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Biological Control of Plant Pathogens: Theory to Application

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It has been customary for the APS presidential address to be more philosophical than technical, and in this respect, the topic chosen for my address may seem like a departure from tradition. My topic is both. It is intended as a technical treatment, but with liberal doses of my own philosophy. A presidential address should also attempt to both challenge and unite us as a profession. Biological control presents one of the greatest challenges of all times to our discipline, and it requires the attention of all facets of our discipline—virology, bacteriology, nematology, and mycology, genetics, molecular biology, ecology, and soil microbiology. It offers something for commercial interests as well as the public sector and to the practitioner as well as the scientist conducting basic research. The topic of a presidential address should be appropriate for the times, and biological control is that. The topic should be dear to the heart of the speaker, and biological control is certainly that to me. Finally, it should not escape our attention that the first experiments on biological control of plant pathogens with antagonists were conducted here in Canada nearly 60 years ago by G. B. Sanford. His first paper (26) on factors affecting the pathogenicity of the potato scab organism was published in PHYTOPATHOLOGY in 1926. Later, Sanford and W. C. Broadfoot (27) published on biological control of the wheat take-all fungus, which was the first usage of the term "biological control" in plant pathology.

Biological Control, A Broad Concept

K. F. Baker and I, in both of our books on biological control of plant pathogens (2,7), define biological control in the broadest sense to include the use of any organism to control a pathogen. An exception, of course, must be people; otherwise biological control would be expanded to include people producing virus-free meristem cultures of plants, people going through fields to eradicate diseased plants, or even people spraying fungicides on plants. On the other hand, our definition includes the use of higher plants as well as microorganisms, and we include host plant resistance as one of the best and most effective biological controls.

This broad definition seems to be generally accepted by plant pathologists today, although some have questioned our broad concept. We have also been chided to the effect that:

> one solution to the poor record of biological control of plant pathogens is to broaden the definition to include the successful cultural practices and breeding for host plant resistance.

However, we have proposed and stuck with this broad definition, not as a way to embellish the record of accomplishments in biological control, but rather as a way to expand the options for the future. Consider, for example, a gene that regulates production of a substance inhibitory to a plant pathogen. If that gene is carried and expressed in cells of a root-colonizing bacterium and that bacterium, when applied as a seed treatment, colonizes and protects the roots of that plant, obviously this is biocontrol. Consider, however, that a genetic engineer manages to transfer this gene into the host plant genome and have it expressed by way of inhibitors released with the root exudates. It would be silly and probably counterproductive if the expression of this gene in a microorganism on the root could be called biocontrol but could not be called biocontrol if expressed in root cells of the host plant itself.

Including the host plant in our concept of biological control should not be strange to plant pathologists. Most of the pathogens with which we deal exist through much or all of their life cycle in intimate association with their host, and most strategies directed at their control have had to consider the host as an integral part of the control. At the very least, the host provides the battleground where antagonists inhibit or displace pathogens. We call this the "passive role" of the host in biological control. However, there is no logical reason to allow for a passive role of the host in biological control but to exclude the active role—active host plant resistance. F. G. H. Lupton, plant breeder at the Cambridge Plant Breeding Institute also holds to this opinion, which he expressed in his 1983 Presidential Address to the Association of Applied Biologist (19). The title of his address was "Biological Control. The Plant Breeder's Objective."

Biological control must no longer be recognized as a science based mainly on the disciplines of ecology, taxonomy, and soil microbiology. Biological control is also based on the disciplines of plant and microbial genetics, molecular biology, cytology, biochemistry, plant physiology, and many others. Moreover, biocontrol is not just applicable to a few nematodes and phytopathogenic fungi; Allen Kerr (14) and others have now shown its potential against bacteria, and the virologists are coming up with some of the best biocontrols, using avirulent and modified virus strains to obtain cross protection against virulent plant viruses (9). Biological control can be accomplished by genetic manipulation of the host, antagonist, or even the pathogen itself and may be directed at the ecosystem, population, or individual level. An example of genetic manipulation of a pathogen at the population level is the use of a mixture of plant cultivars, each having a different gene for resistance to prevent any one virulence gene from becoming dominant in the pathogen population (34). An example of genetic manipulation directed at an individual pathogen is the introduction of hypovirulent *Endothia parasitica* into cankers in chestnut trees to render the pathogen hypovirulent in the canker (1). Biological control, broadly defined, may occur remote from the plant, it may occur on the plant, or it may take place inside the plant; and although it often depends on antagonistic microorganisms in the classic sense, it also depends on the plant and may even use the pathogen against itself. It is the broad concept of biological control that makes it so fascinating as a field of study and potentially so useful as a long-term solution and plant-disease-management strategy.

A Need for Broader Thinking

As broadly defined, biological control has been the cornerstone of our efforts in plant disease management all along. Development of a resistant variety by conventional plant breeding is just as much a way to achieve biological control as is induced resistance, or the development of a resistant variety by genetic engineering; and the use of a crop rotation combined with tillage to permit or accelerate useful biological destruction of inoculum of some pathogen in soil is just as much biological control as is the introduction of a hyperparasite to destroy inoculum. Plant pathologists and breeders have been doing biocontrol research all along—and have been doing a good job as well, I might add. As Lupton (19) stated:

> accelerating or diverting evolutionary processes in order to obtain genotypes adapted to [man's] needs are a most important example of the application of biological control to agricultural and horticultural crops.

However, having conjured up an image that we have been doing

biocontrol research all along, I must point out that the thinking behind much of this research has not been oriented toward biological control. Those who conduct research on pathogen control by cultural practices, in general, have not thought about their controls as biological controls. Similarly, except for a few, such as F. G. H. Lupton, those who work on host resistance have usually not thought of themselves as working on biological control. Maybe the way we think or what we call these and other areas of biological control doesn't matter, but I believe it does. With apologies for singling out those who conduct research on resistance and the host-pathogen interaction, I will use this research area to illustrate my point.

Understanding host and pathogen is challenge enough, but we must also recognize that disease is more than the outcome of an intimate interaction between just two organisms. Disease is the outcome of an interaction between host, pathogen, and a variety of *nonpathogens* that are also poised in the infection court and that have potential to either limit or enhance the activity of the pathogen or the resistance of the host (7). Pathogens do not occur on the host in pure culture, yet they are remarkably successful on the phylloplane as well as in the rhizosphere. Moreover, antagonism from the associated nonpathogenic microbiotia can follow the pathogen deep into the infected tissues and does not necessarily cease at the surface of the host. A pathogen to be successful, therefore, not only must employ certain weapons of offense, required for successful colonization of the host, it must also employ certain weapons of defense, to prevent or avoid being preempted or overrun by the nonpathogens that coexist in the infection court with it.

Most pathogens probably succeed within the milieu of plant colonists by finesse—by careful management of the nutrients and energy supplies in their niche in a way that does not invite or attract unwanted company. A few probably succeed by their ability to liberate secondary metabolites inhibitory to the neighboring nonpathogens. In this regard, a toxin produced by a pathogen is almost invariably studied for its role as a pathotoxin, but maybe it serves the pathogen as an antibiotic to inhibit nonpathogens during pathogenisis. What are the roles of phytoalexins? Perhaps it's to the advantage of a pathogen to initiate phytoalexin accumulation—in concentrations that it can tolerate but that potential competitors in the infection court or lesion cannot tolerate.

My point is that, although excellent progress is being made in understanding the genetics and biochemistry of the host-pathogen interaction, this work is serving to reveal only one aspect of biological control on the host surface or within the host, and even this aspect generally has not been thought of as a study of biological control. Are we in the business of studying mechanisms of host resistance or mechanisms of biological control? The former is somewhat limited in scope compared to the latter, which purports to include not just host resistance but all mechanisms by which the pathogen may be limited or controlled biologically while it is attempting to establish itself in its host. Our goal is to use biological control in the field, and to this end we must broaden our thinking to include all possible biological constraints on the pathogen.

John Naisbitt, in his book "Megatrends" (21), illustrates this point with the U.S. railroad business. He points out that

> . . . railroads should have known that they were in the transportation business and not just railroading. They could have created systems that moved goods by rail, truck, airplane or in combination, as appropriate. Instead, they continued to be transfixed by the lore of railroading that had served the country so well—until the world changed.

Similarly, we should know that we are in the biocontrol business and not just in the host-resistance business. We can then create systems that control pathogens by host resistance, epiphytes that prevent the pathogen from infecting, secondary colonists that limit secondary inoculum formation, or some combination as appropriate.

Strategies for Use of Antagonists

The biological approaches to improving plant health with antagonists of plant pathogens span nearly the full range of approaches possible by other methods of pathogen control. The approaches can be subdivided into three broad strategies (7): biological control of pathogen inoculum, biological protection of plant surfaces, and biological control through induced resistance or cross protection. These categories are a logical sequence of biological control with antagonists remote from the plant, on the plant, or inside the plant.

Biological control of pathogen inoculum involves the destruction or crippling of pathogen inoculum or the prevention of its formation. This approach to biological control is along the lines of the classic concept of biological control by regulation of the pathogen population. It may be accomplished on or within the host plant itself after the host is infected, as with the introduction of hypovirulent *E. parasitica* into blight cankers on chestnut trees. It may also be accomplished after infection, by use of hyperparasites or secondary colonists of lesions to prevent production of secondary inoculum. More commonly, however, this approach is used remote from the host as a means to destroy primary inoculum of pathogens. The traditional long crop rotations permit the time required for biological destruction of pathogen inoculum by resident antagonists in soil, and tillage contributes to biological destruction of inoculum by fragmenting and accelerating the breakdown process of crop residues infested with pathogens. However, antagonists that can also be introduced into soil as a preplant or in-furrow application to destroy pathogen propagules (e.g., *Coniothyrium minitans, Sporidesmium sclerotivorum, Trichoderma* species, and other hyperparasites of sclerotia) give reason to believe that this area may soon become practical as well. We can also take encouragement from the recent successes with *Bacillus penetrans* (30) and certain other hyperparasites as agents for use in nematode control when applied to soil; the only serious obstacle here is the lack of an economical method for mass-rearing *B. penetrans*.

Biological protection of plant surfaces includes most of the recent successes with biological control by introduced antagonists. It is interesting to note that this and the third approach to biological control with antagonists that I have stated went virtually without mention at the 1963 Berkeley symposium on "Ecology of Soilborne Plant Pathogens—Prelude to Biological Control" (3). Examples of this approach now include:

- Biocontrol of *Heterobasidion annosum* by *Peniophora gigantea* applied to freshly cut stumps of pine (25),
- Biocontrol of the crowngall pathogen by *Agrobacterium radiobacter* strain K84 (14),
- Increased growth and yield of crops by seed treatment with *Bacillus subtilis* strain A13 to protect against root pathogens (5).
- The plant growth-promoting rhizobacteria applied on potatoes, beets, and other crops to protect them against subclinical root pathogens (15,31),
- Biocontrol of ice-nucleation active (INA) strains of *Pseudomonas syringae* by INA-negative strains of *P. syringae* or *Erwinia herbicola* to prevent frost injury (18),
- The biocontrols of take-all (32) and now also Pythium root rot (4,33) of wheat by root-colonizing fluorescent pseudomonads.

With all of these examples, an aggressive colonist of the plant's surface is established sufficiently in advance of the pathogen to preempt or inhibit the pathogen. In the case of the soilborne pathogens, the antagonist is usually also inhibitory to the pathogen through production of a bacteriocin, a broad-spectrum antibiotic, or one or more siderophores. More will be said later about this approach to biological control with introduced antagonists. Suffice to say at this stage that this approach seems to offer the most in terms of potential use and commercialization for both field crops and high value ornamentals and fruit crops.

Induced resistance and cross protection is the most intimately dependent on a role of the host, either passively or actively. This may be the only practical biological control possible with antagonists introduced to control viruses and vascular pathogens that exist for most or all of their life cycle inside their host. One

successful case is the use in Brazil and Australia of mild strains of citrus tristeza virus to protect citrus trees against more severe strains of citrus tristeza virus (9). In Japan, biological control of Fusarium wilt of sweet potato is achieved by inoculating the cuttings with a nonpathogenic *Fusarium oxysporum* (22). The excellent work of J. Kuc and his associates (16) during the past 10–15 years on induced resistance in cucurbits, by prior inoculation with nonpathogens or with pathogens of other crops, gives encouragement that this strategy, like the other two I have mentioned, will soon be a commercial success. The major constraint here may be our own reluctance to introduce weak pathogens or modified pathogens into field situations. Obviously the risks must be weighed, but maybe we are too conservative. I think the risks are worth taking in many cases.

Biological Control, A Specific Case

The biological controls under development by D. Weller and myself for *Gaeumannomyces graminis* var. *tritici* and the *Pythium* species on wheat are presented in some detail to show the simplicity of the approaches used and also to show the potential benefits and the problems of this approach to improving root health.

Take-all is easily controlled by crop rotation, a perfectly good biocontrol. The disease can also be controlled by monoculture wheat, which initiates a different biological control—one responsible for take-all decline. We know that the factor responsible for take-all decline is transferable from field to field, is sensitive to pasteurization temperatures of 60° C or greater for 30 minutes, is sensitive to chloropicrin or methyl bromide, and seems to inhibit the pathogen mainly on the root surface or in the lesion after infection, rather than during its saprophytic stages in soil and in the rhizosphere (8). A. D. Rovira and I (8) and also R. W. Smiley (28,29) obtained evidence that the suppression results from root-colonizing fluorescent pseudomonads, but the best evidence for this explanation was obtained by D. M. Weller.

Weller demonstrated that the total population of fluorescent pseudomonads is about the same on roots of wheat growing in suppressive and conducive soils, but the proportion inhibitory to *G. graminis* var. *tritici* is 5–10 times greater on roots in suppressive than on roots in conducive soil. His work clearly indicates a qualitative shift in the makeup of the population of this bacterial group on roots of wheat as the soil changes from conducive to suppressive. Our theory is that the fluorescent pseudomanads, being normal colonists of roots and being quick to respond to readily available sources of nutrients, are among the dominant organisms that establish as secondary colonists in the take-all lesions. We have evidence that these organisms colonize the infected roots as secondaries, in very high populations, and that within the lesion, the intense competition among the bacteria favors mainly the most aggressive and inhibitory strains. This can account for the qualitative shift within the total population of fluorescent pseudomonads toward strains that produce antibiotics. These bacteria, by colonizing the lesion, become cohabitants with *G. graminis* var. *tritici* in the crop residue during its saprophytic existence and are then poised to reestablish on the roots of the next crop infected by *G. graminis* var. *tritici*.

Our approach to biological control of this fungus using these bacteria has been to first isolate them from roots growing in suppressive soil infested with *G. graminis* var. *tritici*. We use suppressive soil to "stack the deck" in favor of finding effective antagonists, and we isolate only from roots in the presence of *G. graminis* var. *tritici* to help insure that the bacteria will then be adapted not just to wheat roots but to wheat roots infected with the take-all fungus. The second step is to screen the isolates for inhibitory activity against the fungus on agar media. These bacteria, to be effective, must be aggressive colonists of the roots and preempt the take-all pathogen, but we think it will be best if the strains also have a strong ability to produce one or more antibiotics, siderophores, or both kinds of inhibitors to limit growth of the take-all pathogen. Our third step is a greenhouse test where the bacteria are applied on the seed and must then colonize the roots as they grow through *G. graminis* var. *tritici*-infested soil. We then test them in field plots with either introduced or natural inoculum of the take-all pathogen.

Many effective strains have been found by this method, but the problem is that control is only partial or it fails completely in at least one of three trials. We are therefore searching for super-strains and may eventually need to use recombinant DNA methods to produce them. We are also beginning to look for variation in wheat genotypes for the ability to support these biocontrol bacteria and thus improve on the efficacy and consistency of control.

For biocontrol of the *Pythium* species responsible for root rot of wheat, we have no known suppressive soils as a source of antagonists. We therefore are taking the next best approach, which is to isolate from roots of the healthiest-appearing wheat seedlings growing in soil naturally infested with *Pythium* species. These isolates are screened in vitro for inhibitory potential against *Pythium ultimum* and then in vivo by methods similar to those used to find strains effective against the take-all fungus (4). Finally, the isolates are tested in the field in soils naturally infested with *Pythium* species. Remarkably, Weller's first field trial was a success, with one strain producing a 27% yield increase over the check in replicated plots with natural infection in the field (33). Again, the evidence is that ability to colonize the rhizosphere and to preempt the pathogens and also to produce antibiotics and/or siderophores all are important traits of these biocontrol bacteria.

This increased growth response of plants to seed bacterization always raises the question of whether the bacteria are producing nutrients or growth factors for the plant. A major breakthrough, and a change in thinking, came with the discovery of *Bacillus subtilis* A13 by P. Broadbent, K. F. Baker, and Y. Waterworth in Australia (5). This strain applied as a seed treatment increased growth and yield of sweet corn, carrots, wheat, barley, oats, and many other economic plant species. The significant trait of A13 was its broad-spectrum antibiotic activity; it was inhibitory to all nine test fungal pathogens used by Broadbent, Baker, and Waterworth in their in vitro screening procedure. This was one of the first clues that ability to produce antibiotic was important and that improvements in root health account for the yield increases in response to seed bacterization. Work by the Berkeley group with the plant growth-promoting rhizobacteria (15,31) and our own work with pseudomonads in wheat (4,32) verify the importance of inhibitors and root protection. In both cases, no increased growth response occurs in fumigated soil and inhibitor-negative mutant strains are ineffective in natural soil. Knowing this, Weller and I would not think of testing our strains in just any field; we test only where our target pathogen is the yield-limiting factor, with the result that we are getting a positive response in one-half to two-thirds of our trials. F. P. Geels and B. Schippers (11) have also shown this for potatoes in Holland; they got highly significant growth responses in plots where potatoes had been grown continuously for many years and where yields had declined, but not in plots where root pathogens were already controlled by a three-year crop rotation.

This tendency to attribute the increased growth response of plants to an increase in the availability of nutrients or growth factors when seed bacterization is used is only one of several examples in which plant and soil scientists have underestimated the importance of root health. Decline of yield with crop monoculture has been attributed in the past to depletion of soil nutrients. Some nutrient depletion may occur, but this cannot explain the yield decline. As pathologists, we know that root pathogens of the crop multiply with monoculture of that crop and are responsible for much or most of the yield decline, including the appearance of nutrient deficiency-like symptoms in the crop. Another example is the increased growth response of plants to soil fumigation, which has been attributed by many to the flush of mineral nutrients released from the killed microbial biomass. Obviously some mineral nutrients are released, but the plant-growth response cannot be duplicated by making an equivalent application of these nutrients. Increased growth response has repeatedly been shown to result from improvements in root health, owing to the elimination of root pathogens. The occasional poor growth of plants in heavy crop residue, and the replant problem, have been attributed to

phytotoxins, allelopathy, and autotoxicity but are now turning out to be the result of root damage caused by soilborne pathogens. Regarding the plant growth response to seed bacterization, except for the well-known nitrogen response to rhizobia, I'm not aware of anyone having shown that a strain effective in promoting plant growth produces significant growth factors and that growth factor-negative mutants do not promote growth. On the other hand, several have now shown that antibiotic- or siderophore-negative mutants do not promote growth. I believe that with biological seed treatments, we have a chance to achieve improvements in root health and increases in yield that presently can only be achieved by crop rotation or soil fumigation, but obviously much more work remains to be done.

Directions for the Future

It would be presumptious of anyone to suggest what directions biological control of plant pathogens might take in the future. The only safe statement is that the directions will be varied, numerous, and limited only by our imagination. It is remarkable to note the number of new agents and approaches to biological control that emerged in the short time between our first and second books—giant amoebae that destroy pathogen propagules in soil, hypovirulence mechanisms in *E. parasitica*, and the plant growth-promoting rhizobacteria, to name just three—and I have no doubt that we will soon discover other new and equally novel approaches to biological control. Nevertheless, I would like to suggest some general areas of research that deserve consideration in the near future.

Making More Effective Use of Antagonists

There are two obvious approaches to more effective use of antagonists in biological control: 1) learn to enhance, or at least not to upset, the benefits of the resident antagonists that operate in suppressive soil or as suppressive populations of endophytes and epiphytes on our crop plants; and 2) find or develop superior antagonists for introduction into soil or for plant inoculation. We need a balanced and simultaneous effort with these two approaches. They are inseparably interrelated. The resident antagonists provide the pool from which we can obtain our candidates or prototype-candidates for use as introduced antagonists, and our goal with introduced antagonists should be to have them then function as residents. Weller and I are encouraged by our results with *Pseudomonas fluorescens* introduced on wheat seed for take-all control (32), but the control achieved by this approach is not nearly as effective as the take-all decline that develops with wheat monoculture. Our goal, therefore, is twofold: 1) to introduce these antagonists to accelerate or enhance take-all decline and 2) to determine the effects of cultural practices on the expression or persistence of the take-all decline phenomenon.

To find effective antagonists for application to soil or planting material, the best approach is to seek them where the target pathogen should be causing disease but is not. Soils from fields where take-all has declined have been our best source of introduced antagonists. The weakly virulent strains of citrus tristeza virus used in Brazil for cross protection against the virulent citrus tristeza virus were isolated originally from citrus trees that were healthy in an otherwise severely diseased citrus orchard (9). K. Ogawa and H. Komada in Japan (22) obtained an effective biocontrol strain of *F. oxysporum* from the vascular tissue of a sweet potato plant that was healthy where other plants had died from wilt caused by *F. oxysporum* f. sp. *batatas*. On the other hand, according to A. Kerr (personal communication), strain K84 effective against crown gall is unlikely to occur naturally in the absence of gall tissues because it, like the pathogen, depends on the opines produced by the gall tissue as a source of carbon and energy. The rule that antagonists should be sought where disease is controlled applies generally, but exceptions are bound to occur. The best rule may be that "antagonists are where you find them."

These latter examples emphasize another point: antagonists are to be found not only in soil, but also on and within the host plant itself. Where we look should be determined by the job to be done: if the antagonist is to live in soil, obviously we should seek our candidates from soil, but those to be used for plant protection should be sought from among the epiphytes or endophytes on and in the plants themselves.

The most promising approach at present is the development of antagonists through breeding, induced mutations, or by genetic engineering. The M-II strain of tobacco mosaic virus used to protect glasshouse tomatoes against virulent tobacco mosaic virus (24) is possibly the first biocontrol agent developed by an artificial approach. G. C. Papavizas and his associates in Beltsville now have mutant strains of *Trichoderma viride* with resistance to specific fungicides that can be used in combination with those fungicides (23). We have also witnessed the first antagonist developed by recombinant DNA technology, namely the INA-negative strains of *P. syringae* of S. Lindow and N. Panopoulos. These strains are identical to the INA-positive strains of *P. syringae*, except that the genetic material for production of the ice-nucleating substance has been removed. The current U.S. Federal Court order that prevents field testing of these biocontrol candidates will delay but will not stop this important approach to protecting plants from pathogens and may ultimately prove beneficial to the process and protocol by which biocontrol agents are evaluated and approved for commercial use.

Use of the Pathogen as an Antagonist

We are only beginning to recognize the many ways the pathogen may be used to bring about its own biological control. Strain K84 of *A. radiobacter*, the hypovirulent *E. parasitica*, the INA-negative strains of *P. syringae*, and the avirulent virus strains used for cross protection all are examples of one strain of the pathogen being used to control another strain. We may ultimately find that our best antagonists will be modified strains of the target pathogen, because they will be best adapted to the niches or sites occupied by the pathogen. Occupancy and preemption of the infection court may be enough by itself, but if the strain can produce an inhibitor such as a bacteriocin, vector an infectious agent such as a dsRNA mycovirus, or trigger a resistance response in the host, obviously the control will be more effective.

Workers in Japan have noted that damping-off of sugarbeets caused by *Rhizoctonia solani* declines with repeated sowings of sugarbeets (13). However, these workers find no evidence of an increase in population of an antagonist associated with the decline in damping-off. Rather, the population of *R. solani* in the soil converts from highly virulent to weakly virulent or avirulent during sugarbeet monoculture (13), and the pathogen is no longer able to cause disease. The phenomenon may be different from that of the transmissible dsRNA mycovirus-like agent reported by B. Castanho, E. E. Butler, and R. J. Shepherd (6). Japanese workers have isolated a DNA plasmid from some (but not all) of the avirulent cultures (12). Take-all decline was once also thought to result from loss of virulence in the population of *G. graminis* var. *tritici* (17). Although the evidence is against this explanation for take-all decline, it is well documented that isolates convert from virulent to avirulent under certain conditions (20). It is possible that some pathogens possess a genetic mechanism whereby they regulate their virulence, perhaps as a way to avoid destroying their hosts. Exploitation of the genetic mechanisms for avirulence offers an approach to biological control and deserves much more study. Even the common phenomonon of loss of virulence during maintenance on agar media, if understood, might offer an avenue to biological control.

Use of the Host Plant

The conventional methods of breeding for resistance to pathogens will continue to be our most productive approach to biological control with the host. However, I repeat my plea for more attention to breeding plant genotypes more supportive of nonpathogenic populations of epiphytes and endophytes that have potential as antagonists of the pathogen.

We should also consider that while higher plants represent a pool of useful genetic resistance, microorganisms are also a source of useful genes for controlling pathogens, and that soon the technology will be available to move these genes into plants. Genes that regulate antibiotic production by microorganisms are

potential resistance genes for plants. The same holds for genes that regulate avirulence in the pathogen or the production of self-inhibitors by pathogens.

I stated earlier that the future of biological control will be limited only by our imagination. I would like to reemphasize this point by adding that from all appearances, we are no longer seriously limited in our research efforts by either institutional constraints or lack of funding. This is a strong but true statement. Biological control is now widely accepted in our profession, a statement that could not be made only 10 years ago. In addition, the private and public sectors both are squarely behind biological control research, with grant moneys and private capital available for this area of research as never before. Moreover, a number of administrators in the U.S. agriculture research establishment, including some distinguished plant pathologists, have done an outstanding job in helping to remove some of the institutional and funding constraints to research and development in all areas of biotechnology, including biological control. The Agricultural Research Service of the USDA has also made significant strides in this direction with the Six-Year Plan and by identification of biological control research among the very high priority areas. My point is this—and I'm speaking to students and bench scientists—it's now up to us! Our commitment to biological control, our confidence in it, and our ability to generate new ideas and to further develop existing ideas are the only real limitation to progress in biological control. Let us accept this challenge that is before us.

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