Annu. Rev. Phytopathol. 2002. 40:349–79
doi: 10.1146/annurev.phyto.40.120501.101443


# PATHOGEN POPULATION GENETICS, EVOLUTIONARY POTENTIAL, AND DURABLE RESISTANCE

Bruce A. McDonald and Celeste Linde
*Institute of Plant Sciences, Plant Pathology Group, Federal Institute of Technology, ETH-Zentrum, LFW, CH-8092 Zürich, Switzerland;*
*e-mail: bruce.mcdonald@ipw.agrl.ethz.ch; celeste.linde@ipw.agrl.ethz.ch*

**Key Words** risk assessment, quantitative resistance, major gene resistance

■ **Abstract** We hypothesize that the evolutionary potential of a pathogen population is reflected in its population genetic structure. Pathogen populations with a high evolutionary potential are more likely to overcome genetic resistance than pathogen populations with a low evolutionary potential. We propose a flexible framework to predict the evolutionary potential of pathogen populations based on analysis of their genetic structure. According to this framework, pathogens that pose the greatest risk of breaking down resistance genes have a mixed reproduction system, a high potential for genotype flow, large effective population sizes, and high mutation rates. The lowest risk pathogens are those with strict asexual reproduction, low potential for gene flow, small effective population sizes, and low mutation rates. We present examples of high-risk and low-risk pathogens. We propose general guidelines for a rational approach to breed durable resistance according to the evolutionary potential of the pathogen.



## INTRODUCTION

Our primary aim in this chapter is to illustrate how principles of population genetics can be applied to guide resistance-breeding strategies. Though the focus will be on plant genetic resistance, these principles should also be relevant for management of fungicides and antibiotics in agroecosystems. A secondary goal in this paper is to develop a flexible framework in which to consider the population genetics of plant pathogens and then relate that framework to the "risk" of pathogen evolution. This framework may prove useful for many aspects of risk assessment related to pathogen-plant interactions, including release of genetically engineered plants and microorganisms. Our final goal is to illustrate how this framework may be used to develop resistance-breeding strategies that aim to attain durable disease resistance.

An important theme running through this paper is the concept of the genetic structure of populations. We define genetic structure as the amount and distribution of genetic variation within and among populations. Genetic structure is a

consequence of interactions among the five forces that affect the evolution of populations. The genetic structure of a population is determined by the evolutionary history of that population. Thus, knowledge of genetic structure gives insight into the evolutionary processes that shaped a population in the past. We hypothesize that knowledge of genetic structure also offers insight into the future evolutionary potential of pathogen populations. We propose that pathogens with the greatest evolutionary potential pose the greatest "risk" of circumventing the effects ("breaking down") of major resistance genes or evolving to counteract other control methods such as applications of fungicides or antibiotics. Knowledge of the evolutionary potential of pathogens may prove useful to optimize the management of resistance genes, fungicides, and antibiotics to maximize their useful life expectancy and minimize the losses that result from loss in efficacy of these control methods (90).

Plant pathologists have witnessed changes in pathogen populations many times over the nearly hundred years since Biffen first described the Mendelian inheritance of disease resistance (4). The most dramatic changes were those that accompanied the breakdown of major resistance genes. Boom-and-bust cycles have been documented most thoroughly with regards to cereal rusts [e.g., (64, 84)] and powdery mildews of cereals [e.g., (11, 136)] that exhibit a gene-for-gene interaction with their hosts (28). In the majority of these cases, a single resistance gene with large effect became widely distributed over a large geographical area (the "boom"). The pathogen population adapted to the presence of a major resistance gene by evolving a new population that could overcome this resistance gene (the "bust"). In these cases, the "breakdown" of genetic resistance was due to the evolution of the local pathogen population because of selection for mutants, recombinants, or immigrants that were better adapted to the resistant cultivar.

In our current understanding of the gene-for-gene interaction, pathogens produce elicitor molecules that are recognized by specific receptors in the plant. When a plant cell receptor recognizes a pathogen elicitor, a defense response is activated that often leads to the death of the infected plant cell and inhibition of the pathogen. Mutations from avirulence to virulence in the pathogen lead to a change in the elicitor, or failure to produce the elicitor at all, that causes nonrecognition by the host receptor. Under this gene-for-gene model, a breakdown in resistance is due to an increase in the frequency of pathogen strains that harbor a mutation from avirulence to virulence. Virulent mutants increase in frequency because host defense systems are not activated early enough to prevent infection and subsequent pathogen reproduction. After selection drives the virulence mutation to a high frequency in the pathogen population, the resistance gene is no longer effective, and we say that its resistance is "broken." Gene-for-gene resistance is often called major-gene resistance or pathotype-specific resistance because its effects are large and effective only against the portion of the pathogen population that produces the elicitor.

Resistance in plants can also be due to other types of genetically encoded products, such as preformed phytoalexins, chemical or physical barriers, PR-proteins, hydrolytic enzymes such as chitinases, and modifiers of host defense responses. We consider it likely that the individual actions of these genes are on

average small and additive, leading to a quantitative resistance response that differs in inheritance and in mode of action from a gene-for-gene interaction. These quantitative responses are sometimes called quantitative resistance, minor-gene resistance, or partial resistance, and they generally do not follow the gene-for-gene pattern of the boom-and-bust cycle. Quantitative resistance rarely provides the total resistance observed in major gene resistance, but it tends to be effective against all strains of a pathogen population, even those that do not produce elicitors. We believe that the population genetic processes described in this chapter also apply to genes governing quantitative resistance, though they may not be as easy to recognize.

To understand the process that leads to breakdown of a resistance gene, we need to understand the processes that govern pathogen evolution. In the next section we briefly illustrate how the five evolutionary forces operate to affect the durability of major gene resistance and quantitative resistance. Then we develop a quantitative framework that can be used to evaluate the risk that a pathogen will evolve to overcome major resistance genes. Finally, we use this framework to propose breeding strategies that we consider most likely to break the boom-and-bust cycle and lead to durable resistance.



## THE FIVE EVOLUTIONARY FORCES AND THE RISK OF PATHOGEN EVOLUTION

Genetic structure refers to the amount and distribution of genetic diversity within and among populations. It is useful to differentiate between the two types of genetic diversity that contribute to genetic structure: gene diversity and genotype diversity. Gene diversity refers to the number and frequencies of alleles at individual loci in a population. Gene diversity increases as the number of alleles increases and the relative frequencies of those alleles become more equal. Genotype diversity refers to the number and frequencies of multilocus genotypes, or genetically distinct individuals, in a population. Genotype diversity is an important concept for plant pathogens that have a significant component of asexual reproduction in their life history.

### Mutation

Mutation is the ultimate source of genetic variation, directly leading to changes in the DNA sequence of individual genes and thus creating new alleles in populations. Mutation is the process that creates new virulent strains of plant pathogens that break major gene resistance. Mutation also creates strains with increased pathogenicity that can erode quantitative resistance. Under our current understanding of the gene-for-gene interaction, a mutation in the avirulence allele, which encodes the elicitor recognized by a resistance gene, is needed to create a virulent pathogen strain. Mutations from avirulence to virulence are rare and operating in

isolation would not cause a breakdown in resistance. However, when mutation is coupled with directional selection (i.e., deployment of a resistance gene), virulent mutants increase in frequency rapidly and cause a resistance gene to lose its effectiveness. Mutation rates are generally low, though they can differ among loci and pathogens (29, 141). Mutation is likely to be especially important for pathogens such as bacteria and viruses that exist as extremely large populations within individual plants. These large population sizes make it more likely that new mutants with higher fitness will emerge within a host, be able to multiply within the infected host, and spread to new, uninfected hosts before the mutation is lost through genetic drift. In our risk model, pathogens with high mutation rates present a greater risk than pathogens with low mutation rates because a high mutation rate increases the likelihood that the mutation from avirulence to virulence or from low to high pathogenicity will be present in a pathogen population. For example, pathogen populations with active transposable elements may exhibit higher mutation rates than populations without active transposons (33a, 69a, 84a). Though it is difficult to imagine how a disease management program could reduce mutation rates and thus limit the creation of new alleles, any activity that slows the movement of active transposable elements or genome rearrangements among populations could potentially affect overall mutation rates for a pathogen species.

## Population Size and Random Genetic Drift

Population size affects the probability that mutants will be present, and it can influence the diversity of genes in a population through a process called random genetic drift. Large populations have more mutants than small populations because mutation rates are generally low. For example, with a mutation rate of $10^{-5}$, a population with $10^6$ individuals is expected to have 10 mutants, and a population with $10^8$ individuals is expected to have 1000 mutants. In small populations, genetic drift leads to a loss of alleles over time. In our risk assessment model, pathogens with large population sizes have greater evolutionary potential than pathogens with small population sizes. Pathogens that undergo regular, severe reductions in population size (bottlenecks), e.g., as a result of crop rotations or annual climatic extremes that kill the majority of individuals, are less diverse and slower to adapt than populations that maintain a high population size year round. Any disease management program that keeps pathogen population sizes small assists control by limiting the gene diversity in the pathogen population [for examples, see (78)].

## Gene and Genotype Flow

Gene flow is a process in which particular alleles (genes) or individuals (genotypes) are exchanged among geographically separated populations. For strictly asexual organisms that do not recombine genes, entire genotypes can be exchanged among populations. We refer to this process as genotype flow. Gene/genotype flow is the process that moves virulent mutant alleles and genotypes among different field populations. Pathogens that exhibit a high degree of gene/genotype flow

are expected to have greater genetic diversity than pathogens with low degrees of gene/genotype flow because high gene/genotype flow increases the effective population size by increasing the size of the genetic neighborhood. Pathogens that produce propagules with the potential for long-distance dispersal, such as rust- and powdery mildew fungi, tend to have large genetic neighborhoods, which may encompass entire continents (e.g., the *Puccinia* pathway in North America). Pathogens with propagules that move only short distances may exist in relatively small genetic neighborhoods, which may encompass only one field or even one section in a field (e.g., nematodes). The size of the genetic neighborhood can be affected by anthropogenic activities. Humans can move many pathogens far beyond their natural dispersal limits through agricultural practices and intercontinental travel and commerce. Thus, the actual degree of gene/genotype flow may be much higher than expected based on life history traits.

Our risk model proposes that pathogens with high gene/genotype flow pose a greater risk than pathogens with low gene/genotype flow. We hypothesize further that gene flow involving asexual propagules (genotype flow) poses a higher risk than movement of sexual propagules (gene flow) because the asexual propagule represents a linked package of coadapted alleles that has already been selected. Any disease management tactic that limits movements of genes and genotypes among pathogen populations limits the spread of mutant alleles and genotypes [for examples, see (78)].

## Reproduction and Mating System

Reproduction and mating systems affect how gene diversity is distributed within and among individuals in a population. Reproduction can be sexual, asexual, or mixed. Mating system is relevant only to the sexual component of reproduction, and can vary from strict inbreeding to obligate outcrossing (Figure 1). In asexual pathogens, measures of genotype diversity are more meaningful than measures of gene diversity because most of the genetic diversity is distributed among clonal lineages. Populations of sexual pathogens usually exhibit a high degree of genotype diversity, so measures of gene diversity are needed to compare the amount of genetic diversity in different populations. Our risk model hypothesizes that pathogens undergoing regular recombination (this can include bacterial conjugation, recombination between viral genomes in plants with mixed infections, and hyphal anastomosis and/or parasexual recombination in fungi) pose greater risks than pathogens that undergo no or little recombination. A recombining pathogen population can put together new combinations of virulence alleles as rapidly as breeders can recombine resistance genes. For this reason, resistance gene pyramids may not be an effective long-term breeding strategy against pathogens that undergo regular recombination. We propose that pathogens that outcross pose a greater risk than inbreeding pathogens because more new genotypes are created through outcrossing. Disease management strategies that prevent the occurrence of sexual reproduction assist with control [for examples, see (78)].

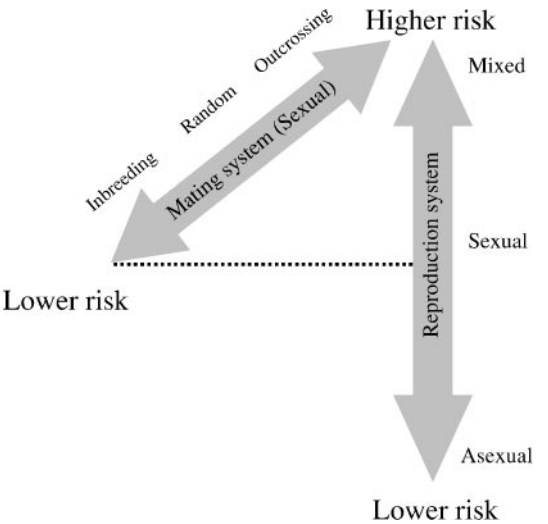



**Figure 1** The interaction between mating system and reproduction system in determining the evolutionary potential of a pathogen population.



We hypothesize that pathogens with mixed reproduction systems pose the highest risk of evolution. During the sexual cycle, many new combinations of alleles (genotypes) are created through recombination. These recombined genotypes can be "tested" in different environments, which may include new resistance genes, fungicides, or antibiotics. Combinations of alleles (genotypes) that are most fit are held together through asexual reproduction and may increase to a high frequency in selected clones. The spatial and temporal distribution of clones or clonal lineages within and among populations will depend mainly on the dispersal potential of the asexual propagules. If the asexual spore or propagule is capable of long-distance dispersal, then the clone(s) with highest fitness can become distributed over a wide area through genotype flow, causing an epidemic. This process of testing recombinants and amplifying selected genotypes occurs for many rust and powdery mildew fungi. If the asexual propagule has limited dispersal potential, then the most damaging clones may be limited to a hot-spot that is only a few meters in diameter in a field. This may occur for sexual pathogens with splash-dispersed conidia such as *Mycosphaerella graminicola* (80) and *Phaeosphaeria nodorum* (82) on wheat and possibly *Rhynchosporium secalis* (110) on barley.

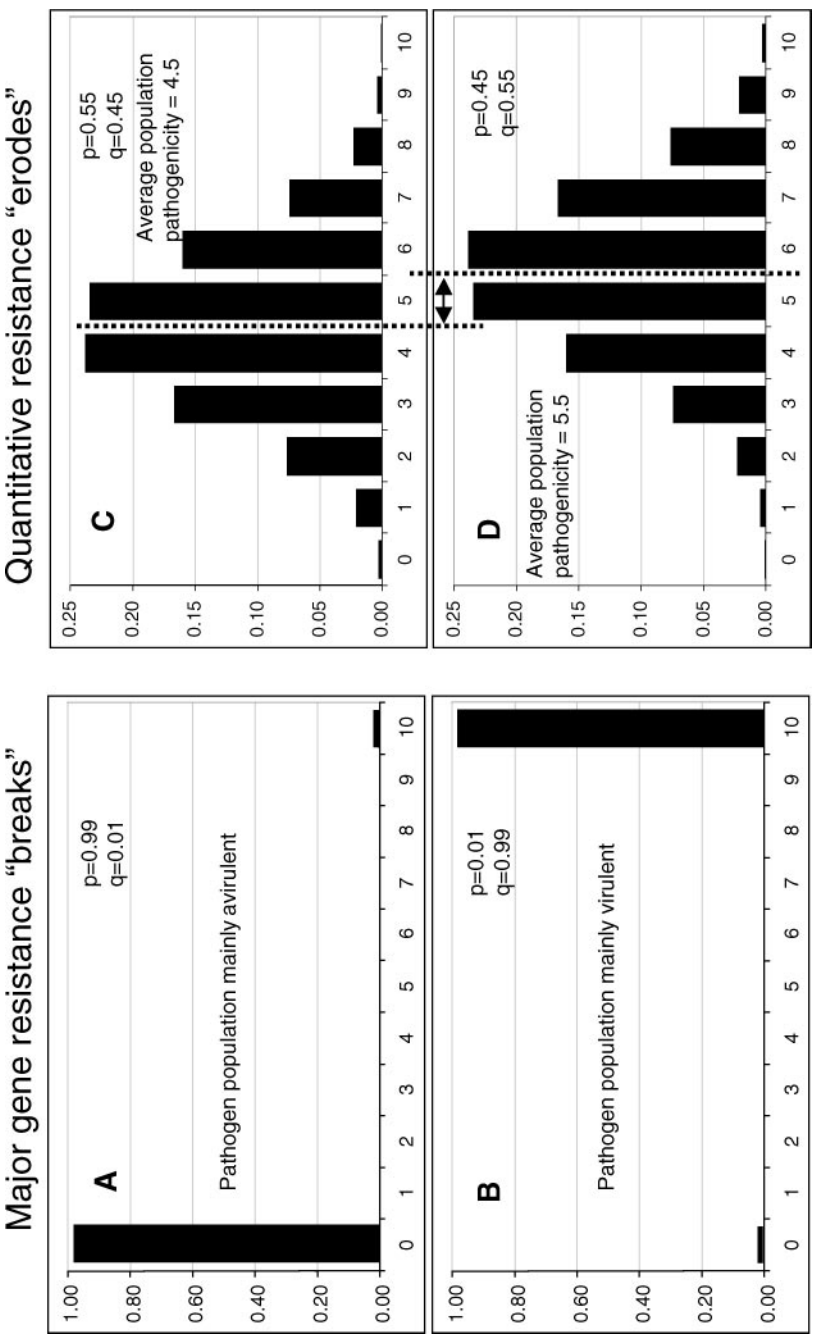
## Selection Imposed by Major Gene Resistance and Quantitative Resistance

Selection is the main force that drives changes in frequencies of mutant alleles. Directional selection occurs when a major resistance gene (encoded by a receptor) becomes widely distributed over a large geographical area. This leads to an increase

in frequency of the virulent mutant that has lost the elicitor (avirulence allele) until the major resistance gene is broken. The many examples of broken major gene resistance offer abundant evidence that selection is efficient in agricultural ecosystems that are based on monoculture and genetic uniformity. There are several possibilities for deploying major gene resistance that can change the way that selection operates on a pathogen population (78) (Figure 2). The most common alternative is to pyramid several major resistance genes into a single cultivar in the hope that the pathogen will not be able to undergo a sequence of mutations corresponding to each resistance gene. Another option is to generate disruptive selection by rotating major gene resistance through time and space or by growing mixtures of cultivars with different resistance genes. These strategies disrupt directional selection by favoring different mutant alleles or genotypes at different times and places, reducing the rate at which the mutant allele or genotype increases in frequency. Gene rotations and mixtures have not been widely exploited in modern agroecosystems, though some preliminary attempts show great promise [e.g., (140)].

Quantitative resistance is another option that plant breeders can utilize to obtain resistant cultivars. One hallmark of quantitative resistance is that it does not exhibit the boom-and-bust cycle characteristic of major resistance genes. It appears likely that this is because quantitative resistance is not based on receptor-elicitor recognition and thus appears to work equally across all pathogen strains. Because quantitative resistance is sensitive to environmental conditions, it can be difficult to determine if pathogen strains differ in their degree of pathogenicity on the same quantitatively resistant cultivar. We consider it likely that pathogen populations also evolve to overcome quantitative resistance in agroecosystems. However, because the nature of this evolution differs from evolution against major gene resistance, it is more difficult to detect and is better characterized as a process of "erosion" rather than as a process of breakdown (Figure 3). The erosion of quantitative resistance is more difficult to observe because corresponding pathogen populations can display a distribution of pathogenicity that may vary considerably from year to year as a result of the strong genotype-by-environment interactions that occur for quantitative characters in both plant and pathogen.

To illustrate the difficulty of detecting erosion of quantitative resistance, we developed a model where resistance was due to five unlinked genes with equal and additive effects (see Supplementary Materials on http://www.annualreviews.org/). For example, the resistance alleles could encode a combination of hydrolases (e.g., chitinases and glucanases) and/or pathogen-specific toxins (e.g., preformed chemical inhibitors or phytoalexins) that slow down or prevent infection by the pathogen. The diploid pathogen in the model had five unlinked genes with equal and additive effects that could counteract the plant resistance genes. For example, the "pathogenicity" alleles might encode enzymes that inactivate preformed chemical inhibitors or modify the pathogen substrate targeted by hydrolases. A continuum in pathogenicity has been described in crosses with *Nectria haematococca* on peas (32) and *Ustilago hordei* (20). If the gene products in pathogen and host interact in an equal and additive manner, then the degree of damage done to the



host (equivalent to pathogenicity) is proportional to the number of pathogenicity alleles. In our model, for example, each pathogenicity allele adds 5% to the leaf area infected on the resistant host. The most aggressive strain will cover 50% of the leaf area, the least aggressive strain will cover only 5% of the leaf area, and a strain with no pathogenicity alleles cannot infect a plant with maximum quantitative resistance.

Following many cycles of pathogen reproduction and selection, the level of pathogenicity in the pathogen population will increase, and the quantitative resistance will erode (see Table, in Supplementary Materials on http://www.annualreviews.org/). However, the year-to-year change will be gradual and hard to detect because the individual strains in the pathogen population exhibit a large range of pathogenicity (Figure 3 and Figure in Supplementary Materials on http://www.annualreviews.org/). Though the erosion of quantitative resistance differs quantitatively from the breakdown of major gene resistance, we believe that the evolutionary processes (and corresponding risk assessment) described in this section apply equally to both types of resistance. Note that resistance genes can differ in the fitness consequences they impose on the corresponding mutants in pathogen populations (67). By choosing major resistance genes that have a large effect on the fitness of virulent mutants, it may be possible to extend the durability of major resistance genes. But under strong directional selection, even the most durable resistance genes may eventually break down because a new mutant or recombinant will emerge (115).

The risk model proposes that pathogen populations exposed to strong (major gene resistance), directional selection over many generations will evolve more quickly than populations that are exposed to weaker selection (quantitative resistance) or to disruptive selection imposed by temporal or spatial patterning of the selective force. Selection is the evolutionary force that is most easily manipulated by humans [e.g., (90)], and thus offers the most practical point for intervention in the evolutionary process. Agroecosystems based on widespread deployment of major gene resistance place maximum directional selection on the pathogen

←

**Figure 3** Shifts in pathogen populations associated with breakdown of major gene resistance and erosion of quantitative resistance. Panels *A* and *B* show the rapid shift from avirulence to virulence associated with breakdown of major gene resistance, where p and q represent frequencies of avirulence and virulence alleles, respectively, in the pathogen population. Differences in pathogenicity between strains that differ for avirulence and virulence are clear and virulence shifts in pathogen populations are easy to detect. Panels *C* and *D* show the erosion of resistance, characterized by a gradual increase in pathogenicity of the pathogen population toward a host with quantitative resistance, associated with a quantitative resistance model described in the text. Vertical lines indicate mean pathogenicity of populations that differ by 10% in the frequencies of five alleles responsible for pathogenicity.

**TABLE 1** Extremes of evolutionary risk posed by plant pathogens and examples of factors that affect risk assessment

| Highest risk of evolution | Lowest risk of evolution |
|---|---|
| High mutation rate | Low mutation rate |
| Transposable elements active | No transposons |
| Large effective population sizes | Small effective population sizes |
| Large overseasoning population | No overseasoning propagules |
| Extinction of local populations rare | Extinction of local populations common |
| No genetic drift, no loss of alleles | Significant genetic drift, alleles lost |
| High gene/genotype flow | Low gene/genotype flow |
| Asexual propagules dispersed by air over long distances | Asexual propagules soilborne |
| Human-mediated long-distance movement common | Quarantines effective |
| Mixed reproduction system | Asexual reproduction system |
| Annual sexual outcrossing and asexual propagules produced | Only asexual propagules produced |
| Efficient directional selection | Disruptive selection |
| R-gene deployed in genetically uniform monoculture | R-genes deployed in mixtures/multilines |
| R-gene deployed continuously over large area | R-genes deployed as rotations in time or space |



population. Agroecosystems that deploy major gene resistance in mixtures, or in rotations through time and space will reduce the efficiency of selection, or impose stabilizing or disruptive selection that can slow the rate of increase in the frequency of virulent mutants.

The individual contributions of each evolutionary factor to the risk assessment framework are summarized in Table 1. The end result of the interactions among these factors is the observed genetic structure of the pathogen population [for examples see (78)]. By using selectively neutral genetic markers and hierarchical sampling to determine the genetic structure of pathogen populations, we can begin to understand the evolutionary forces that shaped these populations, and infer the importance of the individual evolutionary factors (76).

## A MODEL FOR RISK ASSESSMENT

We propose to apply knowledge of the evolutionary forces and pathogen genetic structure to make predictions regarding the relative risks posed by different pathogens for breaking down resistance. Our hypothesis is that much of the durability of resistance genes is due to the nature of the pathogen population rather

than to the nature of the resistance gene. There will be cases where the resistance gene itself plays a key role in durability, e.g., mlo resistance in barley has been durable though *Blumeria graminis* f. sp. *hordei* has a high evolutionary potential according to our risk model (11, 136), and there is good evidence that some resistance genes impose more severe constraints on the fitness of virulent mutants than other resistance genes (67). We offer these guidelines in anticipation that the general pattern will hold true for the majority of pathogens, allowing us to rank their relative evolutionary potential and thus assess the relative risk they pose to agroecosystems. The framework we develop here can be used as a hypothesis to test against a large number of plant pathosystems. The underlying principles of the framework can be tested individually or in combination according to the available knowledge of the population genetics for any pathogen.

Figure 4 is a simplified diagram that we propose as a model framework for assessing the evolutionary risk posed by most plant pathogens. The format used to present the risk categories was inspired by a similar figure presented by Brent & Hollomon (8). Figure 4 considers only the evolutionary risk due to differences in reproduction/mating system, gene/genotype flow, and effective population size. Mutation rate was not included in this diagram because we assumed that mutation rates would be low and relatively constant across pathogens. For pathogens known to have very high mutation rates, or for bacteria and viruses where mutation is likely to play a more important role in evolution, these risk values can be increased accordingly. Selection was not included in this diagram under the assumption that selection is likely to be efficient in the genetically uniform monocultures that dominate modern agricultural ecosystems. Selection risk can be increased by increasing the land area covered to the same resistance gene, or decreased through resistance gene deployment strategies, such as gene rotations or mixtures. We expect that the population size for most pathogen populations is large, so it is likely that virulent mutants will be present and the effects of genetic drift will be small. However, we recognize that some pathogen populations have smaller effective population sizes because of a founder effect, regular bottlenecks, or short-lived overseasoning propagules. Other populations have larger effective sizes due to year-round multiplication, short latent periods, and production of long-lived overseasoning propagules. We modified the risk values we originally proposed (78) by assigning risk values of 1, 2, and 3 for effective population sizes that are small, average, and large, respectively. We also made the effects additive instead of multiplicative. This results in a range of values for each cell in the matrix (Figure 4). The proposed risk categories may need to be adjusted in many cases as a result of anthropogenic activities. For example, gene/genotype flow may be increased beyond the normal biological limits of spore dispersal by movement of inoculum or infected plant material through international commerce and travel. Any activities that reduce the effectiveness of quarantines, such as smuggling or war, may lead to an increase in gene/genotype flow. Similarly, the amount of sexual reproduction may be affected by removal of alternate hosts or by changes in cultivation or sanitation practices.

The risk values presented in Figure 4 are on a 3–9 scale. These numbers are unitless and have no specific biological meaning. The numbers attempt to provide a relative ranking of the evolutionary potential inherent in different pathogen life histories. This ranking system assumes that reproduction/mating system, gene/genotype flow, and effective population size affect evolutionary potential equally. A further assumption is that these effects are additive. As more knowledge accumulates and the hypotheses in this diagram are tested against many different pathosystems, we may learn that the forces do not contribute equally to evolutionary potential or that their effects are multiplicative rather than additive. But the proposed scale offers many possibilities for developing testable hypotheses and assigning relative evolutionary risks. For example, pathogens that have exclusively asexual reproduction and little potential for gene flow are assigned to the lowest risk category. This category includes some bacterial pathogens and the *Fusarium oxysporum* formae speciales (Figure 4). At the other extreme, pathogens that have mixed reproduction and asexual spores that are disseminated over long distances by wind are assigned to the highest risk category. This category includes pathogens such as the powdery mildew fungi. In the intermediate risk categories are pathogens that we expect to have more limited evolutionary potential as a result of lack of an asexual propagule that has high gene flow potential, or lack of regular outcrossing that produces new recombinants (Figure 4). Figure 4 hypothesizes that pathogens with regular sexual cycles will evolve faster than pathogens without recombination. It also hypothesizes that pathogens producing asexual propagules distributed over long distances will break down resistance genes faster than pathogens with short distance dispersal of asexual propagules.

## EXAMPLE PLANT PATHOSYSTEMS FIT INTO THE RISK MODEL

At this time, population genetic structure for most pathogens is unknown and accurate records of the time needed to break down resistance genes or to become resistant to fungicides and antibiotics usually cannot be gleaned from the accessible literature. To properly test the model, we will need to consider a large number of plant pathosystems to determine if the observed evolutionary rate correlates with the predicted evolutionary potential. We conducted a preliminary test of the model by combing the plant pathology literature for examples where genetic structure data were adequate to provide an estimate for expected evolutionary potential, and records of breakdown of resistance could provide an estimate for observed rate of evolution. In total, we considered 52 plant pathosystems. The 43 examples with the most complete data are shown in Table 2. Thirty-four of the pathosystems had adequate information to allow us to approximate values for four evolutionary forces using our risk model. We used Spearman rank order correlation analysis to determine the correlations between the four "expected" risk factors and the "observed" risk values for all 34 pathosystems. We found that $r_s$ was $-0.32$ ($P = 0.063$) for reproduction/mating system, 0.26 ($P = 0.141$) for

effective population size, 0.36 (P = 0.037) for mutation, and 0.26 (P = 0.141) for gene/genotype flow. All significance values were for two-tailed t-tests. When the analysis was conducted using the sum of mutation risk values and gene/genotype flow risk values, the correlation was 0.35 (P = 0.044). When the largest outlier in the correlation matrix, the nematode *Meloidogyne incognita*, was removed from the analysis, the correlation rose to 0.46 (P = 0.007). For *M. incognita*, it is possible that the actual amount of genotype flow is much higher than the predicted amount of genotype flow as a result of movement of contaminated machinery, soil, and water (J. Starr, personal communication), in which case *M. incognita* should be placed in a higher risk category. The correlation between observed and predicted risk values based on the sum of mutation and gene/genotype flow is shown in Figure 5. This preliminary analysis suggests that the contributions of the evolutionary forces may not be equal, as proposed in Figure 4. It also indicates that gene/genotype flow and mutation may be the dominant forces driving pathogen evolution in the 34 plant pathosystems we considered. However, we believe that many more example pathosystems will need to be considered before firm conclusions can be drawn. In the rest of this section, we provide a few illustrative examples.



## *Xanthomonas oryzae* pv. *oryzae* and *Xanthomonas campestris* pv. *vesicatoria*

*Xanthomonas oryzae* pv. *oryzae* reproduces clonally (89) and exhibits limited gene flow as it disperses mainly by rain splash (87), though typhoons may provide a means for long-distance movement. *Xa-3* in rice has been durable for at least 15 years (5, 85) and cultivar Nongken 58 has been resistant for at least 25 years (5). These observations agree well with the prediction of our model. Race 2 of *X. oryzae* pv. *oryzae* took only 3–4 years to increase to high frequencies after the release of cultivars having *Xa-4* in the 1970s (85). However, cultivars with *Xa-4* are still considered resistant and planted widely (5, 69). This resistance is achieved by cumulative effects of multiple QTLs, including the residual effects of the "defeated" *Xa-4* (69). These observations do not correspond with our model, suggesting that the unique properties of the *Xa-4* resistance gene may play a greater role than the biology of the pathogen in determining the durability of this resistance gene. *Xanthomonas campestris* pv. *vesicatoria* also reproduces clonally, but resistance genes in tomato and pepper are often defeated within a single growing season (49, 65, 99). In this pathogen, new pathotypes develop from loss of the plasmid carrying the avirulence gene, from inactivation of the avirulence gene, or from insertion elements that inactivate avirulence genes (65). Pyramiding defeated resistance genes *Bs1*, *Bs2*, and *Bs3* did not provide resistance, as they were defeated within the same growing season during which they were first deployed (65). Though this rapid breakdown of a resistance gene pyramid does not correspond well with expectations for an asexual organism in our model, the fact that two of the avirulence genes were on plasmids (65) increased the likelihood that multiple "mutations" to virulence could occur relatively quickly through asexual propagation.

**TABLE 2** Gene/genotype flow, reproduction/mating system, effective population size, mutation rate, and expected and observed durability of resistance for 43 plant pathosystems

| Organism | Disease | Gene/genotype flow | | Reproduction/ mating system | Effective population size | Mutation[b] | Expected risk[c] | Observed risk[d] | Selected references |
|---|---|---|---|---|---|---|---|---|---|
| | | Sexual H/M/L[a] | Asexual H/M/L[a] | | | | | | |
| *Blumeria graminis* (*Erysiphe graminis*) | Powdery mildew of barley and wheat | L | H | Mixed | Large | 1 | 10 | 5 | (11, 41, 135, 136) |
| *Bremia lactucae* | Lettuce downy mildew | L | H | Mixed | Large | 1 | 10 | 5 | (24) |
| *Cladosporium fulvum* (syn. *Fulvia fulva*) | Tomato leaf mold | — | H | Asexual | Large in greenhouses Small in fields | 1 | 6–8 | 5 | (42, 51, 55, 128) |
| *Colletotrichum graminicola* (*Glomerella graminicola*) | Sorghum and maize anthracnose stalk rot | — | M[e] | Asexual | Medium | 1 | 7 | — | (12, 92, 106) |
| *Colletotrichum lindemuthianum* | Anthracnose of beans | — | M[e] | Asexual | Medium–large | 1 | 6–7 | 5 | (94, 113, 127) |
| *Erwinia amylovora* | Fire blight of apple and pear | — | M | Asexual | Medium | 2 | 5 | — | (46) |
| *Fusarium oxysporum* f. sp. *lycopersici* | Fusarium tomato wilt | — | L | Asexual | Small | 1 | 4 | 1 | (37) |
| *Fusarium oxysporum* f. sp. *melonis* | Vascular wilt of melons | — | L | Asexual | Medium | 1 | 5 | 1 | (7, 37, 68) |
| *Fusarium oxysporum* f. sp. *cubense* | Panama disease of banana | — | L[e] | Asexual | Small | 1 | 4 | 1 | (58, 98, 116) |
| *Heterodera* spp. | Cereal cyst | L | L | Obligatory sexual | Large | 1 | 7 | — | |
| *Leptosphaeria maculans* (*Phoma lingam*) | Blackleg of oilseed rape | M | M[e] | Mixed | Small–medium, founder event | 1 | 7–8 | 5 | (13, 72, 131) |
| *Magnaportha grisea* (*Pyricularia grisea*) | Rice blast | M | H | Mostly asexual | Large | 2 | 9 | 6 | (57, 137–139) |
| *Melampsora larici-populina* | Poplar rust | M | H | Mixed | Large | 1 | 10 | 4 | (97) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *Melampsora larici-epitea* | Willow rust | M | H | Mixed | Large | 1 | 10 | 4 | (75, 96, 101) |
| *Melampsora lini* f. sp. *lini* | Flax rust | M | H | Mostly asexual | Large | 1 | 8 | 6 | (16, 28, 29) |
| *Meloidogyne incognita* | Root-knot nematode of tomato | — | L | Mitotic parthenogenic | Medium | 1 | 5 | 6 | (100, 125) |
| *Mycosphaerella fijiensis* (*Paracercospora fijiensis*) | Black sigatoka of banana | M/H | M | Mixed | Small, founder event | 1 | 7 | 4 | (19, 39, 86) |
| *Mycosphaerella graminicola* (*Septoria tritici*) | Wheat leaf blotch | M/H | M | Mixed | Large | 1 | 9 | 4 | (21, 23, 54, 80, 82) |
| *Phaeosphaeria nodorum* (*Stagonospora nodorum*) | Wheat glume blotch | H | M | Mixed | Large | 1 | 9 | — | (52, 79, 88) |
| *Phytophthora infestans* (new populations) | Potato late blight | L[e] | H | Mixed | Medium–Large | 1 | 9–10 | 5 | (14, 26, 34–36, 73, 117, 118, 129) |
| Old populations | | — | H | Asexual | Small, founder event | 1 | 6 | 5 | |
| *Phytophthora sojae* | Soybean root and stem rot | L | L | Homothallic with low outcrossing | Medium | 1 | 7 | 3 | (1, 31, 53, 108, 109, 111, 112, 126, 132) |
| *Pratylenchus* spp. | Root lesion nematodes | L | — | Obligatory sexual | Large | 1 | 7 | — | |
| *Pseudocercosporella herpotrichoides* (*Tapesia yallundae*) | Wheat eyespot | M | M | Mixed, more clonally | Medium–large | 1 | 8–10 | 3 | (50) |
| *Puccinia coronata* f. sp. *avenae*--Asexual populations | Oat rust | — | H | Asexual | Large | 1 | 8 | 5 | (2, 22, 38, 74, 93) |
| Sexual populations—alternate host present | | M | H | Mixed | Large | 1 | 10 | 5 | |
| *Puccinia graminis* f. sp. *avenae* | Stem rust of oats | — | H | Asexual (No alternate host) | Medium | 1 | 7 | 5 | (74) |
| *Puccinia graminis* f. sp. *tritici* Asexual populations | Wheat stem rust | — | H | Asexual | Medium | 1 | 7 | 5 | (15, 17, 56, 74, 104, 105) |
| Sexual populations—alternate host present | | M | H | Mixed | Large | 1 | 10 | 5 | |

(*Continued*)

**TABLE 2** (*Continued*)

| Organism | Disease | Gene/genotype flow | | Reproduction/ mating system | Effective population size | Mutation[b] | Expected risk[c] | Observed risk[d] | Selected references |
|---|---|---|---|---|---|---|---|---|---|
| | | Sexual H/M/L[a] | Asexual H/M/L[a] | | | | | | |
| *Puccinia sorghi*—Asexual populations | Common rust of maize | — | H | Asexual | Medium | 1 | 7 | 5 | (9, 43, 95) |
| *Puccinia sorghi*—alternate host present | | M | H | Mixed | Large | 1 | 10 | — | |
| *Puccinia striiformis* | Wheat stripe rust | — | H | Asexual: no alternate host | Medium | 1 | 7 | 5 | (27, 47, 48, 56, 120, 130) |
| *Puccinia triticina* (syn: *Puccinia recondita* f. sp. *tritici*)—Asexual populations | Wheat leaf rust | — | H | Asexual | Medium | 1 | 7 | 5 | (15, 18, 38, 56, 61–64, 70, 83, 84, 114) |
| Sexual populations—alternate host present | | M | H | Mixed | Large | 1 | 10 | — | |
| *Pyrenophora tritici-repentis* (*Drechslera tritici-repentis*) | Tan spot of wheat | M | M | Mixed | Large | 1 | 10 | — | (66) |
| *Rhizoctonia solani* | Rice sheath blight | L | L | Mixed? | Medium | 1 | 7 | — | (91, 107) |
| *Rhynchosporium secalis* | Barley scald | H | M | Mixed? | Medium | 1 | 8 | 5 | (40, 44, 81, 110) |
| *Sclerospora graminicola* | Downy mildew of pearl millet | M[e] | H | Mixed | Medium | 1 | 9 | 5 | (45, 123) |
| *Sclerotinia sclerotiorum* | Sclerotinia stem rot of canola | M | H | Mixed, inbreeding | Medium? | 1 | 8 | — | (60) |
| *Setosphaeria turcica* (*Exserohilum turcicum*; syn: *Helminthosporium turcicum*) | Northern corn leaf blight | M | M | Mixed | Small–large | 1 | 7–9 | 2 | (3, 6, 122) |
| *Sporisorium reilianum* | Sorghum and maize head smut | M | M | Sexual, Inbreeding | Small–medium | 1 | 6–7 | — | (124) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *Tilletia tritici* and *T. laevis* | Wheat common bunt (stinking smut) | L | H | Obligatory sexual | Large | 1 | 9 | — | (133) |
| *Ustilago hordei* | Barley smut | L | H | Obligatory sexual | Medium | 1 | 8 | — | |
| *Ustilago maydis* | Maize common smut | L | H | Obligatory sexual | Medium | 1 | 8 | — | |
| *Venturia inaequalis* (*Spilocea pomi*) | Apple scab | M | M | Mixed | Medium–large | 1 | 8–9 | 4 | (71, 103, 121, 134) |
| *Xanthomonas campestris* pv. *vesicatoria* | Bacterial spot of tomato and pepper | — | L[e] | Asexual | Large | 2 | 7 | 6 | (25, 99, 119) |
| *Xanthomonas malvacearum* | Cotton blight | — | L[e] | Asexual | Large | 2 | 7 | 6 | (10) |
| *Xanthomonas oryzae* pv. *oryzae* | Bacterial leaf blight of rice | — | M | Asexual | Large | 2 | 8 | 4 | (69, 85, 102) |

[a]H = high; M = moderate; and L = low gene/genotype flow.

[b]Mutation rates are known for only a small number of pathogens. In pathosystems where mutation rates are known to be high, a risk of 2 was assigned to it, compared to a risk of 1 for other systems with low or unknown mutation rates. All bacteria were assigned a risk of 2.

[c]Expected risk was calculated as the sum of the individual risks for gene/genotype flow of the asexual propagules (high gene/genotype flow = 3; moderate gene/genotype flow = 2; low gene/genotype flow = 1), reproduction/mating system (mixed = 3; sexual = 2; asexual = 1), effective population size (large = 3; medium = 2; small = 1), and mutation rate (high mutation rate = 2; average mutation rate = 1).

[d]This number represents the average number of years before the pathogen caused detectable damage on previously resistant cultivars. These estimates exclude cases where resistance genes remained effective. In many cases these numbers varied widely for different resistance genes and thus should be treated with caution. Risk classes: 6 = 1–3 years; 5 = 4–6 years; 4 = 7–9 years; 3 = 10–12 years; 2 = 13–15 years; 1 = more than 15 years until breakdown. Not enough information was available for pathosystems indicated with a (−).

[e]These pathogens are naturally soilborne and are expected to exhibit low gene/genotype flow. However, because some are seedborne or move on infected plant material, actual gene/genotype flow can be much higher as a result of human activities.

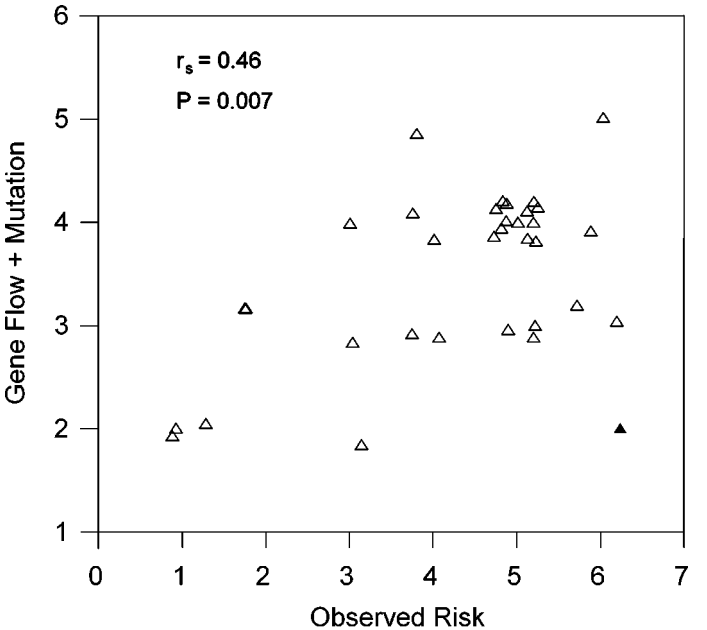



**Figure 5** The correlation between observed risk values and the predicted risk based on the sum of gene/genotype flow and mutation. Values were taken from 34 plant pathosystems shown in Table 2. The dark triangle represents the largest outlier, the nematode *Meloidogyne incognita*. Correlation and significance values (two-tailed t-test) were calculated excluding *M. incognita*.

*X. campestris* pv. *vesicatoria* seems to exhibit limited gene/genotype flow as new pathotypes are often restricted to a specific country (49). However, gene flow is expected to be higher than in *X. oryzae* pv. *oryzae* because *X. campestris* pv. *vesicatoria* can be seedborne (99).

## *Puccinia triticina*

The wheat leaf rust fungus, *P. triticina*, represents a group of asexual rust pathogens that fall in a medium risk category because of long-distance genotype flow. It is asexual (17) in most of the world except in the Mediterranean area (63), where it would be placed in a higher risk category. Large population sizes can be maintained by overwintering of local populations on winter wheat crops (63). Spring wheat breeding programs in North America (62) and Australia (83) have generally been successful in producing cultivars with durable resistance. In contrast, winter wheats grown in the southern plains of the United States often lose effective resistance after only a few years (70). The faster resistance breakdown in the southern United States could be explained by a combination of high gene/genotype flow and large effective population sizes maintained over much of the period when the

wheat crop is in the ground. Thus, this pathogen provides us with an opportunity to compare the evolutionary potential of populations with different effective population sizes. Fewer pathotypes are found in Australia compared to Canada (61), perhaps reflecting lower evolutionary potential in the Australian population due to a founder effect. *Lr*13 broke down within a few years of release in the United States and Canada (61), South Africa, Europe, Mexico, and South America (114), but it remained effective in Australia for more than 20 years (84).

## *Phytophthora sojae* on Soybean

*Phytophthora sojae* (syn. *Phytophthora megasperma* f. sp. *glycinea*) is a homothallic (self-fertile) Oomycetous fungus, causing a root and stem rot of soybean. It is a medium-risk pathogen because it has the potential to outcross, but has limited potential for gene flow because it is soilborne. Already, 46 pathotypes have been described for the *P. sojae* soybean pathosystem (1, 108). Different *P. sojae* pathotypes probably evolved independently from the same clonal lineage, as it is homothallic and a poor correlation was found between RFLPs (132), mtDNA polymorphisms (30), and pathotypes. However, *P. sojae* does outcross at low frequencies (31, 132), and some of the pathotypes may have been created as a result of outcrossing, although mutation is thought to be more important for creating diversity (31). A substantial level of genetic variation using RFLP markers was observed in the U.S. population, suggesting *P. sojae* may be native to the United States (31). Single-gene resistance has been somewhat durable, lasting for 6 to 15 years (108, 111, 126). The longevity of *Rps* resistance may reflect the soilborne nature of this pathogen. The dynamics of infection and subsequent inoculum production and dissemination are limited to the soil environment. Because secondary infection is limited, it is effectively a monocyclic disease, so there is only one chance to develop new pathotypes during a growing season, giving it a lower effective population size.

## *Phytophthora infestans* on Potatoes

*Phytophthora infestans* is heterothallic and has a high potential for genotype flow because it produces airborne asexual spores. *P. infestans* first appeared in the United States in 1843 and migrated to Europe in 1845. There is good evidence that the European population consisted of only one clone introduced from the United States (34). The introduced *P. infestans* population probably consisted of only the A1 mating type and thus was restricted to asexual reproduction (33). As a result of the limited number of founding individuals and lack of recombination, European populations of *P. infestans* have exhibited low levels of gene and genotype diversity over most of the past 155 years. The A2 mating type was first reported in Europe in 1980, but it appears likely that A2 was introduced into Europe some time in the 1970s. Since the introduction of the opposite mating type, *P. infestans* populations in Europe have begun to reproduce sexually and produce oospores that have the potential to overwinter in the soil. Thus, the introduction of the opposite mating type has increased its evolutionary potential in the risk diagram (Figure 4) as a

result of the introduction of a sexual cycle. It is not yet clear if the oospores will increase the population size sufficiently to merit a further increase in the risk value.

### *Blumeria graminis* on Barley and Wheat

*Blumeria graminis* is characterized as a high-risk pathogen with a high potential for gene and genotype flow. It reproduces asexually on the crop and can survive between crops as asexual colonies or as sexual ascospores inside cleistothecia. Green bridges of host plants occur where winter and spring wheat or barley cultivars are grown within the same genetic neighborhood, resulting in a very large effective population size. An annual sexual cycle produces many new allele combinations, and succeeding cycles of asexual reproduction can rapidly increase the frequencies of selected allele combinations. These pathogens have a long history of defeating single, major resistance genes and pyramids of major resistance genes. Barley cultivars with major gene resistance select isolates of *Blumeria graminis* f. sp. *hordei* with matching virulence, and the effectiveness of most major gene resistance is lost through the evolution of corresponding virulence in the pathogen (135). Many barley cultivars with two resistance genes have rapidly become susceptible (135).

## A DECISION DIAGRAM TO AID RESISTANCE BREEDING PROGRAMS

In this section, we propose guidelines based on the evolutionary potential of the pathogen to choose appropriate types of resistance and decide how to deploy major resistance genes in a breeding program. The purpose here is to offer advice on the best way to manage limited genetic resources in order to extend the useful life expectancy of available genetic resistance. We have distilled most of these ideas into a simple decision diagram presented in Figure 6. This diagram offers some broad guidelines to consider before embarking on a resistance-breeding project, with the objective of matching the weapons (resistance-genes) to the targets (pathogens). The breeding goal is to choose the appropriate type of genetic resistance and then apply a resistance gene management strategy that will match the pathogen's biology and minimize the likelihood that the pathogen population will evolve to overcome the resistance. In particular, we have attempted to indicate when single, major gene resistance is likely to be most effective, when resistance gene pyramids are most likely to fail, and when gene deployment options such as cultivar mixtures or multilines should be considered early in the breeding program. Earlier versions of this decision diagram were presented elsewhere (77, 78).

The decision diagram assumes that major gene resistance is based on the receptor-elicitor model characteristic of the gene-for-gene relationship, and that quantitative resistance is a quantitative character based on several unlinked genes that usually show equal and additive effects. It is worth noting that the genes underlying quantitative resistance do not always contribute equally to resistance [e. g., (112a)], and in some cases it appears that only one or a few genes may make

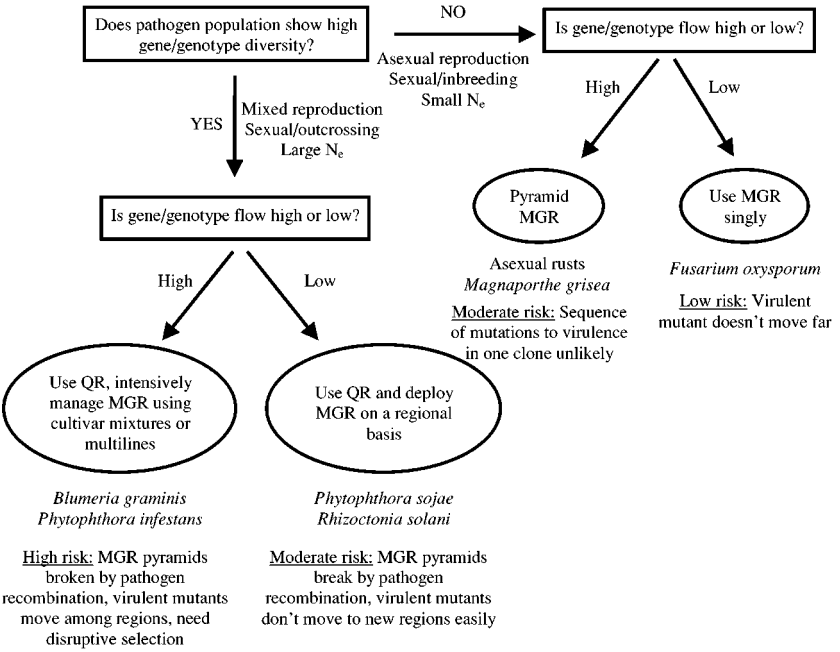



**Figure 6** A simplified decision diagram to assist with developing resistance-breeding strategies to achieve durable disease resistance. Major gene resistance (MGR): resistance that has large effects, is based on the hypersensitive response and follows the receptor-elicitor model of the gene-for-gene interaction. Quantitative resistance (QR): resistance that has, on average, small, nearly equal, and additive effects that are equally effective against all strains of the pathogen.

the major contribution to a quantitative trait. The diagram assumes that both types of resistance are available to the breeder, and that major gene resistance is preferred because it is easier to recognize and is more easily utilized in a breeding program. We did not attempt to include the effects of different mutation rates, population sizes, or the full range of reproduction/mating systems. This diagram can be extended with many additional branch points to encompass the full range of possible interactions among evolutionary forces and potential pathogen population genetic structures. The outcome of the decision diagram is a general recommendation for choosing the type of resistance to use and the optimum deployment method with the aim of maximizing the useful lifespan of the resistance. This diagram should be considered in the appropriate context in a resistance-breeding program, as an aid to assist decision-making. It is not intended as an authoritative guide that will lead to durable resistance.

At one end of the decision diagram are pathogens that have strictly asexual reproduction, a low potential for gene/genotype flow, and small effective population

sizes. In our risk model, these are pathogens with the lowest evolutionary potential. These pathogen populations are characterized by low genotypic diversity that is often arrayed in a limited number of clonal lineages. When a mutation occurs from avirulence to virulence, it occurs randomly within a clonal lineage, and the virulent lineage does not disperse far from its origin due to lack of long-distance dispersal mechanisms. The virulence mutation is "trapped" in the original clonal lineage owing to the absence of meiosis and recombination. For these pathogens, a breeding strategy that relies on single major resistance genes is likely to be durable because the mutation to virulence will occur in a limited number of genetic backgrounds and the virulent lineages that inevitably arise are unlikely to move quickly to new fields planted to the same major resistance gene. An example of a class of pathogens that follow this life history is the *Fusarium oxysporum* wilts on many crops.

The next category in the decision diagram is asexual or inbreeding pathogens that exhibit a high potential for genotype flow. These pathogens also exhibit low genotypic diversity, but when the virulent lineage arises by mutation, it is moved efficiently to neighboring fields or adjacent agricultural regions. In our risk model, these are pathogens with an intermediate evolutionary potential. For these pathogens, a breeding strategy that pyramids major resistance genes is likely to be durable because it is unlikely that a sequence of multiple mutations to virulence (loss of several elicitors simultaneously) will occur in the same clonal lineage. Examples of pathogens that follow this life history are the asexual rusts and *Magnaporthe grisea*. Pathogens that have a sexual cycle, but appear to be mainly inbreeding, such as *Sclerotinia sclerotiorum* (59), may also fall into this category.

Pathogens that exhibit mixed reproduction that includes regular recombination pose a different type of evolutionary risk that requires a different breeding strategy. These pathogens exhibit higher genotype diversity as a result of recombination and have greater potential for local adaptation to a changing environment. After a mutation to virulence occurs, it can be recombined into many different genetic backgrounds, and it can be recombined with other virulence mutations that occur at unlinked loci. Thus pyramids are not an optimum approach for these pathogens. Pathogens with a mixed reproduction system and a low potential for gene/genotype flow are placed in an intermediate risk category. For these pathogens, breeders should focus on quantitative resistance instead of major gene resistance. As a result of the mixed reproduction system, the mutation for virulence can be recombined into many different genetic backgrounds, and it is likely that one or more of the resulting pathogen strains will have a high level of fitness on the corresponding resistant cultivar. A major resistance gene is likely to break down quickly under these circumstances. In the presence of quantitative resistance, the pathogen may evolve increased pathogenicity (the counterpart of plant quantitative resistance), as shown in our model (Figure 1; Figure in Supplementary Materials on http://www.annualreviews.org/). To evolve a higher level of pathogenicity, the pathogen must recombine a number of alleles at independent loci into a single genotype (a coadapted gene complex). Sexual reproduction will tend to break up these coadapted gene complexes in pathogen genotypes that have a high level of

pathogenicity, thus the increase in pathogenicity in sexually reproducing pathogens may occur quite slowly and escape notice if asexual spores are not widely dispersed or if there are few asexual pathogen reproduction cycles per crop generation. If quantitative resistance is not available, then major gene resistance can be deployed in rotations through time or space. Rotations on a regional basis are expected to be effective against low gene flow pathogens because the virulent mutants that arise to overcome a major resistance gene in one region will not be likely to emigrate to other regions. Rotations of major resistance genes through time will produce disruptive selection that may prevent different virulence mutations from accumulating in the same genotype.

The highest risk pathogens have a mixed reproduction system and a high degree of gene/genotype flow. We believe that these pathogens will require the greatest effort to achieve durable resistance because the mutations to virulence can be recombined into many genetic backgrounds until a pathogen clone with high fitness appears, and then this adapted genotype can be dispersed across long distances and into new populations. For pathogens in this risk category, we suggest the breeding effort should concentrate on quantitative resistance that will need to be renewed regularly to stay ahead of the pathogen. If quantitative resistance is not available, then major gene resistance should be managed aggressively, including development of cultivar mixtures and multilines that can be used in combination with regional and temporal deployment strategies.



## GENETICALLY ENGINEERED RESISTANCE

We have entered the era of genetic engineering of our major crops with caution. Genetic engineering technologies clearly offer great potential, but genetically engineered crops present a number of uncharacterized risks that require further investigation. One risk is that genetically engineered resistance genes will face the same boom-and-bust cycles as the major resistance genes incorporated by traditional breeding methods. As molecular characterization of resistance genes proceeds, it will become progressively easier to manipulate genetic resistance and transfer resistance genes within and among species. Our present knowledge indicates that plants evolved leucine-rich repeat (LRR)-types of receptors to recognize a diverse array of pathogen elicitors, and it is likely that pathogens coevolved with these receptors for millions of generations before agriculture arose. With this long history of coevolution, it seems unlikely that we will be able to eliminate plant diseases by engineering new receptors or combinations of receptors and putting them into our crops. Pathogens will continue to evolve. However, genetic engineering offers new opportunities to stay a few steps ahead of the pathogen. Genetic engineering can be used to create novel pyramids of major resistance alleles that can be transferred into plants as a cassette of linked genes. It may become possible to create a pyramid more quickly through a single transformation step than through a series of hybridizations and backcrosses. Of course, plants already have evolved cassettes

of linked resistance genes over evolutionary timescales, and pathogens are still with us. Genetic engineering also could be used to synthesize multilines quickly and efficiently by inserting different resistance alleles into superior agronomic genotypes as they are developed. This approach may allow us to impose disruptive selection that slows pathogen evolution, but it is unlikely to eliminate the pathogen. It is most likely that pathogen populations will continue to evolve and respond to the new forms of genetic resistance that we deploy through genetic engineering. But with careful management of these new, engineered resistance genes, we may be able to create truly durable forms of genetic resistance. The best way to insure the durability of these new engineered resistance genes is to manage them wisely using knowledge of the evolutionary potential of the pathogen population.

**The *Annual Review of Phytopathology* is online at http://phyto.annualreviews.org**



## LITERATURE CITED

1. Abney TS, Melagar JN, Richards TL, Scott DH, Grogan J, Young J. 1997. New races of *Phytophthora sojae* with *Rps*1-d virulence. *Plant Dis.* 81:653–55
2. Bartos P, Fleischmann G, Samborski DJ, Shipton WA. 1969. Studies on asexual variation in the virulence of oat crown rust, *Puccinia coronata* f. sp. *avenae*, and wheat leaf rust, *Puccinia recondita*. *Can. J. Bot.* 47:1383–87
3. Bergquist RR, Masias OR. 1974. Physiologic specialization in *Trichometasphaeria turcica* f. sp. *zea* and *T. turcica* in Hawaii. *Phytopathology* 76:546–49
4. Biffen RH. 1905. Mendel's laws of inheritance and wheat breeding. *J. Agric. Sci.* 1:4–48
5. Bonman JM, Khush GS, Nelson RJ. 1992. Breeding rice for resistance to pests. *Annu. Rev. Phytopathol.* 30:507–26
6. Borchardt DS, Welz HG, Geiger HH. 1998. Genetic structure of *Setosphaeria turcica* populations in tropical and temperate climates. *Phytopathology* 88: 322–29
7. Bouhot D. 1981. Some aspects of the pathogenic potential in formae speciales and races of *Fusarium oxysporum* on Cucurbitaceae. In *Fusarium: Diseases, Biology, and Taxonomy*, ed. PE Nelson, TA Toussoun, WFO Marasas, pp. 318–26. University Park, PA: Penn. State Univ. Press
8. Brent KJ, Hollomon DW. 1998. Fungicide resistance: the assessment of risk. *FRAC Monogr. No. 2, Global Prot. Fed.* 48 pp.
9. Brewbaker JL. 1983. Breeding for disease resistance. In *Challenging Problems in Plant Health*, ed. T Kommedahl, PH Williams, pp. 441–49. St. Paul, MN: Am. Phytopathol. Soc.
10. Brinkerhoff LA. 1970. Variation in *Xanthomonas malvacearum* and its relation to control. *Annu. Rev. Phytopathol.* 8:85–110
11. Brown JKM, Foster EM, O'Hara RB. 1997. Adaptation of powdery mildew populations to cereal varieties in relation to durable and non-durable resistance. In *The Gene-for-Gene Relationship in Plant-Parasite Interaction*, ed. IR Crute, EB Holub, JJ Burdon, pp. 119–38. Wallingford, UK: CABI
12. Browning M, Rowley LV, Zeng PY, Chandlee JM, Jackson N. 1999. Morphological, pathogenic, and genetic comparisons of *Colletotrichum graminicola* isolates from poaceae. *Plant Dis.* 83:286–92
13. Brun H, Levivier S, Somda I, Ruer D,

Renard M, Chèvre AM. 2000. A field method for evaluating the potential durability of new resistance sources: application to the *Leptosphaeria maculans–Brassica napus* pathosystem. *Phytopathology* 90:961–66

14. Brurberg MB, Hannukkala A, Hermansen A. 1999. Genetic variability of *Phytophthora infestans* in Norway and Finland as revealed by mating type and fingerprint probe RG57. *Mycol. Res.* 103:1609–15
15. Burdon JJ, Luig NH, Marshall DR. 1983. Isozyme uniformity and virulence variation in *Puccinia graminis* f. sp. *tritici* and *P. recondita* f. sp. *tritici* in Australia. *Aust. J. Biol. Sci.* 36:403–10
16. Burdon JJ, Roberts JK. 1995. The population genetic structure of the rust fungus *Melampsora lini* as revealed by pathogenicity, isozyme and RFLP markers. *Plant Pathol.* 44:270–78
17. Burdon JJ, Roelfs AP. 1985. The effect of sexual and asexual reproduction on the isozyme structure of populations of *Puccinia graminis*. *Phytopathology* 75:1068–73
18. Burdon JJ, Roelfs AP. 1985. Isozyme and virulence variation in asexually reproducing populations of *Puccinia graminis* and *Puccinia recondita* on wheat. *Phytopathology* 75:907–13
19. Carlier J, Lebrun MH, Zapater MF, Dubois C, Mourichon X. 1996. Genetic structure of the global population of banana black leaf streak fungus, *Mycosphaerella fijiensis*. *Mol. Ecol.* 5:499–510
20. Caten CE, Person C, Groth JV, Dhahi SJ. 1983. The genetics of pathogenic aggressiveness in three dikaryons of *Ustilago hordei*. *Can. J. Bot.* 62:1209–19
21. Chen RS, McDonald BA. 1996. Sexual reproduction plays a major role in the genetic structure of populations of the fungus *Mycosphaerella graminicola*. *Genetics* 142:1119–27
22. Chong J, Kolmer JA. 1993. Virulence dynamics and phenotypic diversity of *Puccinia coronata* f. sp. *avenae* in Canada from 1974 to 1990. *Can J. Bot.* 71:248–55
23. Cowger C, Hoffer ME, Mundt CC. 2000. Specific adaptation by *Mycosphaerella graminicola* to a resistant wheat cultivar. *Plant Pathol.* 49:445–51
24. Crute IR. 1992. From breeding to cloning (and back again?): a case study with lettuce downy mildew. *Annu. Rev. Phytopathol.* 30:485–506
25. Dahlbeck D, Stall RE. 1979. Mutations for change of race in culture of *Xanthomonas vesicatoria*. *Phytopathology* 69:634–36
26. Drenth A, Tas ICQ, Govers F. 1994. DNA fingerprinting uncovers a new sexually reproducing population of *Phytophthora infestans* in the Netherlands. *Eur. J. Plant Pathol.* 100:97–107
27. Dubin HJ, Rajaram S. 1996. Breeding disease-resistant wheats for tropical highlands and lowlands. *Annu. Rev. Phytopathol.* 34:503–26
28. Flor HH. 1956. The complementary genic systems in flax and flax rust. *Adv. Genet.* 8:29–54
29. Flor HH. 1958. Mutation to wider virulence in *Melampsora lini*. *Phytopathology* 48:297–301
30. Förster H, Kinscherf IG, Leong SA, Maxwell DP. 1989. Restriction fragment polymorphisms of the mitochondrial DNA of *Phytophthora megasperma* isolated from soybean, alfalfa, and fruit trees. *Can. J. Bot.* 67:529–31
31. Förster H, Tyler B, Coffey MD. 1994. *Phytophthora sojae* races have arisen by clonal evolution and by rare outcrosses. *Mol. Plant-Microbe Interact.* 7:780–91
32. Funnell DL, Matthews PS, VanEtten HD. 2000. Breeding for highly fertile isolates of *Nectria haematococca* MPVI that are highly virulent on pea and *in planta* selection for virulent recombinants. *Phytopathology* 91:92–101
33. Goodwin SB. 1997. The population

genetics of *Phytophthora*. *Phytopathology* 87:462–73

33a. Goodwin SB, Cavaletto JR, Waalwijk C, Kema GHJ. 2001. DNA fingerprint probe from *Mycosphaerella graminicola* identifies an active transposable element. *Phytopathology* 91:1181–88

34. Goodwin SB, Cohen BA, Fry WA. 1994. Panglobal distribution of a single clonal lineage of the Irish potato famine fungus. *Proc. Natl. Acad. Sci. USA* 91:11591–95

35. Goodwin SB, Drenth A. 1997. Origin of the A2 mating type of *Phytophthora infestans* outside Mexico. *Phytopathology* 87:992–99

36. Goodwin SB, Sujkowski LS, Dyer AT, Fry BA, Fry WE. 1995. Direct detection of gene flow and probable sexual reproduction of *Phytophthora infestans* in Northern America. *Phytopathology* 85:473–79

37. Gordon TR, Martyn RD. 1997. The evolutionary biology of *Fusarium oxysporum*. *Annu. Rev. Phytopathol.* 35:111–28

38. Groth JV, Roelfs AP. 1982. Effects of sexual and asexual reproduction on race abundance in cereal rust fungus populations. *Phytopathology* 72:1503–7

39. Hayden HL. 2000. *Population genetic studies of Mycosphaerella species infecting banana*. PhD thesis. Univ. Queensland, St. Lucia, Aust.

40. Houston BR, Ashworth LJ Jr. 1957. Newly determined races of the barley scald fungus in California. *Phytopathology* 47:525

41. Howard HW, Johnson R, Russell GE, Wolfe MS. 1970. *Problems in breeding for resistance to diseases and pests.* Rep. Plant Breed. Inst. 1969, Cambridge

42. Hubbeling N. 1978. Breakdown of resistance of the CF5 gene in tomato by another new race of *Fulvia fulva*. *Med. Fac. Landbouww. Rijksuniv. Gent* 43:891–94

43. Hulbert SH, Lyons PC, Bennetzen JL. 1991. Reactions of maize lines carrying *Rp* resistance genes to isolates of the common rust pathogen, *Puccinia sorghi*. *Plant Dis.* 75:1130–33

44. Jackson LF, Webster RK. 1976. Race differentiation, distribution, and frequency of *Rhynchosporium secalis* in California. *Phytopathology* 66:719–25

45. Jeger MJ, Gilijamse E, Bock CH, Frinking H. 1998. The epidemiology, variability and control of the downy mildews of pearl millet and sorghum, with particular reference to Africa. *Plant Pathol.* 47:544–69

46. Johnson KB, Stockwell VO. 1998. Management of fire blight: a case study in microbial ecology. *Annu. Rev. Phytophathol.* 36:227–48

47. Johnson R. 1992. Reflections of a plant pathologist on breeding for disease resistance, with emphasis on yellow rust and eyespot of wheat. *Plant Pathol.* 41:239–54

48. Johnson R, Taylor AJ. 1980. Pathogenic variation in *Puccinia striiformis* in relation to the durability of yellow rust resistance in wheat. *Ann. Appl. Biol.* 94:283–86

49. Jones JB, Stall RE, Bouzar H. 1998. Diversity among *Xanthomonas* pathogenic on pepper and tomato. *Annu. Rev. Phytopathol.* 36:41–58

50. Jones SS, Murray TD, Allan RE. 1995. Use of alien genes for the development of disease resistance in wheat. *Annu. Rev. Phytopathol.* 33:429–43

51. Joosten MHAJ, Cozijnsen TJ, de Wit PJGM. 1994. Host-resistance to fungal tomato pathogen lost by a single base-pair change in an avirulence gene. *Nature* 367:384–86

52. Jørgensen HJL, Smedegaard-Petersen V. 1999. Host pathogen interactions in the Septoria-disease complex. See Ref. 70a, pp. 131–60

53. Keeling BL. 1982. Four new physiologic races of *Phytophthora megasperma* f. sp. *glycinea*. *Plant Dis.* 66:334–35

54. Kema GHJ, Sayoud R, Annone JG, Van Silfhout CH. 1996. Genetic variation for

virulence and resistance in the wheat–*Mycosphaerella graminicola* pathosystem. II. Analysis of interactions between pathogen isolates and host cultivars. *Phytopathology* 86:213–20

55. Kerr EA, Patrick ZA, Bailey DL. 1971. Resistance in tomato species to new races of leaf mold (*Cladosporium fulvum* Cke.). *Hortic. Res.* 11:84–92
56. Kilpatrick RA. 1975. New wheat cultivars and longevity of rust resistance, 1971–75. *US Dep. Agric. Res. Serv.* NE 64:1–20
57. Kiyosawa S. 1982. Genetics and epidemiological modelling of breakdown of plant disease resistance. *Annu. Rev. Phytopathol.* 20:93–117
58. Koenig HC, Ploetz RC, Kistler HC. 1997. *Fusarium oxysporum* f. sp. *cubense* consists of a small number of divergent and globally distributed clonal lineages. *Phytopathology* 87:915–23
59. Kohli Y, Brunner LJ, Yoell H, Milgroom MG, Anderson JB, et al. 1995. Clonal dispersal and spatial mixing in populations of the plant pathogenic fungus, *Sclerotinia sclerotiorum*. *Mol. Ecol.* 4:69–77
60. Kohn LM. 1995. The clonal dynamic in wild and agricultural plant-pathogen populations. *Can. J. Bot.* 73:S1231–40
61. Kolmer JA. 1989. Virulence and race dynamics of *Puccinia recondita* f. sp. *tritici* in Canada during 1956–1987. *Phytopathology* 79:349–56
62. Kolmer JA. 1991. Effect of sexual recombination in two populations of the wheat leaf rust fungus *Puccinia recondita*. *Can. J. Bot.* 70:359–63
63. Kolmer JA. 1992. Diversity of virulence phenotypes and effect of host sampling between and within populations of *Puccinia recondita* f. sp. *tritici* in Canada. *Plant Dis.* 76:618–21
64. Kolmer JA. 1996. Genetics of resistance to wheat leaf rust. *Annu. Rev. Phytopathol.* 34:435–55
65. Kousik CS, Ritchie DF. 1996. Race shift in *Xanthomonas campestris* pv. *vesicatoria* within a season in field-grown pepper. *Phytopathology* 86:952–58
66. Lamari L, Sayoud R, Boulif M, Bernier CC. 1995. Identification of a new race in *Pyrenophora tritici-repentis*: implications for the current pathotype classification system. *Can. J. Plant Pathol.* 17:312–18
67. Leach JE, Cruz CMV, Bai JF, Leung H. 2001. Pathogen fitness penalty as a predictor of durability of disease resistance genes. *Annu. Rev. Phytopathol.* 39:187–224
68. Leary JV, Wilbur WD. 1976. Identification of the races of *Fusarium oxysporum* f. sp. *melonis* causing wilt of muskmelon in California. *Phytopathology* 66:15–16
69. Li Z-K, Luo LJ, Mei HW, Paterson AH, Zhao XH, et al. 1999. A "defeated" rice resistance gene acts as a QTL against a virulent strain of *Xanthomonas oryzae* pv. *oryzae*. *Mol. Gen. Genet.* 261:58–63

69a. Linde C, Zhan J, McDonald BA. 2002. Population structure of *Mycosphaerella graminicola:* From lesions to continents. *Phytopathology.* In press

70. Long DL, Roelfs AP, Roberts JJ. 1992. Virulence of *Puccinia recondita* f. sp. *tritici* in the United States during 1988–1990. *Plant Dis.* 76:495–99

70a. Lucas JA, Bowyer P, Anderson HM, eds. 1999. *Septoria on Cereals: A Study of Pathosystems.* Wallingford, UK: CABI

71. MacHardy WE, Gadoury DM, Gessler C. 2001. Parasitic and biological fitness of *Venturia inaequalis*: relationship to disease management strategies. *Plant Dis.* 85:1036–51
72. Mahuku GS, Goodwin PH, Hall R, Hsiang T. 1997. Variability in the highly virulent type of *Leptosphaeria maculans* within and between oilseed rape fields. *Can. J. Bot.* 75:1485–92
73. Malcolmson JF. 1969. Races of *Phytophthora infestans* occurring in Great Britain. *Trans. Br. Mycol. Soc.* 53:417–23

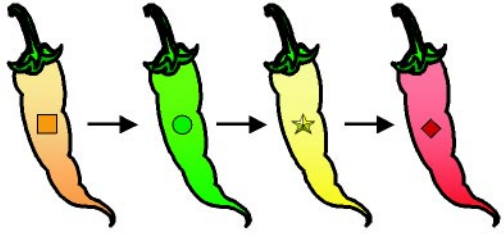
74. Martens JW, Dyck PL. 1989. Genetics of resistance to rust in cereals from a Canadian perspective. *Can. J. Plant Pathol.* 11:78–85
75. McCracken AR, Dawson WM. 1998. Short rotation coppice willow in Northern Ireland since 1973: development of the use of mixtures in the control of foliar rust (*Melampsora* spp.). *Eur. J. For. Pathol.* 28:241–50
76. McDonald BA. 1997. The population genetics of fungi: tools and techniques. *Phytopathology* 87:448–53
77. McDonald BA. 1999. The population genetics of plant pathogens and resistance breeding strategies. *Vortr. Pflanzenzücht.* 46:235–44
78. McDonald BA, Linde C. 2002. Pathogen population genetics and the durability of disease resistance. *Euphytica.* In press
79. McDonald BA, Miles J, Nelson LR, Pettway RE. 1994. Genetic variability in nuclear DNA in field populations of *Stagonospora nodorum*. *Phytopathology* 84:250–55
80. McDonald BA, Pettway RE, Chen RS, Boeger JM, Martinez JP. 1995. The population genetics of *Septoria tritici* (teleomorph *Mycosphaerella graminicola*). *Can. J. Bot.* 73(Suppl.):S292–S301
81. McDonald BA, Zhan J, Burdon JJ. 1999. Genetic structure of *Rhynchosporium secalis* in Australia. *Phytopathology* 89:639–45
82. McDonald BA, Zhan J, Yarden O, Hogan K, Garton J, Pettway RE. 1999. The population genetics of *Mycosphaerella graminicola* and *Phaeosphaeria nodorum*. See Ref. 70a, pp. 44–69
83. McIntosh RA. 1992. Pre-emptive breeding to control wheat rusts. *Euphytica* 63:103–13
84. McIntosh RA, Brown GN. 1997. Anticipatory breeding for resistance to rust diseases in wheat. *Annu. Rev. Phytopathol.* 35:311–26
84a. Mes JJ, Haring MA, Cornelissen BJC. 2000. Foxy: an active family of short interspersed nuclear elements from *Fusarium oxysporum*. *Mol. Gen. Genet.* 263:271–80
85. Mew TW, Vera Cruz CM, Medalla ES. 1992. Changes in race frequency of *Xanthomonas oryzae* pv. *oryzae* in response to rice cultivars planted in the Philippines. *Plant Dis.* 76:1029–32
86. Mouliom-Pefoura A. 1999. First observation of the breakdown of high resistance in Yangambi km 5 (*Musa* sp.) to the black leaf streak disease in Cameroon. *Plant Dis.* 83:78
87. Mundt CC, Ahmed HU, Finckh MR, Nieva LP, Alfonso RF. 1999. Primary disease gradients of bacterial blight of rice. *Phytopathology* 89:64–67
88. Mundt CC, Hoffer ME, Ahmed HU, Coakley SM, DiLeone JA, Cowger C. 1999. Population genetics and host resistance. See Ref. 70a, pp. 115–30
89. Nelson RJ, Baraoidan MR, Vera Cruz CM, Yap IV, Leach JE, et al. 1994. Relationship between phylogeny and pathotype for the bacterial blight pathogen of rice. *Appl. Environ. Microbiol.* 60:3275–83
90. Palumbi SR. 2001. Humans as the world's greatest evolutionary force. *Science* 293:1786–90
91. Pan XB, Rush MC, Sha XY, Xie QJ, Linscombe SD, et al. 1999. Major gene, nonallelic sheath blight resistance from the rice cultivars Jasmine 85 and Teqing. *Crop Sci.* 39:338–46
92. Pande S, Thakur RP, Karunakar RI, Bandyopadhyay R, Reddy BVS. 1994. Development of screening methods and identification of stable resistance to anthracnose in sorghum. *Field Crops Res.* 38:157–66
93. Park FF, Oates DD, Meldrum S. 2000. Recent pathogenic changes in the leaf (brown) rust pathogen of wheat and the crown rust pathogen of oats in Australia in relation to host resistance. *Acta Phytopathol. Entomol. Hung.* 35:387–94

94. Pastor-Corrales MA, Otoya MM, Molina A, Singh SP. 1995. Resistance to *Colletotrichum lindemuthianum* isolates from Middle America and Andean South America in different common bean races. *Plant Dis.* 79:63–67
95. Pataky JK, Pate MC, Hulbert SH. 2001. Resistance genes in the *rp1* region of maize effective against *Puccinia sorghi* virulent on the *Rp1-D* gene in North America. *Plant Dis.* 85:165–68
96. Pei MH, Yuan ZW, Hunter T, Ruiz C. 2000. Heterogenous nature of a 'new' pathotype of *Melampsora* rust on *Salix* revealed by AFLP. *Eur. J. Plant Pathol.* 106:771–79
97. Pinon J, Frey P. 1997. Structure of *Melampsora larici-populina* populations on wild and cultivated poplar. *Eur. J. Plant Pathol.* 103:159–73
98. Ploetz RC, Pegg KG. 1999. Fusarium wilt. In *Diseases of Banana, Abaca and Enset*, ed. DR Jones, pp. 143–59. Wallingford, UK: CABI
99. Pohrenezny K, Stall RE, Caneros BI, Kegley M, Datnoff LE, Subramanya R. 1992. Sudden shift in the prevalent race of *Xanthomonas campestris* pv. *vesicatoria* in pepper fields in southern Florida. *Plant Dis.* 76:118–20
100. Prot JC. 1984. A naturally occurring resistance breaking biotype of *Meloidogyne incognita* on tomato. Reproduction and pathogenicity on tomato cultivars Roma and Rossol. *Rev. Nematol.* 7:3–28
101. Ramstedt M. 1999. Rust disease on willows—virulence variation and resistance breeding strategies. *Forest Ecol. Manag.* 121:101–11
102. Reddy OR, Ou SH. 1976. Pathogenic variability in *Xanthomonas oryzae*. *Phytopathology* 66:906–9
103. Roberts AL, Crute IR. 1994. Apple scab resistance from *Malus floribunda* 821 (*Vf*) is rendered ineffective by isolates of *Venturia inaequalis* from *Malus floribunda*. *Norw. J. Agric. Sci.* 17:403–6
104. Roelfs AP. 1985. Epidemiology in North America. In *The Cereal Rusts*, ed. WR Bushnell, AP Roelfs, pp. 403–34. New York: Academic
105. Roelfs AP, Groth JV. 1980. A comparison of virulence phenotypes in wheat stem rust populations reproducing sexually and asexually. *Phytopathology* 70: 855–62
106. Rosewich UL, Pettway RE, McDonald BA, Duncan RR, Frederiksen RA. 1998. Genetic structure and temporal dynamics of a *Colletotrichum graminicola* population in a sorghum disease nursery. *Phytopathology* 88:1087–93
107. Rosewich UL, Pettway RE, McDonald BA, Kistler HC. 1999. High levels of gene flow and heterozygote excess characterize *Rhizoctonia solani* AG-1 1A (*Thanatephorus cucumeris*) from Texas. *Fungal Genet. Biol.* 28:148–59
108. Ryley MJ, Obst NR, Irwin JAG, Drenth A. 1998. Changes in the racial composition of *Phytophthora sojae* in Australia between 1979 and 1996. *Plant Dis.* 82:1048–54
109. Ryley MJ, Obst NR, Stovold GE. 1991. A new race of *Phytophthora megasperma* f. sp. *glycinea* on soybean in Australia. *Aust. Plant Pathol.* 20:97–100
110. Salamati S, Zhan J, Burdon JJ, McDonald BA. 2000. The genetic structure of field populations of *Rhynchosporium secalis* from three continents suggests moderate gene flow and regular recombination. *Phytopathology* 90:901–8
111. Schmitthenner AF. 1985. Problems and progress in control of *Phytophthora* root rot of soybean. *Plant Dis.* 69:362–68
112. Schmitthenner AF, Hobe M, Bhat RG. 1994. *Phytophthora sojae* races in Ohio over a 10-year interval. *Plant Dis.* 78: 269–76
112a. Shaner G, Buechley G, Nyquist WE. Inheritance of latent period of *Puccinia recondita* in wheat. *Crop Sci.* 37:748–56
113. Sicard D, Michalakis Y, Dron M, Neema C. 1997. Genetic diversity and pathogenic variation of *Colletotrichum*

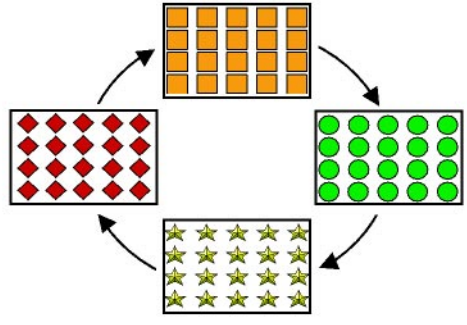
*lindemuthianum* in three centers of diversity of its host, *Phaseolus vulgaris*. *Phytopathology* 87:807–13
114. Singh RP, Rajaram S. 1992. Genetics of adult-plant resistance of leaf rust in 'Frontana' and three CIMMYT wheats. *Genome* 35:24–31
115. Staskawicz BJ, Mudgett MB, Dangl JL, Galan JE. 2001. Common and contrasting themes of plant and animal diseases. *Science* 292:2285–89
116. Stover RH, Buddenhagen IW. 1986. Banana breeding: polyploidy, disease resistance and productivity. *Fruits* 41:175–91
117. Sujkowski LS, Goodwin SB, Dyer AT, Fry WE. 1994. Increased genotypic diversity via migration and possible occurrence of sexual reproduction of *Phytophthora infestans* in Poland. *Phytopathology* 84:201–7
118. Swiezynski KM, Sieczka TM, Sujkowski LS, Zarzycka H, Guzowska-Zimnoch E. 1991. Resistance to *Phytophthora infestans* in potato genotypes originating from wild potato species. *Plant Breed.* 107:28–38
119. Swords KMM, Dahlbeck D, Kearney B, Roy M, Staskawich BJ. 1996. Spontaneous and induced mutations in a single open reading frame to both virulence and avirulence in *Xanthomonas campestris* pv. *vesicatoria avrBs2*. *J. Bacteriol.* 178:4661–69
120. Ten Houten JG. 1974. Plant pathology: changing agricultural methods and human society. *Annu. Rev. Phytopathol.* 12:1–11
121. Tenzer I, Gessler C. 1997. Subdivision and genetic structure of four populations of *Venturia inaequalis* in Switzerland. *Eur. J. Plant Pathol.* 103:565–71
122. Thakur RP, Leonard KJ, Jones RK. 1989. Characterization of a new race of *Exserohilum turcicum* virulent on corn with resistance gene *Ht*N. *Plant Dis.* 73:151–55
123. Thakur RP, Rai KN, Rao VP, Rao AS. 2001. Genetic resistance of pearl millet male-sterile lines to diverse Indian pathotypes of *Sclerospora graminicola*. *Plant Dis.* 85:621–26
124. Torres-Montalvo JH. 1998. *The population genetics of Sporisorium reilianum, the head smut pathogen of sorghum and maize*. PhD thesis. Texas A&M Univ. 90 pp.
125. Triantaphyllou AC. 1971. Genetics and cytology. In *Plant Parasitic Nematodes*, ed. BM Zuckerman, WF Mai, RA Rohde, pp. 1–32. New York: Academic
126. Troedson RJ, Ryley MJ, Byth DE, Irwin JAG. 1991. Effect of Phytophthora root and stem rot on the response of field-grown soybean to saturated soil culture. *Aust. J. Agric. Res.* 42:791–99
127. Tu JC. 1992. *Colletotrichum lindemuthianum* on bean. Population dynamics of the pathogen and breeding for resistance. In *Colletotrichum—Biology, Pathology and Control*, ed. JA Bailey, MJ Jeger, pp. 203–24. Wallingford, UK: CABI
128. Vos P, Hogers R, Bleeker M, Reijans M, van der Lee T. 1995. AFLP: a new technique for DNA fingerprinting. *Nucleic Acid Res.* 23:4407–17
129. Webb RE, Bonde R. 1956. Physiologic races of the late blight fungus from potato dump-heap plants in Maine in 1955. *Am. Potato J.* 33:53–55
130. Wellings CR, McIntosh RA. 1990. *Puccinia striiformis* f. sp. *tritici* in Australasia: pathogenic changes during the first 10 years. *Plant Pathol.* 39:316–25
131. West JS, Kharbanda PD, Barbetti MJ, Fitt BDL. 2001. Epidemiology and management of *Leptosphaeria maculans* (phoma stem canker) on oilseed rape in Australia, Canada and Europe. *Plant Pathol.* 50:10–27
132. Whisson SC, Drenth A, Maclean DJ, Irwin JAG. 1994. Evidence for outcrossing in *Phytophthora sojae* and linkage of a DNA marker to two avirulence genes. *Curr. Genet.* 227:77–82
133. Wiese MV. 1991. *Compendium of Wheat Diseases*. St. Paul, MN: APS Press
134. Williams EB, Brown AG. 1968. A new

physiological race of *Venturia inaequalis*, incitant of apple scab. *Plant Dis. Rep.* 52:799–801

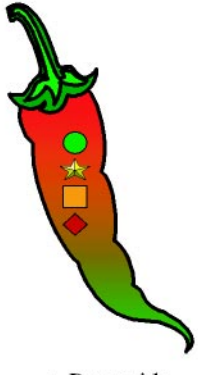
135. Wolfe MS. 1984. Trying to understand and control powdery mildew. *Plant Pathol.* 33:451–66
136. Wolfe MS, McDermott JM. 1994. Population genetics of plant pathogen interactions: the example of the *Erysiphe graminis-Hordeum vulgare* pathosystem. *Annu. Rev. Phytopathol.* 32:89–113
137. Xia JQ, Correll JC, Lee FN, Marchetti MA, Rhoads DD. 1993. DNA fingerprinting to examine microgeographic variation in the *Magnaporthe grisea* (*Pyricularia grisea*) population in two rice fields in Arkansas. *Phytopathology* 83:1029–35
138. Zeigler RS, Scott RP, Leung H, Bordeos AA, Kumar J, Nelson RJ. 1997. Evidence of parasexual exchange of DNA in the rice blast fungus challenges its exclusive clonality. *Phytopathology* 87:284–94
139. Zeigler RS, Tohme J, Nelson RJ, Levy M, Correa VF. 1994. Lineage exclusion: a proposal for linking blast population analysis to resistance breeding. In *Rice Blast Disease*, ed. RS Zeigler, SA Leong, PS Teng, pp. 267–92. Wallingford, UK: CABI
140. Zhu Y, Chen H, Fan J, Wang Y, Li Y, et al. 2000. Genetic diversity and disease control in rice. *Nature* 406:718–22
141. Zimmer DE, Schafer JF, Patterson FL. 1963. Mutations for virulence in *Puccinia coronata*. *Phytopathology* 53:171–76



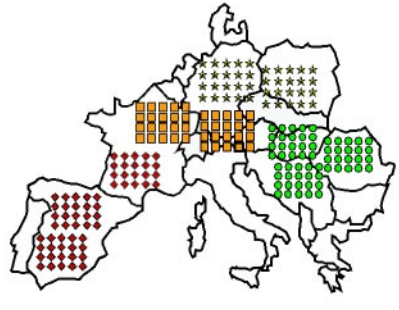
a. Traditional approach: plug, plant, and pray



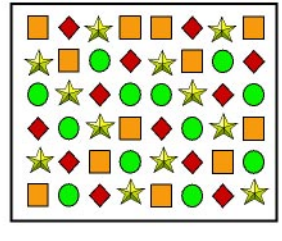
b. Rotations in space and time



c. Pyramids



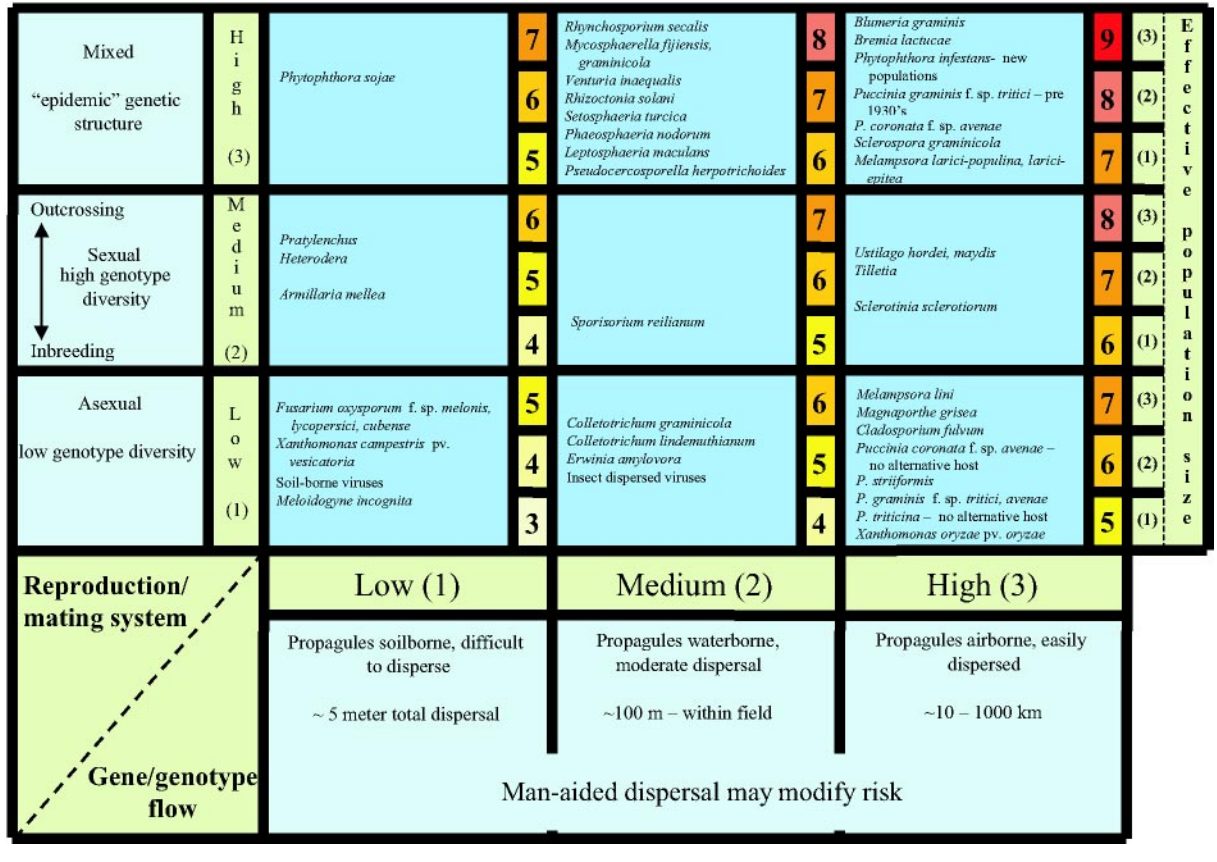
d. Regional deployment



e. Multilines and mixtures

See legend on next page

**Figure 2** (See figure on previous page) Strategies for deployment of major resistance genes (R-genes). (*A*) The traditional "plug, plant, and pray" approach of deploying single R-genes one at a time in a sequence that matches the boom and bust cycle. (*B*) Rotations of R-genes in time or space. Each R-gene is deployed over a limited number of years or area, and is withdrawn before the corresponding virulence allele achieves a high frequency in the pathogen population. (*C*) R-gene pyramid. All R-genes are placed together in one plant genotype. (*D*) Regional deployment. Different R-genes are grown in different regions. This can be part of a gene rotation as described in panel B. (*E*) Cultivar mixtures and multilines. Individual R-genes are grown as an intimate mixture in the same field.




See legend on next page

**Figure 4** (See figure on previous page) Scale of evolutionary risk organized according to reproduction/mating system, gene/genotype flow and effective population size. The organization of this diagram is modified from Figure 2 of Brent & Holloman (8). Effective population size ($N_e$) is on a 1–3 scale where 1 is small $N_e$, 2 is average Ne, and 3 is large $N_e$. Assignment of total risk value assumes that all effects are additive. This risk model assumes that mutation rates are constant and that selection is efficient for all pathogens. Placement of example pathogens is according to principles explained in the text or from Table 2.

*Annual Review of Phytopathology*
*Volume 40, 2002*

# CONTENTS