nearly 40 years ago Vanderplank (1963) outlined the epidemiological principles relevant for assessing the threat of plant pathogens as biological weapons. A common feature of plant epidemics is that plants can become infected at any time by contacts between disease-free plants and (a) inoculum produced during past epidemics or in epidemics in other host populations (known as primary infection) or (b) inoculum produced by infectious plants in the current epidemic (known as secondary infection) (Campbell and Madden 1990).

A key parameter in predicting several features of epidemics is the basic reproduction number, R_0 (Diekmann et al. 1990), which is defined as the mean number of new infected individuals that results from one infected individual introduced into a susceptible (disease-free) host population (over the lifetime of the infectious individual). R_0 must exceed 1 for disease invasion and persistence (Mollison 1995): The epidemic will not die out when each diseased individual leaves, on average, more than one new diseased individual. The magnitude of R_0 can be used to determine final epidemic size (either abundance or proportion of diseased individuals in the population), provided there is sufficient time for either a steady state to be achieved (if there is host growth) or an asymptote to be approached (for nongrowing host). *Host growth* can refer to changes in either the numbers of host individuals or the amount of host tissue available for infection. Thus, for long-lived perennial plant species with continuous disease development, current epidemic theory can, in general, be used to predict epidemic outcomes from accidentally or deliberately introduced pathogens (Jeger and van den Bosch 1994, Swinton and Gilligan 1996, Madden et al. 2000). However, most major crops are annuals (Hanson 1990), often with long periods between seasons, or perennials with only seasonal growth, such that there are long intervals in which there is no susceptible host tissue (e.g., because of natural leaf senescence) or the environment is unfavorable for disease development or crop growth.

This article deals with epidemics of annual crops but has applicability to nonsystemic diseases of perennial crops with seasonal growth. The abrupt elimination of the annual-crop host at regular times (during harvesting), independent of disease status, and the subsequent introduction or reintroduction of the host at a later time (e.g., next season, when crops are planted), independent of the amount of pathogen inoculum in the soil or surrounding area, are complications not typically considered in theoretical epidemic models. A major challenge in plant protection is to develop the theoretical and experimental approaches for studying these so-called polyetic (multiple-season) epidemics (Zadoks 1999). In human host populations, forcing functions (such as cosine functions for the transmission rate parameter) are often used to represent temporal cycles of high and low disease transmission (Bolker and Grenfell 1993, Earn et al. 2000). This approach does not adequately represent the disappearance of the host nor the potential survival of the pathogen as a saprophyte or parasite of other plant species.

Model

To help assess the risk associated with a plant pathogen being introduced—deliberately or accidentally—into a susceptible annual crop, we developed a coupled differential-equation model for the long-term (multiseason) dynamics of plant disease for annual crops. The within-season dynamics are represented with equations for the rate of change in the abundance of disease-free plant individuals (S), and latently infected (E), infectious (I), and postinfectious or removed (R) plant individuals (Figure 1; Box 1). Total disease, Y, is given by $E + I + R$. Although all variables depend on time (t) (e.g., $S[t]$), for convenience we suppress the t notation when that can be done without causing ambiguity. It is assumed that P_0 units of pathogen inoculum are introduced into a disease-free crop at the start of a season ($t = 0$), considered below as the first season. The introduced inoculum then decays expo-

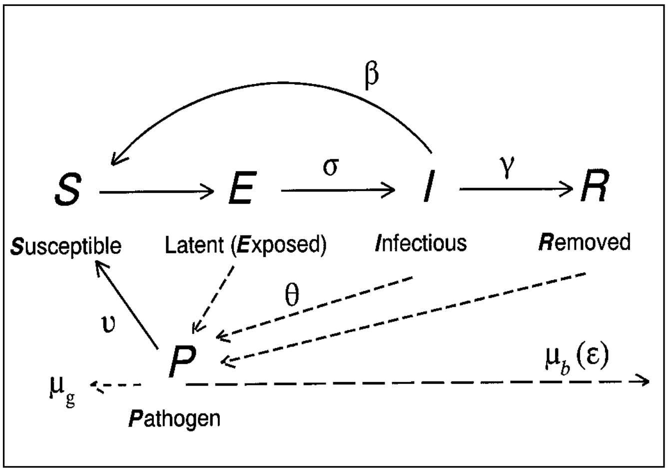

Figure 1. Schematic drawing of disease model, representing within-season dynamics of disease-free (S), latently infected (E), infectious (I), and postinfectious (R) plants; the production of inoculum or pathogen individuals (P); and mortality of inoculum within and between seasons.

nentially. New infections occur based on the contact between S and P, and the rate depends on the primary infection rate parameter, υ. Infected individuals initially are in the latent state (with a mean duration of $1/\sigma$), and then are in the infectious state (for a mean duration of $1/\gamma$). New infections can occur from infectious plant individuals; the rate of this secondary infection depends on the secondary infection rate parameter, β. One example of secondary infection would be through the production of spores on foliar lesions caused by a fungal disease and the dispersal of some of these spores to disease-free plants, some of which become infected. The overall model can be written in pseudo-equation form as

Box 1. Plant epidemic model

Let S, E, I, and R represent the abundance of the disease-free, latently infected, infectious, and postinfectious plant individuals (Figure 1). Also let P represent the abundance of pathogen inoculum. When P_0 units of pathogen inoculum are introduced into a disease-free crop at time (t) 0, new infections occur at rate υSP (with υ being the primary infection rate parameter [constant]) during the growing season. υS is the mean number of new infected plant individuals per unit of inoculum per time. Infected plants are first in the latent state; they become infectious at a rate σ. Infectious plant individuals become postinfectious or removed from the epidemic at a rate γ. New infections can occur from infectious plant individuals at a rate βSI (with β being the secondary infection rate parameter [constant], sometimes called the transmission rate) (Figure 1). βS is the mean number of new infected individuals per infected individual per time, and depends, for fungal pathogens, on the production of spores and the probability of a spore causing an infection (Campbell and Madden 1990). The introduced pathogen inoculum decays exponentially at a natural mortality rate $\mu_g P$ (with μ_g being the mortality rate parameter) and depletion rate $\upsilon' P$ (with υ' here equal to υ, because each unit of inoculum that produces a plant infection is one less unit of inoculum available for infecting another plant). The model can be written as

$$
\begin{aligned}
& dS/dt = -\,\upsilon SP - \beta SI \\
& dE/dt = +\,\upsilon SP + \beta SI - \sigma E \\
(1)\quad & dI/dt = +\,\sigma E - \gamma I \\
& dR/dt = +\,\gamma I \\
& dP/dt = -\,(\mu g + \upsilon')P.
\end{aligned}
$$

Numerical integration can be used to solve equation 1 for S, E, I, and R using any set of parameter values. An analytical solution is obtained for P.

A pure contagious (secondary-infection-only or "compound interest") epidemic can be obtained from the model if one allows $\upsilon \rightarrow \infty$ and $\upsilon' + \mu_g \rightarrow \infty$, with $\upsilon/(\upsilon' + \mu_g) = \phi$ held constant. Then, $\phi P_0 S_0$ is the initial number of diseased plant individuals, and P equals 0 after time 0; ϕS_0 is the number of diseased plants infected at the beginning of the growing season per unit of initial inoculum. Under these circumstances, $\beta S_0/\gamma$ is the within-season basic reproduction number, which Vanderplank (1963) called the progeny–parent ratio in a different modeling structure. To obtain a pure primary-infection-only epidemic, one lets σ go to 0 in the limit. Other special cases also are possible. For instance, if γ is very small (or $1/\gamma$ is large), infected plants remain infectious for the entire epidemic after they pass through the latent period. When μ_g is negative, an increase in P due to saprophytic growth is described.

The growing season and epidemic end at $t = T_g$, to represent crop harvest. All plant abundances are set to 0 immediately after T_g ($t = T_g^+$); that is, $E(T_g^+) = I(T_g^+) = R(T_g^+) = S(T_g^+) = 0$. The "+" superscript represents the instant after the end of the season. The "–" superscript (see below) indicates the instant before the end of the season. New inoculum at T_g^+, which may survive between growing seasons, is proportional to disease intensity at T_g^-, or to a weighted function of diseased individuals over the last T_1 days of the epidemic. If θ_I, θ_E, and θ_R represent the number of spores (or other infectious units or amount of inoculum) produced per diseased individual at the end of the season, then $\kappa_I = \theta_I I(T_g^-)$, $\kappa_E = \theta_E E(T_g^-)$, and $\kappa_R = \theta_R R(T_g^-)$ represent the total number of spores (or amount of inoculum) at $t = T_g^+$ from infectious, latent, and removed diseased individuals at $t = T_g^-$. For a generalization, assume that only postinfectious disease that is not too old can produce new P. If R that is less than T_1 days old can produce P, then

$$\kappa_R = \theta_R \gamma \int_{T_g - T_1}^{T_g} I(t)dt.$$

Inoculum production could be defined by more complicated functions of E, I, and R, but we restrict our attention to the simple functions described above. Because of the exponential decline in P over time, the amount of introduced inoculum (in the first season) still present at T_g^+ is given by $\kappa_P = P_0 \exp[-(\upsilon' + \mu_g)T_g^-]$. Thus, inoculum at T_g^+ is given by $P(T_g^+) = \kappa_P + \kappa_I + \kappa_E + \kappa_R$.

As a simple example, if no inoculum survives until the end of the season and E, I, and R all produce new inoculum at the same magnitude (θ), $P(T_g^+)$ is given by $\theta[E(T_g^-) + I(T_g^-) + R(T_g^-)]$, or $\theta Y(T_g^-)$.

$$\frac{dS}{dt} = -\begin{bmatrix}\text{primary}\\ \text{infections}\end{bmatrix} - \begin{bmatrix}\text{secondary}\\ \text{infections}\end{bmatrix}$$

$$\frac{dE}{dt} = +\begin{bmatrix}\text{primary}\\ \text{infections}\end{bmatrix} + \begin{bmatrix}\text{secondary}\\ \text{infections}\end{bmatrix} - \begin{bmatrix}\text{latent infections}\\ \text{becoming infectious}\end{bmatrix}$$

$$\frac{dI}{dt} = +\begin{bmatrix}\text{latent infections}\\ \text{becoming infectious}\end{bmatrix} - \begin{bmatrix}\text{removal of}\\ \text{infectious}\end{bmatrix}$$

$$\frac{dR}{dt} = +\begin{bmatrix}\text{removal of}\\ \text{infectious}\end{bmatrix}$$

$$\frac{dP}{dt} = -\begin{bmatrix}\text{mortality of}\\ \text{primary inoculum}\end{bmatrix}$$

The more formal single-season model is presented in Box 1 as equation 1. This is a generalization of the classic SEIR (susceptible, exposed, infectious, and recovered) model and is based on some of the models of Gilligan and colleagues for mixtures of primary and secondary infection (Gilligan and Kleczkowski 1997, Gilligan et al. 1997, Bailey and Gilligan 1999); the model also has similarities to those developed for animal epidemics in which the pathogen has a saprophytic stage (Godfray et al. 1999). For initial simplicity, growth or mortality of S during the growing season is not considered here.

Depending on the values of the parameters of equation 1, pure primary-infection-only (i.e., "simple interest") and pure secondary-infection-only ("compound interest") epidemics can be obtained (Box 1). Moreover, most single-season epidemics of crops can be characterized through the model parameters. One composite parameter, $\beta S_0/\gamma$, is especially useful in this regard; $\beta S_0/\gamma$ equals the within-season basic reproduction number (Diekmann et al. 1990) for secondary-infection-only epidemics. Both increasing transmission rate (β) and increasing length of the infectious period ($1/\gamma$) lead to increases in $\beta S_0/\gamma$.

The single-season model of equation 1 can now be expanded for multiple seasons. Crop harvest occurs at $t = T_g$. After this time, all plant abundances are set to 0. We assume that new inoculum, which may survive between growing seasons, is produced by diseased individuals. Although only the I individuals produce inoculum that can cause secondary infections during the within-season epidemic, disease in all states theoretically could produce inoculum for the next season. For instance, spores may be produced or released (or both) from diseased noninfectious roots as they decay in the soil or on the soil surface (Agrios 1997). Moreover, this new inoculum may be in the form of infected alternate perennial (weed) hosts. The number of spores (or amount of inoculum) produced per diseased individual at the end of the season is given by θ_I, θ_E, and θ_R for the plants in the infectious, latent, and removed states, respectively; total number of spores produced is then given by κ_I, κ_E, and κ_R for the three infection categories (see Box 1).

As an example, new inoculum immediately after the end of the season (T_g^+) originating from infectious individuals is given by $\kappa_I = \theta_I I(T_g^-)$, where T_g^- is the time immediately before the end of the season. For convenience, we use θ without a subscript when the parameters for per-unit inoculum production are the same for each disease state, or when we refer to inoculum production in general. Some of the pathogen individuals introduced at the beginning of the season may still be present at the end of the season (depending on the mortality rate); this remaining inoculum is indicated by κ_P (see Box 1). Thus, inoculum at T_g^+ is given by $\kappa_P + \kappa_I + \kappa_E + \kappa_R$.

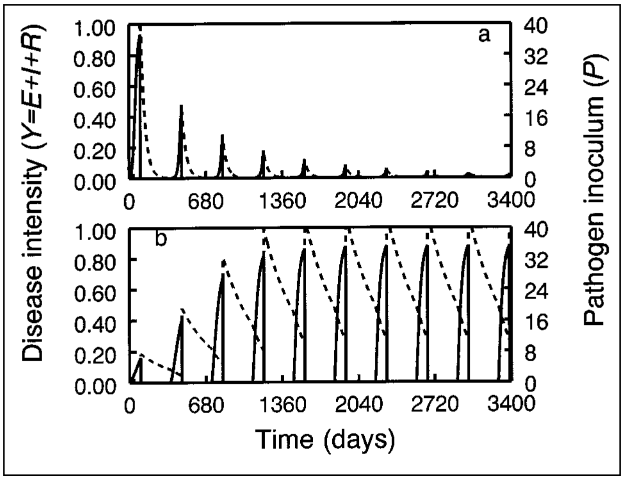

Figure 2. Infected plant individuals (Y; solid line, left side of panels) and inoculum density (P; broken line, right side of panels) over 10 years for an annual crop with a growing season of 100 days. Each growing season starts with a disease-free and fixed crop abundance of $S_0 = 1$, and disease and pathogen dynamics proceed as in equation 1. Initial P (P_0) for season 1 equals 1. (a) High rate of within-season disease increase (with a corresponding within-season basic reproduction number, $\beta S_0/\gamma$, of 3.1), but with a high inoculum decay rate between seasons ($\mu_b = 0.027$ per day). The multiseason basic reproduction number, R_0, equals 0.72 (equation 4). (b) Low rate of within-season disease increase (with $\beta S_0/\gamma = 0.81$), but with a low decay rate between seasons ($\mu_b = 0.003$ per day), so that R_0 equals 4.80. The primary infection rate, within-season inoculum mortality rate, mean latent period, mean infectious period, and per-unit production of inoculum are the same for both graph panels.

Between growing seasons, P decays exponentially with rate parameter μ_b, so that $dP/dt = -\mu_b P$. Therefore, at the start of the next growing season, T_b days after the end of the first season, the fraction of inoculum remaining is given by $\varepsilon = \exp(-\mu_b T_b)$. The amount of inoculum (or the number of P individuals) at the start of the next season resulting from each P individual (each unit of inoculum) at the start of the present season is thus given by

$$Q = [(\kappa_P + \kappa_I + \kappa_E + \kappa_R)\varepsilon]/P_0.$$

As exemplified in Figure 2, it is possible, depending on the parameters, for disease intensity (proportion of plant individuals infected) to be high in the first season and then to decline over each successive season. Or disease intensity may be low in the first season and increase over successive seasons.

Model terms for primary and secondary infection, latent and infectious periods within seasons, and inoculum decay within and between seasons are consistent with empirical data and modeling evidence (Zadoks 1961, Sumner et al. 1985, 1990, Campbell and Madden 1990, Hall and Phillips 1992, Jeger and van den Bosch 1994, Hall 1996, Bailey and Gilligan 1999); however, in no study have all these factors been simultaneously considered. Although the proportionality between disease in one season and the amount of overwintering inoculum is well accepted (Zadoks 1999), quantitative information about the relationship of disease at the end of a growing season to newly produced *P* is scant. It should be emphasized that the expression for *Q* is not dependent on the simple functions used in Box 1 for the κ values; other functions could be substituted when information becomes available. Our model is similar to that developed by Gubbins and Gilligan (1997) and Truscott and colleagues (1997), although we used a simpler equation for *S* (in the current work) to facilitate derivation of a persistence threshold.

Box 2. Plant epidemic with density independence

The solution to the model for a plant epidemic in equation 1 when S is replaced by a constant, S_0, is given by

$$E(t) = P_0C_0\left(C_4e^{\lambda_1 t} + C_5e^{\lambda_2 t} + e^{\lambda_3 t}\right)$$
$$I(t) = P_0C_0\left(C_1e^{\lambda_1 t} + C_2e^{\lambda_2 t} + C_3e^{\lambda_3 t}\right)$$
$$R(t) = P_0C_0\gamma\left(\frac{C_1}{\lambda_1}(e^{\lambda_1 t}-1) + \frac{C_2}{\lambda_2}(e^{\lambda_2 t}-1) + \frac{C_3}{\lambda_3}(e^{\lambda_3 t}-1)\right) \tag{2}$$
$$P(t) = P_0e^{\lambda_3 t}$$

in which C_0 to C_5 and λs are constants, defined by

$$C_0 = \upsilon\left(\sigma + \lambda_3 - \beta S_0\frac{\sigma}{\gamma + \lambda_3}\right)^{-1}$$
$$C_1 = -\frac{(\sigma+\lambda_1)(\sigma+\lambda_2)}{\beta S_0(\lambda_2-\lambda_1)} + \frac{\sigma(\sigma+\lambda_1)}{(\lambda_2-\lambda_1)(\gamma+\lambda_3)}$$
$$C_2 = \frac{(\sigma+\lambda_1)(\sigma+\lambda_2)}{\beta S_0(\lambda_2-\lambda_1)} - \frac{\sigma(\sigma+\lambda_2)}{(\lambda_2-\lambda_1)(\gamma+\lambda_3)}$$
$$C_3 = \frac{\sigma}{\gamma+\lambda_3}$$
$$C_4 = \frac{\sigma\beta S_0}{(\lambda_2-\lambda_1)(\gamma+\lambda_3)} - \frac{\sigma+\lambda_2}{\lambda_2-\lambda_1}$$
$$C_5 = \frac{\sigma+\lambda_1}{\lambda_2-\lambda_1} - \frac{\sigma\beta S_0}{(\lambda_2-\lambda_1)(\gamma+\lambda_3)}$$
$$\lambda_{1,2} = -½(\sigma+\gamma) \mp ½\sqrt{(\sigma+\gamma)^2 - 4\sigma(\gamma-\beta S_0)}$$
$$\lambda_3 = -(\upsilon' + \mu_g)\,.$$

The original parameters are defined in the text and in Box 1. The amount of inoculum produced by the diseased individual in the three states (i.e., the κs) is calculated by setting $t = T_g$ in equation 2 and multiplying by the appropriate θs (e.g., $\kappa_I = \theta_I I(T_g^-)$). If the more general expression for κ_R is used, substitute exp $\lambda_*(T_g - T_1)$ for each 1 in the expression for $R(t)$ (in which the "$*$" subscript represents 1, 2, or 3), and then multiply by θ_R.

Persistence of disease over multiple growing seasons

Although *Q* can indicate short-term behavior of the process (e.g., between the first and second seasons), it does not necessarily indicate long-term dynamics. To determine persistence formally, we assume that the epidemic in the first season starts from a small (infinitesimal) P_0 so that the introduced inoculum or the inoculum produced by *I* individuals does not contact a diseased individual during the epidemic. This assumption is reasonable in practice, because it is unlikely that a large amount of inoculum, relative to the size of the crop, would be introduced accidentally or deliberately. With this assumption, there is in effect no limitation to the increase in diseased individuals, and the variable *S* is replaced by the constant S_0 in equation 1. This results in the elimination of the equation for *S*. The equations can be solved analytically for *E, I, R*, and *P*. Results are shown as equation 2 in Box 2.

Basic reproduction number. With the density-independence assumption we use the term Q_0 for *Q* and express it here as

$$Q_0 = [(\kappa_P + \kappa_I + \kappa_E + \kappa_R)\varepsilon]/P_0. \tag{3}$$

Q_0 is defined as the mean number of *P* individuals at the start of the *next* season resulting from each *P* at the start of the *present* season when an infinitesimal amount of *P* is introduced into a pathogen-free and disease-free crop. Although Q_0 is a measure of persistence, it is not necessarily equal to a multiseason basic reproduction number because—for pathogen inoculum with a low mortality rate—a portion of the introduced inoculum in the present season can survive until the next (or later seasons), and infections from this initial inoculum can then occur over more than 1 year. A new multiseason R_0 can be determined using the following argument.

When P_0 units of inoculum are introduced at the start of season 1, there are $(\kappa_I + \kappa_E + \kappa_R)\varepsilon$ new *P* individuals at the start of season 2, and $\kappa_P\varepsilon$ old (i.e., original) *P* individuals remaining. These old *P* individuals at the start of season 2 result in $(\kappa_P\varepsilon)[(\kappa_I + \kappa_E + \kappa_R)/P_0]\varepsilon$ new *P* individuals at the start of season 3, with $\kappa_P\varepsilon(\kappa_P/P_0)\varepsilon$ old *P* individuals still remaining, which can result in new *P* individuals at the start of season 4. If one sums over all seasons the number of new infections that result only directly from the original P_0 individuals, and then divides by P_0, one obtains the basic reproduction number. After some algebra, R_0 can be written as

$$R_0 = \frac{(\kappa_I + \kappa_E + \kappa_R)\varepsilon}{P_0\left(1 - (\kappa_P\varepsilon/P_0)\right)} = \frac{Q_0 - (\kappa_P\varepsilon/P_0)}{1 - ((\kappa_P\varepsilon/P_0))} \tag{4}$$

which can be defined as the mean number of P individuals resulting from each P individual during its entire "lifetime" when an infinitesimal amount of P is introduced into a pathogen-free and disease-free crop. R_0 will be greater than or equal to Q_0 whenever Q_0 is greater than or equal to 1. It can be shown that the two terms will be equal when there is high mortality (i.e., when $\kappa_P = 0$, so that there is no surviving inoculum at the end of the season) or when $R_0 = 1$. As with Q_0, R_0 can be calculated for any set of reasonable epidemic parameter values without a numerical solution to equation 1.

The necessary condition for persistence (of the pathogen or disease) over multiple seasons is an R_0 greater than or equal to 1. A key result is that even if a large amount of inoculum is introduced, so that disease dynamics can be accurately described only by the density-*dependent* model (equation 1), R_0 as defined in equation 4 is still the correct predictor of persistence. A heuristic argument explains this conclusion. Suppose R_0 (or Q_0) is less than 1, and recall that Q_0 is equal to or greater than Q (by definition); thus, Q also is less than 1 in this situation. P_0 at the start of season 2 will be less than P_0 at the start of season 1, even if a large amount of inoculum is introduced and all (or nearly all) plant individuals become diseased by the end of the season. P_0 declines each season until eventually it is low enough for the density-independent model to hold (with the solution in equation 2). Then, P_0 at the start of subsequent seasons is directly determined from $P_0(Q_0)^\eta$, in which η is the season number beginning when density-independence holds.

Now consider a situation in which a large amount of inoculum is introduced, Q is less than 1, but R_0 is greater than 1. In this case, P_0 initially declines for a number of seasons (because $Q < 1$) until inoculum is low enough that the density-independent model (equation 2) holds. However, the disease does not go extinct because—at low inoculum levels—each unit of inoculum produces more than one new unit of inoculum (because R_0 [or Q_0] > 1).

Thresholds for persistence. To determine the conditions necessary for persistence or no persistence, one can solve equation 4 for the parameter values that give $R_0 = 1$. This is demonstrated in Figure 3 for situations in which plant individuals in the I and R states contribute to inoculum production at the end of the season. Persistence occurs whenever the parameter values for a given disease lie above the appropriate curve. Although the basic reproduction number for continuous "season-less" crops ($\beta S_0/\gamma$) must be greater than 1 for persistence with pure contagious (secondary-infection-only) epidemics, $\beta S_0/\gamma$ can be considerably less than 1 and the disease and pathogen will still persist over multiple seasons. This will happen if inoculum mortality (μ_b, μ_g) is low, the production of P from infected plant individuals (i.e., θs) is high, or, for diseases with both primary and secondary infections, the primary infection rate (υS_0) is moderate to high. For instance, consider Figure 3c, which represents a disease with low inoculum mortality during and between seasons. When there are 10 P individuals (units of inoculum) produced per infectious and removed diseased plant at the end of the growing season (i.e., $\theta = 10$), persistence will occur at a low primary infection rate of $\upsilon S_0 = 0.002$ per day when $\beta S_0/\gamma$ is greater than 0.62. When υS_0 is increased to 0.005 per day, persistence will occur with $\beta S_0/\gamma = 0$ (i.e., no secondary infections during the season are required). At higher

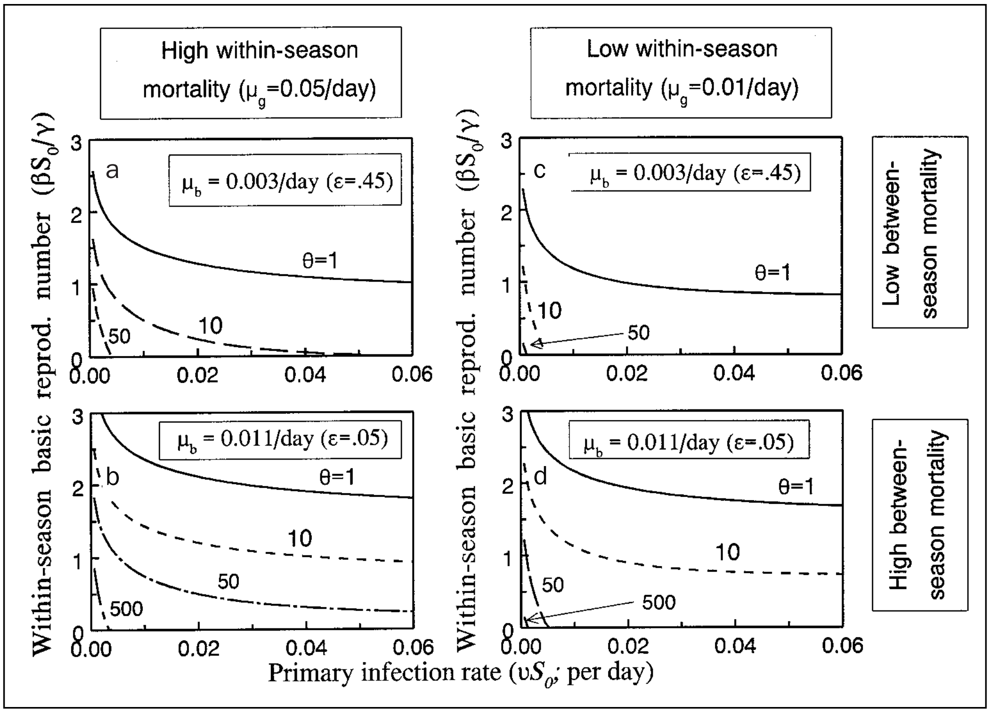

Figure 3. Parameter values of the plant epidemic model that produce a multiseason basic reproduction number (R$_0$; equation 4) of 1. For all graphs, the growing season is 100 days, mean latent period is 7 days, the per-unit production of inoculum is the same for infectious and removed diseased individuals (labeled simply as θ), and latently infected plant individuals do not produce new inoculum. Disease and pathogen persistence occur when the primary infection rate, υS_0, and the within-season basic reproduction number, $\beta S_0/\gamma$, are above the curve for the indicated θ and other parameters given above or within the panels. The panels on the left and right correspond to two different values of the within-season inoculum mortality rate (μ_g); the upper and lower panels correspond to two different values of the between-season mortality rate (μ_b).

θ (e.g., $\theta = 50$) for these same inoculum mortality conditions (Figure 3c), almost any positive value of primary infection rate and $\beta S_0/\gamma$ will result in persistence because so much inoculum is produced per infected plant individual. On the other hand, at a low θ value (e.g., $\theta = 1$), persistence will still occur at $\beta S_0/\gamma < 1$ if the primary infection rate is high enough ($\upsilon S_0 > 0.02$ per day, a high value). Even for pure contagious (secondary-infection-only) epidemics, persistence can occur when $\beta S_0/\gamma < 1$.

With high inoculum mortality within and between seasons, as shown in Figure 3b, persistence can also occur at $\beta S_0 / \gamma < 1$, but only if the per-unit production of inoculum (θ) and primary infection rate (υS_0) are high. For example, at $\theta = 50$, persistence occurs at $\upsilon S_0 = 0.01$ per day (a high value) and $\beta S_0/\gamma > 0.74$. These persistence situations with low $\beta S_0/\gamma$ represent crop diseases, typical of those caused by soilborne pathogens, that manifest relatively little increase in the number of diseased individuals the first year after a pathogen is introduced and then a gradual increase in diseased individuals each year as inoculum builds up (Hall 1996); the same pattern of gradual increase holds for crops planted in areas where P is initially low.

Conversely, $\beta S_0/\gamma$ may need to be considerably above 1 for persistence (Figure 3), especially if the primary infection rate (υS_0) is low, production of inoculum from diseased individuals is low, between-season mortality (μ_b) of inoculum is high, or within-season mortality of inoculum (μ_g) is high (so that little inoculum survives until the next season). Likewise, for pure contagious epidemics, $\beta S_0/\gamma$ may also need to be considerably above 1 for persistence if only a small number of plant individuals become infected per unit of inoculum (ϕS_0; see Box 1). For instance, persistence will occur at $\theta = 1$ and $\upsilon S_0 = 0.006$/day only if $\beta S_0/\gamma$ is greater than 2.5 (Figure 3b). With 10 times as much inoculum produced at the end of the season (i.e., $\theta = 10$) and other conditions unchanged, persistence will occur if $\beta S_0/\gamma$ is more than 1.7. For pure contagious epidemics, a value of $\beta S_0/\gamma$ greater than 1 generally will be required for persistence if the number of new plant infections at the beginning of a season per unit of inoculum (ϕS_0; see Box 1) is less than 0.01 and θ is low. These persistence situations with high $\beta S_0/\gamma$ would correspond to many foliar diseases with a rapid increase in the number of infected individuals during the season but little inoculum survival without the host (Zadoks 1961). Latent period ($1/\sigma$) has no influence on persistence for a continuous, seasonless crop because all latently infected individuals eventually become infectious (in the model), but the latent period can have a large influence on persistence in a multiseason situation when $\theta_E = 0$. This is because not all infected individuals will necessarily be infectious by the end of each season, and thus not all infected individuals will produce inoculum.

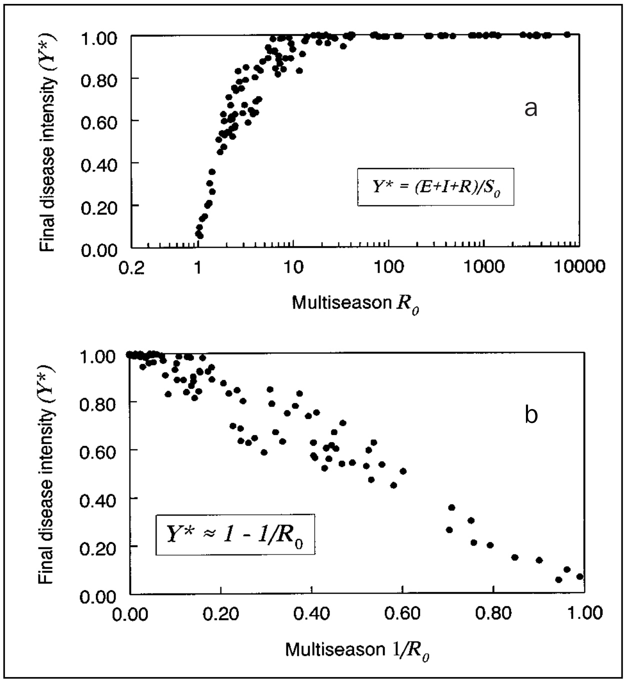

Figure 4. The seasonally recurrent value of the fraction of infected plant individuals at the end of each season (Y*)—after the epidemic has settled into a fixed within-season pattern—based on the numerical solutions of density-dependent equation 1, in relation to (a) the multiseason basic reproduction number (R_0; equation 4) or to (b) the inverse of R_0. Solutions were obtained for a wide range of parameter values, with a growing season of 100 days in all cases. Length of the growing season may affect the exact results, but not the basic relationship.

Density dependence. Although R_0 (equation 4) is a measure of disease persistence in the density-*independent* situation, we found that it can be used to calculate numerically the seasonally recurrent state of total disease at the end of the season, $Y^* = Y(T_g^-)/S_0$, for the density-*dependent* model (equation 1) when R_0 is fixed (Figure 4). This relationship for the seasonally recurrent state in Figure 4 is not exact, but it can be described approximately by $Y^* = 1 - (R_0)^{-1}$ for $R_0 > 1$. At $R_0 < 1$, Y^* goes to 0 within a few seasons, because there is less inoculum each year than in the previous year. The relationship between Y^* and R_0 is not calculated from equation 1, but is based on calculating R_0 from equation 4 and calculating Y^* from the numerical solutions of equation 1. Y^* can be considered as a steady state. For a 100-day annual crop epidemic, Y^* is predicted to be 0.5 when $R_0 = 2$, and 0.9 when $R_0 = 10$. This can be seen in Figure 2b as the final value of Y for each season for one set of parameter conditions. Interestingly, R_0 does not predict the seasonally recurrent state of P_0 at the start of each season for the density-dependent model; a large R_0, for instance, can be associated with a large or small (but nonzero) value of P_0. Although the time required to reach Y^* has not been determined analytically, it was generally considerably less than 10 seasons (Figure 2b).

Implications

Many factors determine whether a pathogen introduced deliberately or accidentally will be a successful invader, survive between seasons, and ultimately persist (Yang et al. 1991, Schaad et al. 1999). Classic epidemiological theory can be used to predict invasion and persistence for situations in which there is no interruption of disease development by harvesting or other externally imposed condition (Vanderplank 1963, Anderson and May 1990, Campbell and Madden 1990, Jeger and van den Bosch 1994). We have expanded on this theory by explicitly considering disease in annual crops over multiple seasons, and we have presented a conceptual framework to determine which combinations of within-season and between-season population characteristics will lead to persistence in annual crops. This framework fits into the epidemiological surveillance program for human, animal, and crop diseases advocated by Wheelis (1992) to strengthen biological weapons control efforts; it can constitute the first step in a comprehensive evaluation, or risk assessment, of threatening pathogens (MacKenzie 1999, Schaad et al. 1999). In particular, one could ultimately replace the subjective weighting of some pathogenic traits with the multiseason basic reproduction number (R_0 [equation 4]) in scoring systems (Schaad et al. 1999) used to determine the most threatening pathogens of crops. Additionally, one can use graphs such as Figure 3 to determine whether persistence is likely for a given threatening pathogen under a range of scenarios summarized by model parameters.

As Figure 3 shows, more than one set of pathogenic or disease traits can lead to persistence and high disease intensity. Rust diseases, which have traditionally been considered and developed as bioweapons (Whitby and Rogers 1997, Rogers et al. 1999), have high within-season basic reproduction number ($\beta S_0/\gamma$) values (Vanderplank 1963), leading to high disease intensities (Ys) in a single season. Such a pathogen could have a major economic impact during the year of its introduction, but without overwintering hosts its between-season survival may be very low (because of low ε or high μ_b), leading to extinction locally; thus, this type of introduced rust disease is unlikely to cause long-term economic problems unless pathogen inoculum is reintroduced yearly. It should be emphasized that $\beta S_0/\gamma$ and other parameters (and hence R_0) are heavily dependent on the environment (Vanderplank 1963, Campbell and Madden 1990). Therefore—even for diseases with very high within-season rates of increase (potato late blight, stem rust of wheat)—those rates may be low or very low during many other years, resulting in R_0 being less than 1.

On the other hand, pathogens with low mortality in the absence of the host, or with a wide range of alternate perennial hosts, could persist even when disease development within growing seasons is quite limited. An example is the soil-borne fungus *Fusarium oxysporum*, which has been considered as a biological agent for killing narcotic poppy, the source of opium (Connick et al. 1998). This species also has been extensively studied as a mycoherbicide for narcotic coca and marijuana (Kleiner 1999). *Fusarium oxysporum* is a soil-borne pathogen that causes a plant wilt, and there is little if any secondary spread of disease between plants; an increase in disease within a growing season is mostly due to primary infections. However, many *Fusarium* species can readily survive in the soil between growing seasons, which could result in a high multiseason R_0. The introduction of such a pathogen may not cause large direct economic losses in a single year unless a very large amount of inoculum has been introduced into a crop, in which case substantial efforts would have to be made to reduce the amount of surviving inoculum and prevent persistence.

Another example of a disease without secondary infection during the growing season but with low mortality rates between seasons is bunt, or covered smut of wheat, caused by two fungi, *Tilletia tritici* and *T. laevis*. It is now known that Iraq was working to develop these pathogens as anticrop weapons (Whitby and Rogers 1997). Other plant pathogens may exhibit a combination of moderate $\beta S_0/\gamma$, primary infection rate, and between-season survival, resulting in R_0 greater than 1 if environmental conditions are favorable. One possible example is another pathogen considered for killing poppy (Bailey et al. 2000), *Pleospora papaveracea*, which is characterized in a limited number of studies (so far) by a moderate increase in disease within a growing season and in spore survival between seasons.

The advantage of the modeling approach discussed in this article is that order-of-magnitude estimates are available for most of the model parameters for many diseases being assessed (and others related to them); if they are not known, the parameters can be indirectly estimated from other known population terms, such as the intrinsic rate of increase (r) for selected diseases (Campbell and Madden 1990, Madden et al. 2000). With these parameter estimates, R_0 can be calculated (equation 4) and used to predict persistence. When persistence is expected ($R_0 > 1$), the relationship between the seasonally recurrent fraction of infected plants (Y^*) and R_0 (Figure 4) can be very informative in predicting the seriousness of the disease threat. When Y^* is expected to be high, disease control strategies can be developed by focusing on altering the epidemic components that determine R_0 (e.g., primary and secondary infection rates, inoculum survival). However, much more precise parameter estimates will be needed if specific predictions about final epidemic outcomes are desired. The modeling work here also shows that one weakness in our knowledge of polyetic diseases (Zadoks 1999) concerns the production of new overwintering inoculum from diseased individuals (the κ functions and corresponding θ terms). Field experimentation is urgently needed to provide estimates of the θ terms or to demonstrate that more complicated functional relationships need to be considered. The model can be augmented in various ways for greater realism; crop growth during the growing season (Gubbins and Gilligan 1997) can be incorporated, for example, as well as metapopulation dynamics, heterogeneity, and expansion of disease foci through spore dispersal.

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