The many types of disease resistance

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This paper deals with diseases caused by microorganisms as parasites when they grow inside higher plants. For a particular plant the extent to which a parasite does not grow and, therefore, cause disease is a measure of disease resistance. The causes of resistance are the conditions in the plant that limit growth. They are of two main types. The condition may be independent of the parasite as when cell walls of uninfected plants are lignified and therefore potentially resistant to the penetration and degradation upon which growth of the parasite in the plant may depend. Or the condition may be a response to the parasite so that, for example, unlignified cell walls become lignified and again impede growth of a parasite. This second induced type of resistance is almost certainly much more important and is therefore the subject of this paper. It will be discussed under three main headings for which the least unsatisfactory terms probably are race-specific, race non-specific and non-host resistance.

1. Race-specific resistance

In this, by far the most studied, cultivars of a plant are differentially resistant to races of a parasite in patterns which in some diseases have been shown to reflect a matching of a host gene for resistance (R) and a pathogen gene for low virulence (P) for a series of pairs of such genes.

Resistance almost always is dominant and in the few diseases in which genetic analysis of the pathogens has been possible, avirulence is dominant to virulence. When a pair of matching genes (P x R) which would confer resistance occurs with another (p x r) which alone would mean susceptibility, then the phenotype is resistant. From these and related facts it may be inferred that it is P x R that is determinative and that when it does not occur (p x R, P x r, p x r) then the phenotype is susceptibility. This inference is the basis of most past and current research on resistance. Its aim has been to determine how a low virulence gene P matched by a resistance gene R leads to conditions which limit growth of the parasite. As might be expected it has been usual to select for study diseases in which P x R allows very little growth of the parasite and little disease whereas the other combinations allow much more of both. The highly resistant reaction is usually associated with death of one cell or of a few cells to which the parasite is confined. It is usually referred to as a hypersensitive reaction or response (HR). Whether or not the parasite remains alive in the killed cells has rarely been determined but its death is not critical in the context of resistance. Neither need be the death of host cells which is usually regarded as an essential feature of HR. Changes in host cells falling short of death could be and almost certainly are in some diseases every bit as effective in...
severely limiting growth of a parasite. The essential feature of HR is perhaps not so much the nature and expression of the changes in cells containing or close to the parasite as the effect of these changes in drastically restricting its growth. And even thus it must be remembered that in some diseases and for different pairs of $P \times R$ genes there is a continuum between HR as high resistance and the parasite confined to one cell or a few cells and intermediate resistance (or low susceptibility) involving many more cells not all of which are killed. Plant pathologists have perhaps become too preoccupied with death of cells as a criterion of HR. Some have gone so far as to describe the killing of cells by an abiotic agent as HR. This would possibly be justified if the agent were also the agent from a parasite which caused HR or if it acted through the same mechanism. But any less discriminating use is hardly justified and can be confusing.

Next and briefly the conditions that restrict growth and first of the obligate parasite which continues to grow only in association with host cells that remain alive although, of course, almost certainly different and possibly very different from corresponding cells in uninfected tissues. Death of cells no matter how caused could explain resistance but from this it must not be assumed that it does. The parasite may cause other changes which prevent growth of the obligate as they do of the facultative parasite and these may or may not depend upon cell death.

Death of cells almost always will not explain resistance to facultative parasites which can grow on dead cells. Neither would damage short of death because probably this would release substances that would be expected to sustain the growth of a parasite. Therefore what mechanisms of resistance are induced by changes in host cells? The one most studied is the accumulation of substances toxic to parasites, phytoalexins, to concentrations sufficient to limit their growth as seen in resistant reactions. In uninfected tissues phytoalexins either are undetectable or present in concentrations insufficient to decrease significantly growth of the parasite. In resistance responses, they may accumulate as products of new biosynthetic pathways, of activated existing pathways which operate at much lower levels in normal cells, or because of decreased breakdown of phytoalexins in such pathways. Such evidence as there is indicates that phytoalexins are usually the products of new pathways. In view of the emphasis of past and current research on phytoalexins as the final cause of resistance it is surprising that there is so little quantitative evidence about rates and timing of their accumulation in resistant and susceptible reactions and whether these can explain differences in growth of a parasite. Much of the evidence is not much more than the demonstration that phytoalexins do accumulate more rapidly in resistant than in susceptible responses.

Phytoalexins act in resistance because they are toxic to parasites. If one or more do not accumulate sufficiently, then clearly something else must decrease the growth of the parasite. Lignification or closely related changes in cell walls has been studied in this context but only in a few diseases. No doubt there are also other mechanisms particularly in resistance to obligate parasites. The rest of the paper will be confined largely to phytoalexins as causes of resistance but almost all would apply to other mechanisms.

1.1 Cell damage and phytoalexins

In resistant responses phytoalexins accumulate in and around cells damaged and usually killed by the parasite. But almost from the start of research on phytoalexins it
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has been known that phytoalexins may accumulate at similar rates following damage caused by other agents. Thus a bewildering variety of substances cause pisatin to accumulate in pea tissues. Substances may have these effects in concentrations that do not kill plant cells; UV radiation may act similarly. Therefore it seems that accumulation, probably because of new or greatly increased synthesis, follows damage to cells of which that caused by parasites is only one of the many forms, and thus I come to elicitors a word introduced some years ago for substances which elicit responses associated with resistance. "To elicit" means to "draw forth (what is latent; usu. fig.); draw out, evoke, (admission, answer from person)" (The Concise Oxford Dictionary, 1976). In the context of resistance it means not much more than "to cause" and "an elicitor" essentially means "a cause". Nevertheless there need be no harm and there can be some benefit from using elicitor in relation to resistance so long as the way in which it is being used makes clear that which is being elicited. Usually this is or is assumed to be the accumulation of phytoalexins.

It is comparatively easy to obtain from fungi, pathogens or otherwise, substances which in low concentration elicit the accumulation of phytoalexins when applied to plants. Most of them are polymers, carbohydrates or glycoproteins, which also are toxic to plant cells. Potent among these elicitors are branched β-glucans similar to those known to be major structural components of fungal cell walls (Albersheim and Valent 1978). Such elicitors can be extracted by drastic chemical treatment. Similar substances may also occur in culture fluids probably after autolysis of the cell walls. Much lower molecular weight products of degradation of such glucans also are active elicitors. Chitosan, a polymer of β-1,4 linked glucosamine residues is also an active elicitor (Hadhiger and Loschke 1981). An interesting recent finding is that β-1,3 glucanases from soybean tissues rapidly release from cell walls of Phytophthora megasperma f. sp. glycinea a glucomannan which elicits accumulation of glyceollin in soybean tissues (Keen and Yoshikawa 1983).

Interesting as are these glucans both as elicitors of the accumulation of phytoalexins and for their toxicity to plant cells at low concentrations, they are unlikely to be important in race-specific resistance simply because they are not specific in their activity. Such elicitors from races of a pathogen have similar effects on differential cultivars of a host plant and may even be active on non-host plants. Also, glucan elicitors have been isolated from yeasts.

Certain glycoproteins from fungi are also active elicitors. Evidence for their specificity has been obtained for the following: soybean and P. megasperma f. sp. glycinea (Keen and Legrand 1980) or Pseudomonas glycinea (Bruegger and Keen 1979); Phaseolus vulgaris and Colletotrichum lindemuthianum (Anderson 1980); Pisum sativum and Fusarium solani (Daniels and Hadwiger 1976). These glycoproteins have not been characterized and their role in the diseases remains to be established. Another glycoprotein has been isolated and characterized from Rhizopus stolonifer as an endo-polygalacturonase which is an active elicitor of the synthesis of casbene in castor bean (Ricinus communis) (Lee and West 1981). But R. stolonifer is no more than a weak pathogen, usually of storage tissue, so this interesting work is not directly relevant to race-specific resistance. Similar results have been obtained for an endo-pectate trans eliminase from Erwinia carotovora (Davis et al 1982). Such enzymes rapidly kill plant cells so it is possible that it is death of cells that leads to the synthesis and accumulation of phytoalexins in ways to be referred to later; such activity would be very largely non-specific. These enzymes rapidly degrade pectic polysaccharides in cell walls.
to lower molecular compounds which are known to be active elicitors (Bruce and West 1982; Northnagel et al. 1983). Other substances may also be released from cell walls by these enzymes. But again their activity is likely to be non-specific certainly in the context of race X cultivar systems.

The most promising research so far reported is for races of *Fulvia fulva* (*Cladosporium fulvum*) and cultivars of tomato (De Wit and Spikman 1982). Cell-free extracts from leaves infected with virulent races contained substances which when applied to appropriate cultivars caused necrosis and chlorosis in patterns similar to those caused by the races themselves. The specifically active substances are produced in leaves irrespective of genotype so long as they are susceptible (De Wit et al. 1984). It is to be hoped that in spite of formidable technical difficulties more will soon be reported about the activity and nature of these substances because the lack of progress in isolating elicitors that act specifically has been frustrating particularly in light of the efforts that have been made and the expertise of those who have made them. On present evidence the best candidates for elicitors seem to be glycoproteins with specificity based on the carbohydrate moieties the structure of which would be determined by glycosyl transferases coded for by genes for avirulence in races of a pathogen (Albersheim and Anderson-Prouty 1975). Other possibilities would be of carbohydrates with specific activities which are released from the pathogen by host enzymes or from host cell walls by enzymes of the pathogen. Little is known about the products (elicitors) from races that determine their specificity still less, indeed almost nothing, is known about the complementary products in cultivars. It has been suggested that elicitors act directly on host DNA and in so doing depress transcription of one or more of the genes involved in synthesis of phytoalexins (Hadwiger and Schwochau 1969). But comparison with other systems suggests that plasma membranes are more likely to be sites of the products that react with elicitors and there is some evidence that they are (Yoshikawa 1983). If so there is the problem as to how a reaction in the plasma membrane leads to the synthesis of phytoalexins. This would require the formation of a secondary messenger that conveys information to the host cell nucleus followed by transcription of the genes controlling synthesis of phytoalexins. This second messenger may be constitutive elicitor which is released from plant cells damaged by freezing or in other ways and which causes accumulation of phytoalexins when applied to plant tissues (Hargreaves and Bailey 1978). One asks whether elicitor should be used for such substances if the elicitor also is used for a primary product of a pathogen that causes them to be released; it could be confusing to use the same term for substances of different origin and function unless it were suitably qualified to emphasize these differences. Endogenous "elicitors" may also be released from plant tissues by chemical or enzyme treatments that yield low molecular weight pectic polysaccharides some of which can cause the accumulation of phytoalexins. What now needs to be investigated is the connexion, if any, between the primary response, probably in plasma membranes, and the release or activation of enzymes which produce low molecular weight products as secondary messengers. Whatever their origin and nature the secondary messengers almost certainly must be able to move from cell to cell, at least locally, because the available evidence suggests that phytoalexins are synthesized in a small number of cells around the cell in which the primary response occurs. They then are assumed to move back into the infected cell where they accumulate to prevent growth of the pathogen. Almost always this cell is dead and it is usually assumed that death is a primary response to the pathogen. But because certain phytoalexins are known to be quite toxic to plant cells
there is the possibility that it is the accumulation of phytoalexins that kills the cell containing the pathogen. There would then be the problem of why they do not kill the cells in which they are synthesized but which usually remain alive around the cell containing the pathogen. If in some diseases they did so and if these cells also released a secondary messenger that induced synthesis of phytoalexins in adjacent living cells then a lesion could develop containing many more cells than in a typical hypersensitive response and similar to certain leaf spots in which tissue occupied by the pathogen is smaller than the lesion itself. Necrosis in such diseases is usually attributed to toxins produced by the pathogen. Then one must ask why the pathogen does not colonize the dead cells and continue to kill more and thus cause a spreading rather than a restricted lesion. Is it possible that the agent that kills host-cells is the phytoalexin that confines the growth of the pathogen. If so, there remains the problem of the restriction in size.

A last point relates to the abiotic agents that non-specifically cause accumulation of phytoalexins. If the sequence of events leading to this starts in plasma membranes how does the damage caused compare with that caused specifically by products of P genes which require complementary products of R genes to be effective, and are the secondary messenger and subsequent events similar?

So much for the model upon which most research on race-specific resistance has been based. There is another model which has attracted much less research but which may attract more in the future. Thus in potatoes and Phytophthora infestans, certain water soluble, low molecular weight glucans from the pathogen suppress necrosis and accumulation of phytoalexins otherwise caused by high molecular weight substances from the pathogen which act non-specifically (Doke et al 1980). The suppressors were specific in that they suppressed resistant responses only in cultivars that were susceptible to the race from which they were obtained. There is the difficulty that non-specific elicitors from the pathogen are many times more active than are the specific suppressors but if this can be resolved for conditions in vivo then there will be good evidence that it is the suppressors that are the determinants of specificity, at least in this disease. If so would the model cope with the fact that genes for resistance to P. infestans are dominant and so probably are genes for low virulence? One explanation is that specificity depends on reactions between mutable suppressors from races of the pathogen which prevent the binding of a common, non-specific elicitor to mutable receptors in the host which would be the primary reaction of a hypersensitive response leading later to accumulation of phytoalexins. In the absence of this response the pathogen would grow in the host plant. The credibility of this explanation depends on the concept of a non-specific elicitor and conversion of a progenitor to a pathogen by production of a species-specific suppressor which establishes a “basic compatibility” between plant and micro-organism which will be referred to later.

1.2 Host selective toxins

There are now about ten diseases in which such toxins and their receptors in plants are considered to be the determinants of specificity in the following manner. A virulent pathogen of susceptible plant X produces a toxin which damages plant X at concentrations much lower than those at which it damages other plants which are resistant to the pathogen. Production of the toxin and of virulence may be controlled by one gene as is susceptibility to the toxin and to the pathogen; both genes are usually dominant. Therefore it is susceptibility and not resistance that is determined by a
reaction between the two gene products; otherwise the plant is resistant. In considering this explanation one should consider the behaviour of the pathogen in resistant and susceptible responses. The resistant response has all the features of hypersensitivity—death of one cell or of a few cells to which the pathogen is confined. What kills the cell? It cannot be the host-selective toxin. And if the pathogen by some other mechanism kills one cell why does it not proceed to kill many more in the same way? Unless, of course, the killing of the cell leads to other changes that prevent growth of the pathogen as described in §2.1. In susceptible reactions in certain diseases the pathogen may grow for some time and not kill cells as in other diseases in which host selective toxins have not been implicated. Later many host cells are killed, presumably by the toxin which kills at low concentrations only cells with a receptor coded for by the gene for susceptibility. But at this stage the selectivity is redundant. The toxin could as well be non-specific as it is in many other diseases. It has also been suggested that the host-selective toxin first acts in susceptible plants by suppressing the hypersensitive response thus allowing the pathogen to grow and produce more toxin. In which case one must ask about the levels of toxin sufficient to suppress the hypersensitive response but insufficient to kill susceptible cells. Another puzzling feature of Victoria blight of oat and the host selective toxin victorin of Helminthosporium victoriae is that the gene-controlling susceptibility to the toxin is probably at the same locus as the gene controlling resistance to races of Puccinia coronata which have the matching gene for low virulence. How does the product of this gene compare with the toxin controlled by the gene for virulence in H. victoriae if they have a common receptor in oat plants? It seems to me that the explanation of resistance and susceptibility in diseases caused by pathogens that do produce host-selective toxins may not be so simple as commonly has been assumed.

2. Race non-specific resistance

In the above sections diseases in which resistance and susceptibility are controlled by pairs of matching genes have been considered. Despite this simplest of relationships we know little about how reactions between different gene products in pairs lead to a common mechanism of resistance and on how the same mechanism is induced by abiotic agents. The type of resistance now to be considered has been far less studied. It has been called race non-specific, minor gene, polygene, adult plant, durable, horizontal to name most of the terms. For present purposes the most useful refers to the lack of specificity between races and cultivars, race non-specific, which usually depends on more than one gene, usually many and undetermined. How do these genes control the mechanism of resistance in the light of race specific resistance, the only other system about which more than a little is known, and in which resistance is controlled by reactions between specific products of genes in pairs, \( P_1 \times R_1 \) or \( P_2 \times R_2 \) and so on, which do something that limits disease. This something may be the same for different gene pairs such as accumulation of the same phytoalexin (\( P_1 \times R_1 \) and \( P_2 \times R_2 \to X \)) or it may be different as when cultivars with different genes for resistance react differently to races of Erysiphe graminis f. sp. hordei (\( P_1 \times R_1 = X_1, P_2 \times R_2 = X_2 \) and so on). Does polygenic resistance compose a series of matching genes for low virulence (\( Pm \)) and for resistance (\( Rm \)). If so does \( Pm_1 \times Rm_1 \to Xm \) and \( Pm_2 \times Rm_2 \to Xm \) and so on such that \( \Sigma Xm \) is the mechanism of resistance and is less than \( X \) as almost always it is in
polygenic compared with monogenic resistance. Or does $Pm_1 \times Rm_1 \rightarrow Xm_1$ and $Pm_2 \times Rm_2 \rightarrow Ym_2$ and so on where $Xm_1$ and $Ym_2$ are different responses in which case what does $\Sigma Xm_1 + Ym_2 \ldots$ amount to, or do $Pm_1 \times Rm_1$ and $Pm_2 \times Rm_2$ cause effects quite different from those caused by $P_1 \times R_2, P_2 \times R_2$ in monogene systems? A related point is the one made some years ago along the following lines. In the absence of $P \times R$ let resistance be $X_0$ which is susceptibility. For $P \times R$ let resistance be $X$ which is high. Reaction $P_1 \times R_1$ gives $Xm_1$ which is much lower than $X$ but significantly higher than $X_0$. If this happens for a succession of $p$ genes then polygenic resistance may be $\Sigma Xm$ dependent on many relic $R$ genes now matched by complementary $p$ genes. This could also explain in part the persistence of this type of resistance in that such genes for low virulence would be unlikely to change to genes for higher virulence as they do so often in race-specific resistance. In biochemical terms it would be possible to speculate about the effects of the different genes in polygenic resistance in terms of gene dosage, changes in composition of gene products, resulting in different affinities, rates of reactions and so on but at present there is very little data upon which to base such speculations.

Finally under this heading may be considered the resistance of “land races”, the cultivars of less highly developed farming. They respond to pathogens much as do cultivars with race non-specific polygenic resistance which is probably land race resistance not lost in plant breeding programmes as other properties have been changed. But this resistance is sometimes lost. How does this happen if the effect of each of the many genes is small, even if each confers no more than a slight disadvantage in the absence of the pathogen. If land race resistance is polygenic resistance which depends on many genes each contributing to resistance then how does it relate to the resistance of the wild plant progenitors of the land races to common pathogens bearing in mind that wild plants carry many genes which confer high race specific resistance when transferred singly to crop plants but to which pathogens often and quickly become virulent. Also, it is now known for a few pathogens that such genes may function in wild plants much as they do in crop plants. The implications of findings such as these for a better understanding of race non-specific resistance should stimulate much more research on the behaviour of plant pathogens in populations of wild plants.

3. Non-host resistance

Although a minority of pathogens cause disease in many species of plants which are not closely related the great majority are highly specialized parasites of only relatively few of the vast range of plant species that potentially are available. Almost always a plant species is resistant to all micro-organisms except the few that are its pathogens. This has come to be called non-host resistance. It is of course by far the predominant form of resistance in wild and cultivated plants and it is also the type least studied because there seems rarely to have been the inclination and still less the money to investigate why a micro-organism is not a pathogen. Also, for non-host resistance there is the overriding difficulty that the genetics of crosses between a host and non-host plant almost always cannot be investigated. Nevertheless there is no good reason why this resistance should not be studied in other ways.

An interesting point about non-host resistance is that it was the basis of some of the earliest work which led to the concept of phytoalexins. And it is perhaps surprising that the earliest responses and the later accumulation of phytoalexins are, at least in some
non-host responses, similar to those in race × cultivar resistance where the product of race gene $P_1 \times$ product of cultivar gene $R_1 \rightarrow X_1$ the mechanism of resistance. In non-host resistance in which $X_1$ may be similar what replaces $P_1 \times R_1$? Are there multitudes of genes corresponding to $P_1$ in each micro-organism to match multitudes of complementary genes corresponding to $R_1$ in all the non-host plants with all the complications and ramifications which this would imply (Wood 1976). This seems improbable but how much evidence is there to refute it? Other hypotheses are based on an assumption that all plants have mechanisms for recognizing and reacting against non-self including microorganisms. Therefore, to become a pathogen of a particular plant a microorganism either must not induce this non-specific response or must later nullify its effects and thus allow a “basic compatibility” to be established; gene-for-gene systems are a later development (Bushnell and Rowell 1981; Ellingboe 1976; Heath 1982). I have raised elsewhere the difficulties of reconciling the postulated and general response of plants with the host of specific “basic compatibilities” i.e. all the diseases of plants, other than by schemes which are as complex as hypotheses based on gene-for-gene responses (Wood 1984). In the same paper I also considered briefly the following problems about non-host resistance: how does a saprophyte which is not a parasite of any plant differ from a highly specialized parasite which is not a parasite of all but a few plants; how do saprophytic members of a genus e.g. *Penicillium* or even of a species e.g. *Fusarium oxysporum*, differ from members that are specialized parasites; what happens when an isolate of a highly specialized parasite loses its pathogenicity so that it becomes essentially a saprophyte; stating that a microorganism becomes “compatible” with a plant, in other words a parasite, means that before this happened it was a non-parasitic symbiont (and therefore compatible in the better sense of the word) or a saprophyte. It is, perhaps not difficult to imagine the transition from symbiosis but much more difficult for the very different life styles of saprophytes and parasites. One hopes that these and other problems of non-host resistance will attract a much larger proportion of research on resistance than they have in the past but I doubt that they will.

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