CAN THE EVOLUTION OF HERBICIDE RESISTANCE IN WEEDS BE DELAYED?

Jonathan Gressel*

*Plant Genetics, Weizmann Institute of Science, Rehovot, Israel

ABSTRACT - Changes in weed spectrum due to changing technologies and continuous use of herbicides are not new. Herbicide resistance almost inevitably evolves with continuous use of single herbicides in monocultures. Weeds that evolved resistance are no longer laboratory curiosities; they cover tens of millions of hectares and cause considerable additional weed control expenses and/or reduced yields. Models have been constructed to predict herbicide resistance to identify gaps of knowledge and suggest resistance-delaying strategies. Resistances have evolved most rapidly to the heavily used groups of single target site herbicides affecting acetolactate synthase (ALS), acetyl CoA-carboxylase (ACCase), photosystem II (PS2), and tubulin biosynthesis, in that order. The most disturbing resistances are those to virtually all selective herbicides used in wheat, usually where underdosing was practiced. The advent of metabolic broad spectrum cross resistances to wheat-selective herbicides is a major setback requiring concerted efforts. Strategies to delay the evolution of resistance can be practiced, but there has been little impetus to do so, as it is a long-term investment in agriculture, where short-term thinking is the norm.

Introduction

Herbicides play a leading role, with fertilizers, in allowing breeding of crops for higher yields. New cultivars need not compete with weeds for space, light, water and minerals when herbicides are used. This is especially evident with grains, where dwarfing reduced partitioning of photosynthate into straw, greatly increasing the yield index, and preventing fertilizer-induced lodging. The dark side of this success story is that herbicide use encouraged monoculture, allowing breeders to ignore fertilizer efficiency, and crops to become less efficient mineral extractors than the weeds, furthering the need for herbicides. Resistance is an inevitable outcome of relying on single methods, as has been learnt with other pests and pesticides.

Changes in weed spectra due to changing technologies are not new. Many previously pernicious weeds have been virtually eliminated. Seed cleaning equipment eliminated some weeds, deep cultivation eliminated many perennials, draining eliminated wetland weeds, fertilizers selected against those that did not respond well (15). Rotations kept many weeds at bay. Weeds often mimic crops in morphology and phenology (1), and rotation of crops having different phenologies and morphologies prevents any

species from building up to the explosive levels possible in monoculture. Herbicide rotations had the same effect, as different herbicides left different weeds, and rotations controlled most weeds during the cycle. Despite all this, we still have weeds.

Wheat fields were transformed from mustard yellow in color to drab green with the advent of 2,4-D. Few weeds have evolved resistance to 2,4-D, but as ecology abhors a vacuum, empty niches were rapidly filled by weeds that always had been resistant to 2,4-D. More powerful herbicides replaced 2,4-D, and resistant weed strains rapidly evolved. The message from this and innumerable other cases is that farmers and their advisors can no longer rely on indiscriminate spray, spray, spray. They must understand the crop, its weeds, the physiological and biochemical modes of action, as well as crop resistance to the available herbicides, and the full implications arising from the use of each herbicide and their mixtures. Only then should farmers decide when to spray and when not, and what to spray and what not. Alternatives to herbicides must be sought, so that we will still have the herbicides available when needed.

Enormous pressures are being imposed to lower pesticide use based on some real and some perceived dangers to humanity and the environment. Agricultural economists teamed with weed scientists to provide computer programs for thresholds showing when herbicides provide cost-effective weed control. The economists' "less is better" can fit well with the greens' "use less", resulting in less expensive weed control, less environmental impact *and* often less, or delayed resistance. The case with reduced rates is far more complex.

Definitions: *Herbicide resistance* is the inherited ability not to be controlled by a herbicide. The term resistance should always be followed and/or preceded by modifiers. An important modifier is the rate applied. Resistance to agricultural rates is assumed here, but rates should be stated. Crops are *naturally resistant* to the selective herbicides used to control weeds in each crop. Evolution of resistance is then the process whereby the rare *resistant individual* becomes the majority - i.e., a *resistant-population. Resistance factors* are usually described as the I_{50} or better yet the I_{90} to I_{99} of the resistant individual divided by the I_{50} or I_{90} to I_{99} of the susceptible. There may be *full resistance* at an agricultural use-rate, or *partial resistance* (in the past termed tolerance) when the weed is severely inhibited but still produces some seed.

Some weed biotypes have evolved resistance to more than one herbicide. If this is due to a sequential selection where one herbicide was used until resistance evolved, then another until resistance evolved to it, this is *multiple resistance.* Each resistance was a separate evolutionary event due to mutations in different genes. If evolution of resistance to one herbicide immediately endowed resistance to other herbicides there is *cross resistance.* It is target-site cross-resistance if all the herbicides affect the same precise target, or metabolic cross resistance if all the herbicides or their toxic products are degraded by the same mechanism. Negative cross resistance occurs when the resistant plant is more susceptible to some other herbicide than the wild type susceptible biotype.

The Resistance Situation

Weed control failures are usually due to factors other than resistance. The best way to guess if a patch of weeds in an otherwise weed-free field is resistant, or uncontrolled due to other shortcomings, is to observe weed species distribution. If a patch contains a mixture of species, the herbicide application probably failed. If a patch is comprised of a single weed species, with

clear control of other species, resistance may have evolved.

The first verified resistances to evolve were to the triazine herbicides, along rights of way, in orchards, and in monoherbicide monoculture maize, with resistance now estimated on over 6 million hectares of crop land, split mainly between North America and Europe. Of the > 50 triazine-resistant species only one evolved by clearly degrading the atrazine. The rest are target site mutants, having PS2-target site cross resistance to all triazines, many phenylureas (but not diuron), uracils and other PS2-inhibiting herbicides (18).

Target site resistance to the highly persistent, soil residual, chlorsulfuron and other ALS-inhibiting herbicides appeared in five species within 3 to 5 years of use, and many more are now resistant (28). Millions of hectares are infested, especially in North America, Europe and Australia. Many resistant biotypes have cross resistance among ALS inhibitors (28).

Target site resistance evolved to the tubulin-binding trifluralin in *Eleucine indica* in the U.S. South in cotton (31) and in *Setaria viridis* in vast areas of western Canada (21) where used in wheat and oilseed rape for 20 years.

Resistance at the level of the target site has easily evolved in grass weeds to the -fop and -dim herbicides inhibiting ACCase, throughout North America and Australia, in a number of important weeds, in various crops (14, 21).

Paraquat resistance evolved in three *Conyza=Erigeron* species, as well as in many other species around the world (8,27). There are various thoughts on the modes of resistance, which may vary from species to species. There is often a low level cross-resistance to PS2 and diphenylether-type herbicides, where resistance is due to the oxidants generated by all these herbicides (8).

The most disturbing resistances are those to virtually all selective herbicides used in wheat. *Alopecurus myosuroides* evolved resistance to chlorotoluron in England and there are new reports yearly of co-evolution in other areas (23). *Lolium rigidum* has evolved resistance to diclofop-methyl at many sites in throughout Australia with millions of hectares affected (26). Many of the biotypes of these two weeds have cross-resistance to all other wheat herbicides. In many instances, they never saw these other herbicides. This type of resistance is clearly a threat to wheat growing areas worldwide, and we must learn how to prevent similar cases from evolving. The recent first instances of isoproturon-resistant *Phalaris minor* in India (19), is especially disturbing, as this *Phalaris* biotype is not as easily controlled by other wheat-selective herbicides as is the isoproturon-susceptible biotype.

Understanding Evolution to Prevent or Delay Resistance

If the relative importance of each of the factors controlling the rates of evolution is understood, practices can be modified to delay resistance. The relative importance of each factor can be assessed by modelling, and verified by epidemiology and/or experimentation. The first model describing different rates of evolution of herbicide resistance under different conditions was published 19 years ago (9). This basic model, which deals only with resistance due to major-gene mutations has been slightly modified through the years to consider more information that has appeared (10, 11, 20, 22). Such models assist in prediction, and suggest delaying tactics but also delineate gaps of knowledge that suggest research priorities. Models describe why the vast majority of cases of resistance have evolved in monoculture, monoherbicide situations. Monoherbicide is defined as repeatedly using one or more herbicides with the same

precise site of action, or one or more herbicides that are degraded in the same manner, or whose toxic products are degraded in the same manner for the control of a given weed. There are many cases where a large number of generations have been treated with a given herbicide, but not in consecutive years due to herbicide rotation, and resistance did not evolve. The same numbers of treatments in monoherbicide culture elicited resistance.

The factors leading to major monogene resistance include

The initial frequency of resistant mutations in the gene pool. Mutations are always occurring, whether we use a herbicide or not. Most major-gene mutations are lethal. Virtually all of the non-lethal mutants are deleterious in the natural environment, and are present at a lower frequency than the mutation frequency as they are less competitive (unfit) compared with the wild type.

Genes conferring resistances at various herbicide targets are at different natural frequencies. The alleles conferring resistance to sulfonylurea and other ALS-inhibiting herbicides appears in about one in a million plants as a semi-dominant mutation in the target site. This nuclear-inherited trait is phenotypically dominant at most agricultural rates. In contrast, target-site PS2 resistance is recessively inherited on the chloroplast genome (18). Chloroplast mutations appear phenotypically at far lower frequencies than nuclear mutations, and the frequency, is guessed to be near 10-20. Thus PS2 resistance evolves much more slowly than ALS resistance, which appeared within 3 years of limited use, whereas triazine-resistant populations were only evident after 7 to 10 years of continual use on a much larger scale.

The frequency of resistance to some herbicides, such as the thiocarbamates is unknown. They are thought to be multi-site inhibitors (because *no* specific sites have been found). The frequencies of resistance to all targets is the *compounded* frequencies of resistance to each target. Evolution of resistance with more than three targets would be highly unlikely. A weed would probably have to evolve a degradation mechanism to be resistant to thiocarbamates. The frequencies of detoxification mutants, must be far rarer than single target site mutations, based on their rare evolutionary appearance.

Some pest species evolve resistance more quickly than others for yet obscure reasons. *Lolium* spp. have such a propensity to evolve resistance very rapidly, even where many weed species co-exist with them. *Lolium* evolved a multiplicity of means to protect itself. In two places (at least) it has evolved resistance to oxidants (paraquat and SO_2) by elevating levels of the oxygen detoxification pathway under polygenic control (8). *Lolium* seems to have evolved different methods to cope with diclofop methyl; in North America it is resistant at the level of ACCase (14, 21). A major reason for the propensity of *Lolium* to evolve resistance is its huge populations due to copious seed production. The Australian *Lolium* seems to have evolved a metabolic type cross-resistance in wheat as it is resistant to all wheat selective herbicides that are oxidized by monooxygenases in wheat (4). Lines have been recently found that also have a target site resistance (27). Simultaneous evolution of many target site mutations in the various sites (which seems genetically impossible) has been experimentally ruled out (26).

Selection pressure - the greatest influence. Selection pressure is the relative ability exerted by different herbicides to decimate the wild type and leave resistant individuals. Selection pressure is measured as the ratio of survival of resistant to susceptible propagules over a growing season. The longer a herbicide remains

persistent (active), the greater its selection pressure, as many weeds germinate throughout the season. Weeds germinating after a herbicide has dissipated can leave susceptible seeds. The short activity herbicides can have higher selection pressure when weeds germinate in a single flush. Additionally, in post-emergence usage, some susceptible weed seedlings are "shaded" by the crop and escape herbicides, lowering selection pressure.

Some herbicides exert exceedingly strong selection pressures because of their soil persistence. Chlorsulfuron, atrazine, simazine, and trifluralin are often residual in soil at levels that still control some weed species after a year or more, selecting for widespread resistance. Resistance has also evolved to herbicides with no biological persistence. Paraquat is inactive within hours, but by spraying monthly, farmer persistence replaced chemical persistence.

Fitness - a major modulator. Most mutants are less fit than the wild type when the selector is not present, otherwise the mutant would be the wild type. Fitness should be measured as competition between the resistant mutant and susceptible wild type, throughout their life cycles, from seed to seed. Under such competitive situations, triazine-resistant mutants yield 10-50% less seed than the susceptible wild type (9,10,18). Where the modifications conferring resistance in a target enzyme are far from the active site of the enzyme, as occurred with ALS resistance (29), the fitness differential is minimal, but still must exist.

The lesser fitness of resistance will not assist in delaying the rate of evolution of resistance to high persistence herbicides used in monoherbicide culture; there is no occasion for the fitness difference to be expressed. Herbicide rotation can allow for fitness to depress the rate of enrichment of resistant individuals in a population, but only in the "off" years when the particular herbicide is not used. These resistance-suppressing rotational strategies have been modelled (10). The models suggest that there can be adequate weed control in the years when the herbicide is used, which can even preserve ALS-inhibiting herbicides usable for many years. There are even some strategies where there is negative enrichment for resistance or just a negligible enrichment of resistance. These strategies do not preclude the use of herbicides in the off years; they require that the "off" year herbicides do not select for the same resistance genes as the "on" year herbicides (10). This requires understanding the weed biology and the chemistry of the herbicides.

The soil seed bank. Weed seed can be incorporated into the soil seed bank, and proportions continually released. The few resistant seeds entering the soil are diluted by the susceptible seed from previous years. The longer the life in the seedbank, the greater the buffering effect of susceptible seed from previous years, decreasing the rate of evolution of resistance. Resistance evolves more quickly to the same weed species in a no-tillage system, where few seeds enter the seedbank, than in a tillage situation where most seed is incorporated.

Integrating the factors

Population-dynamics models integrate these factors (9,10,20,22). The integrations become clear when hypothetical curves are generated from different selection pressures and from an average seed-bank life-span, with different fitnesses (Fig. 1). It is possible to move the frequency scale in Fig. 1 to fit any initial field frequency. It is clear from the slopes that the proportion of herbicide-resistant individuals increases year by year. The slopes indicate that it will take many years to reach a frequency of resistant weeds that will be noticeable, i.e. more than the 1 to 10% viable weeds. Thus, farmers do not realize that they are enriching for herbicide resistance until it is upon them.

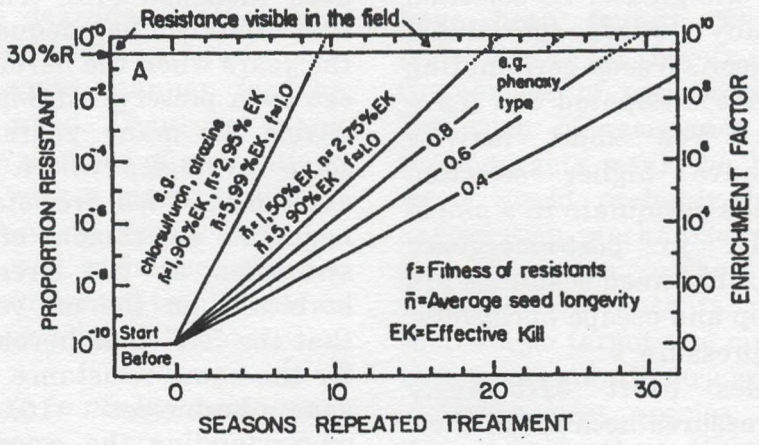

Figure 1 *- Modelling evolution of major gene traits following repeated herbicide treatments. Repeat treatments with highly persistent herbicides that control throughout a cropping season follow the acute slope. The effect of short-lived herbicides that allow the expression of the fitness difference between resistant and sensitive individuals after the herbicide has been dissipated follow the obtuse slopes. Note the logarithmic scale for enrichment of resistant individuals in the population. Based on equations in (9).*

Such models allow one to plot scenarios as is done in Fig. 1. One can easily surmise that the very acute slope with rapid evolution of resistance describes what actually happened with persistent ALS-inhibitors and triazines. The reason that resistance typically appears to the former after 3 to 5 years of use, and the latter after 7 to 10 years is probably due to the much lower initial frequency of chloroplast-inherited PS2 resistance in weed populations.

The lower more obtuse-angled slopes showing slow evolution are typical of post-emergence herbicides with imperfect cover, missing a proportion of the weeds and lowering selection pressure. Field epidemiology has clearly shown that these models work only in monoherbicide culture. If it takes six years for resistant populations to appear in monoherbicide cultures, it has typically taken much more than 12 years when the same herbicide chemistry was used every second year. Even the models that consider fitness differentials, seed bank, etc., during rotation (10), underestimate the delaying effects of rotations.

Creeping multi-genic resistances

We have become used to the appearance of target-site resistances to potent mono-site herbicides, inherited in a monogenic fashion (30), and will probably see more of them with the increasing use of inhibitors of ALS and ACCase. More worrisome is the recent paucity of cases of non target site resistances appearing in some of the major crops; e.g. wheat and rice. These latter cases are typified by a slow, incremental, creeping increases in the LD50 of the whole population as a function of repeated treatments. This was well documented for diclofop-methyl resistance in field populations of *Lolium rigidum* in Australia, where low rates (375g/ha) are typically used (16) (Fig. 2), and no target site resistances were initially found. In Canada, where three times this

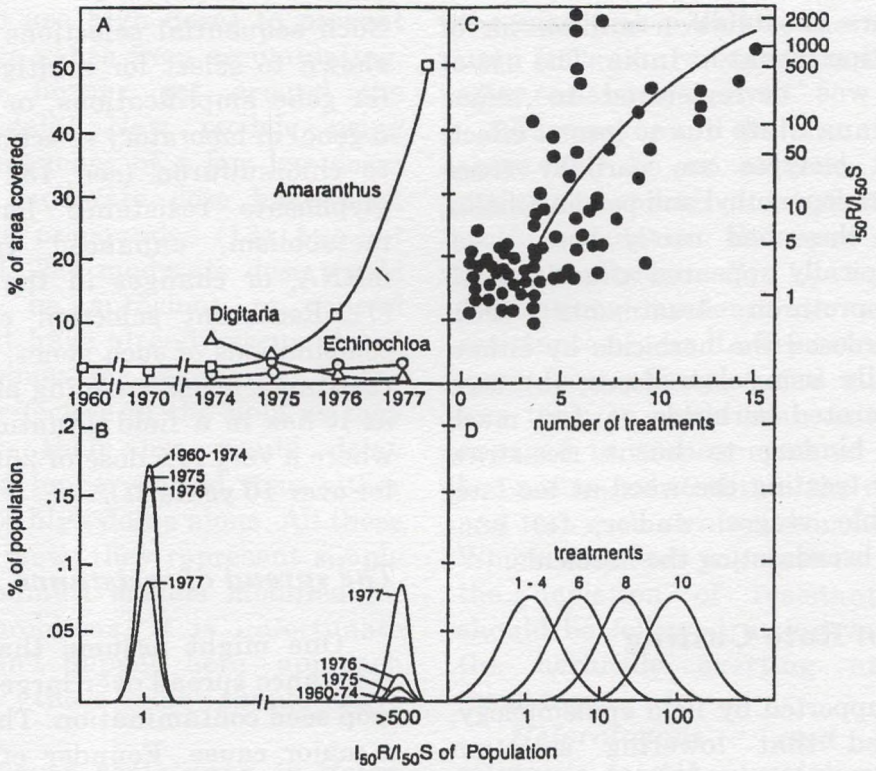

Figure 2 *- "Sudden" appearance of major monogene resistance vs. slow incremental creep of multigenic resistance.* ***A.*** *Changes in weed populations in monoculture maize treated annually with atrazine. Amaranthus retroflexus, Echinochloa crus-galli, and Digitaria sanguinalis, the foremost weeds, were counted in a maize field that was treated with atrazine from 1970. Plotted from Table I in (24).* ***B.*** *A population distribution description of the same data for Amaranthus in A, where the relative resistance (R/S) is arbitrarily plotted on the horizontal axis.* ***C.*** *Slow incremental increase in the level of resistance in repeatedly treated Lolium populations. Lolium rigidum was treated with a typical annual rate of 375 g/ha diclofop-methyl. The relative dose level needed to control resistance in populations is shown as a function of the number of diclofop-methyl treatments. The populations of seeds were collected in fields. Modified and redrawn from (16).* ***D.*** *A population distribution description of the data in C where the relative resistance on the horizontal axis is arbitrarily plotted.*

rate of diclofop-methyl are used, a *Lolium* sp. evolved only target-site resistance (21), and resistant individuals were totally resistant to much higher levels of the herbicide, without any change in the LD50 with repeated treatments. Creeping resistances have been found earlier (12) but their incidences have been overshadowed by the target site resistances, until the rampant creeping resistances covered much of Australian wheat fields (26). Many herbicides have been considered to be immune to the evolution of resistance, with resistant populations appearing after only 15 to 25 repeated uses in monoculture. This seems to have been true for the phenoxy and chloroacetamide herbicides, as well as glyphosate. Thus, it has been disturbing to see resistances creeping within these groups following recurrent selection (13,17). This is a field problem in *Echinochloa crus-galli* with butachlor and thiobencarb in rice (17) as described above. An equally problematic situation is the creeping non-target site resistance of *Phalaris minor* to isoproturon (19), which

already covers over half a million ha of green revolution wheat in India. The use of isoproturon was de-registered in major parts of Haryana State due to loss of effect. The resistant biotypes are partially cross-resistant to diclofop-methyl and pendimethalin, even though they had rarely been used. Resistance typically appeared after 10 to 15 repeated isoproturon treatments when farmers underdosed the herbicide by either: (a) purposefully using low doses; (b) used heavily adulterated herbicide; (c) lost much herbicide to binding to burnt rice-straw carbon; (d) by treating the weed at too late, less susceptible stages, and/or; (e) non-uniform hand broadcasting the herbicide.

Outcomes of Rate Cutting

Theory, supported by field epidemiology, has suggested that lowering selection pressure (by lowering herbicide persistence and/or rates) delays the evolution of major monogene resistances. Conversely, substantially lowering rates to the minimum effective levels enhances the rapidity of evolution of multigenic (or multi-changes in a gene)-inherited resistances. This is clearly a biological "Catch 22" when it comes to designing resistance management strategies (13). The explanation of this enhanced creeping evolution at low dose rates is as follows: there are many alleles that can mutate, and each confers enough resistance to overcome a small increment of herbicide. An unlikely confluence of many such mutations has to be present to confer resistance to higher doses. As there are many such minor alleles compared to the rarer major alleles for resistance, it is more likely that low, marginally-effective doses will select for these ubiquitous minor mutations. Many different minor mutations will accumulate in the population under repeated selection, conferring higher and higher levels of resistance, especially when the dose is gradually increased after signs of incipient resistance become apparent. Such sequential selections have also been shown to select for multigenic resistances (or gene amplifications, or changes within a gene) in laboratory selections for resistance to chlorsulfuron (see 13). Increments of glyphosate resistance have come from metabolism, enhanced transcription of mRNA, or changes in the target enzyme (7). Recurrent selection could select for combinations of such genes, with glyphosate resistance levels creeping above field rates, as it has in a field situation in Australia, where a very low dose of 250 g/ha was used for over 10 years (7).

The spread of resistance

One might assume that much of the resistance spread over large areas is due to crop seed contamination. This has not been a major cause. Founder effect studies on many PS2 resistant populations showed that each population evolved separately; not by movement of seed (2). The slight differences in the cross resistance patterns to different herbicides in the resistant Australian *Lolium* and the British *Alopecurus* species indicate that there must have been concurrent evolution at many foci, and not by spread of seed or pollen. Harvesting equipment blows weed seeds within a field (25), and manure spreaders will spread undigested weed seeds. Vehicles move resistant seed along rights of way as evidenced by tens of thousands of kilometers of *Kochia scoparia* along U.S. railroads (18). Spread of resistant seed should be contained by quarantine; but it is the concurrent evolution that must be precluded.

Delaying Tactics

Models show that the best way to delay single major gene resistances is to lower selection pressure; i.e. cut the dose or use less persistent herbicides within a chemical group. The best way to delay multigenic

resistance is to use high doses to prevent minor resistance genes from accumulating. How can the farmer get around the conflicting models? New models using cycles with a sequence of a few low doses followed by a moderate dose have been constructed and propounded (13), but not yet field tested. The moderate dose would be chosen to be sufficient to control individuals that have already accumulated a few minor genes for resistance. If the models are as effective in the field as they are on paper, their use would delay resistance for a longer period than either the use of low or high doses alone. All these models are not new, they represent simple population dynamics models modified for weed-specific problems. It is unfortunate that the "it can't happen here" approach was taken by those who should have known better.

Negative cross resistance to delay resistances. Some herbicides are more toxic to individuals resistant to other herbicides than to susceptible ones, i.e. there is negative cross resistance. Negative cross resistance can be elucidated and incorporated into rotational strategies for preventing resistance, both before and after populations become resistant. The delaying effect of negative cross resistance must be added or compounded to the lack of fitness of resistant weeds when considering rotations. The most explicable instances of negative cross-resistances are with PS2-resistant weeds and herbicides that act at or near the same site in PS2 (dinoseb, ioxynil, and pyridate)(11). There are some field data on this potentially powerful tool resistance management (3). There can even be a "negative enrichment", where the resistant individuals are depleted to a lower than natural frequency at normally used rates (11). For example, mixtures presently used affect atrazine-resistant biotypes to a far greater extent than the sensitive biotypes. The selection pressure is then negative This is probably the case with pyridate, the main herbicide used (in mixture with atrazine) in Europe after resistance evolved.

Farmers could balance rates so that there will be no selection pressure for resistance and no enrichment of resistance in the population. Balanced rates could be used prophylactically, i.e. before resistant populations predominate, or just after resistance occurs. Lower rates will be much more "cost effective" and may be slightly less toxic to crops than full rates. Those engaged in management of weeds should be encouraged to obtain the necessary data and test such strategies in field situations. Where resistant populations have evolved, the depletion of resistant populations should be followed, using various rates of the herbicide exerting negative cross resistance.

Heterologous and synergistic mixtures to delay resistance. There can also be simple heterologous mixtures and synergistic mixtures having interrelated and/or overlapping spectra of weed control that are effective in resistance management. *Heterologous mixtures* act at different sites of action on a weed. The best documented case is that of alachlor and atrazine, which both control *Amaranthus* spp. and *Chenopodium* spp., species often evolving triazine resistance. Such mixtures lower the initial frequency, by compounding the frequencies of resistance to both herbicides in those weeds controlled by both. If the frequency of resistance to one herbicide is 10^{-6} and that of the other is 10^{-5}, the compounded frequency to both is 10^{-11}. If all else is equal, it will take at least twice as long for resistance to evolve. As fitness losses are also compounded, it should take longer yet, giving a synergistic effect on resistance management. In the case of the alachlor/atrazine mixture, there is no information on the frequency of resistance to the mixture, as no resistance has evolved despite 30 years of extensive use of the mixture. Only one case of resistance

has evolved where alachlor was used alone, due to degradation. There probably can be no target-site resistance to alachlor; its target is unknown.

A *synergistic mixture* in the general sense is one where the herbicidal effect of the mixture is greater than the effect of the sum of the components. This allows using less of each component, often giving an economic advantage to a mixture. The atrazine-alachlor mixture has been shown to be synergistic against some weeds (cf.5) and smart farmers have reduced their rates of both. The lowering of the herbicide use rates lowers the selection pressure for resistance to each herbicide, depressing the rate of evolution for each. This effect is synergistic beyond the compounded frequencies. The best clear-cut case of use of a synergist mixture to manage an evolved resistance problem was pioneered in Costa-Rica. There and elsewhere, the problematic rice weed *Echinochloa* spp. evolved resistance to herbicides. In Costa-Rica, Columbia, Greece, and the U.S., resistance evolved to propanil (32), in China there are over 2 million hectares of rice paddies with *Echinochloa* cross-resistant to butachlor and thiobencarb (17). Piperophos or related herbicides added to propanil prevent propanil degradation by *Echinochloa,* allowing the use of much less propanil and a minute amount of piperophos (32), and costs less than propanil alone, so there is a $ynergy as well as a synergy. The mixture controls wild-type *Echinochloa* (32), and if used earlier it would have delayed resistance, saved farmers herbicide , as well as crop losses due to resistance.

Will abstinence help? It is axiomatic that total abstinence from herbicide use will fully delay herbicide-selected evolution of resistance. What about occasional abstinence? Will it delay resistance for as many treatment cycles as were missed? The answer probably depends upon what the farmer allows to happen. If the farmer uses good monitoring techniques and abstains from herbicide use when there was little or no reason for chemical weed control, there should be mainly positive, resistance-delaying effects. This is especially so when individuals resistant to the last-used herbicide are less fit, and will be competed away by more fit, susceptible individuals. Conversely, abstinence that allows a huge build-up of weed seed populations can be very negative. Evolution is a quantitative selection process; the more individuals to choose from in a field, the more likely resistant individuals will be found in that field, and the more likely outcrossing weeds will be near to mates. Field epidemiology has shown time and again that resistance is most likely to appear first in weeds with heavy seed infestations, especially if they are generally hard to control.

Meaningful rotations - still the best prevention. The best time-proven resistance delaying tactic has been to rotate crops and herbicides in such a way that weed seed banks are kept suppressed, and that different modes of action and modes of crop selectivities are used. The use of meaningful herbicide mixtures (33) and synergies (5) can also be of value. This is easier said than done in many agricultural ecosystems. Too many areas can only support one type of crop, e.g. the otherwise marginal lands where much of the world's wheat is cultivated, and wheat seems to have but one mechanism of herbicide detoxification (4) leading to graminaceous weeds evolving the same system. In general, the variety of herbicide chemistries available for such rotations is decreasing instead of increasing, due to deregistering older herbicides faster than the registering of new chemistries/modes of action. Thus, genetic engineering to introduce new modes of herbicide resistance into crops such as wheat seems to be imperative (6), if not to resistance-prone or already heavily used herbicides.

Concluding Remarks

The war we have with weeds was hard enough before resistances evolved. We can continually win battles if we use wise strategies (but the war is never ending). We cannot successfully continue using a single strategy; the enemy will overcome it. We must use a wide variety of strategies, herbicide and crop rotations, cultivation and fallows, molecular biology and biochemistry, to continually confuse the enemy and not to lose too many battles due to resistance. We must prolong the use life of herbicides or the continual war with weeds will be lost. The advent of metabolic, broad-spectrum cross resistances to rice and wheat-selective herbicides was a major set-back. We have waited far too long to "know thine enemy" and have put in too little intelligent effort, too late. Some strategies are self-evident and others require research. The few, albeit excellent, researchers grasping at the problem are not enough, considering the magnitude of potential losses. Scientists in Brazil who are coping with their first resistance problems have the backing of, and can rely upon, the advice of those scientists who have already coped with similar problems elsewhere. Evolutionary processes do not know global barriers.

Acknowledgements

The organizers are gratefully thanked for their invitation. The author has the Gilbert de Botton Chair of plant sciences.

References

1. Barrett, S.C.H. 1983. Econ. Bot. 37: 255-282.

2. Darmency, H. and Gasquez, J. 1983. New Phytol. 95: 289-297.

3. De Prado, R., Sanchez, M., Jorrin, J. and Dominguez, C. 1992. Pestic. Sci. 35: 131-136.

4. Gressel, J. 1988. Oxford Surv. Plant Molec. Cell Biol. 5: 195-203.

5. Gressel, J. 1990. Rev. Weed Sci. 5 :49-82.

6. Gressel, J. 1995 In: Herbicide Resistant Crops: Agricultural, Economic, Environmental, Regulatory and Technological Aspects.(Ed. Duke, S.O.), (Boca-Raton: Lewis Publishers), pp.231-250.

7. Gressel, J. 1996. Pest Resistance Management 8(2), 2-5

8. Gressel, J. and Galun, E. 1994. In: Photooxidative Stresses in Plants, Causes and Amelioration. (Eds. Foyer, C. and Mullineaux, P.) (CRC Press: Boca Raton) pp.258-273.

9. Gressel, J. and Segel, L.A. 1978. J. Theor. Biol. 75: 349-371.

10. Gressel, J. and Segel, L.A. 1990. Weed Technol. 6: 509-525

11. Gressel, J. and Segel, L.A. 1990. Z. Naturforsch. 45c: 470-473.

12. Gressel, J.; Ammon, H. U., Fogelfors, M., Gasquez, J.,. Kay, Q. O. N. and Kees, H. 1982 In: Herbicide Resistance in Plants. (Eds. Le Baron, H. and Gressel, J.) (Wiley:New York) pp.31-55.

13. Gressel, J. Gardner, S.N. and Mangel, M. 1996. In: Molecular Genetics and Ecology of Pesticide Resistance, (Ed. Brown, T.M.). (Amer. Chem. Soc.: Washington DC) pp.169-186.

14. Gronwald, J.W., Eberlein, C.V., Betts, K.J., Baers, R.J Ehlke, N.J., and Wyse, D.L. 1992. Pestic. Biochem. Physiol. 44: 126-139.

15. Haas, H. and Streibig, J.C. 1982. In: Herbicide Resistance in Plants. (Eds. LeBaron, H.M. and Gressel, J.) (Wiley: New York). pp.57-80.

16. Heap, I. (1988) Resistance to Herbicides in Annual Ryegrass (*Lolium rigidum)* Ph.D. thesis, Waite Agric. Inst., Univ. of Adelaide.

17. Huang, B.Q. and Gressel, J. 1997. Resistant Pest Management (in press)

18. LeBaron, H.M. and Gressel, J. (Eds). 1982. Herbicide Resistance in Plants. (Wiley: New York). 449 pp.

19. Malik, R. K. and Singh, S. 1995. Weed Technol. 9:419-425..

20. Maxwell, B.P., Roush, M.L. and Radosevich, S.R. 1990. Weed Technol. 4:2-13.

21. Morrison, I.N. and Bourgeouis, L. 1995. Brighton Crop Protect. Conf. pp.567-576.

22. Mortimer, A.M., Ulf-Hansen, P.F. and Putwain, P.D. 1992. In: Achievements and Developments in Combating Pesticide Resistance (Eds. Denholm, I., Devonshire A.L. and Hollomon, D.) (Elsevier: London) pp.148-164.

23. Moss, S. 1992. In: Achievements and Developments in Combating Pesticide Resistance (Eds. Denholm, I., Devonshire A.L. and Hollomon, D.) (Elsevier: London) pp.28-47.

24. Nosticzius, A., Muller, T. and Czimber, G. 1979. Bot. Kozl. 66: 299-305.

25. Porterfield, J.W. 1989. Agric. Eng. (Jan/Feb), 11.

26. Powles, S.B. and Matthews, J.M. In: Achievements and Developments in Combating Pesticide Resistance (Eds. Denholm,I. Devonshire A.L. and Hollomon,D.)(Elsevier: London) pp.75-87.

27. Powles, S.B. and Holtum, J.A.M., Eds., 1994. Herbicide Resistance in Plants: Biology and Biochemistry (Lewis: Boca Raton), 353 pp.

28. Saari, L. L., Cotterman, J.C. and Thill, D.C., 1994. In: Herbicide Resistance in Plants: Biology and Biochemistry (Eds. Powles, S.B. and Holtum, J.A.M.), (Lewis: Boca Raton) pp.80-139.

29. Schloss, J.V., Ciskanik, L.M., and Van Dyk, D.E. 1988. Nature 331: 360-362.

30. Shaner, D. 1995. Brighton Crop. Prot. Conf. - Weeds. pp.537-546.

31. Smeda, R.J. and Vaughn, K.C. 1994.. In: Herbicide Resistance in Plants: Biology and Biochemistry (Eds. Powles, S.B. and Holtum, J.A.M.), (Lewis: Boca Raton) pp. 215-228

32. Valverde, B.E. 1996. In: Proc. 2nd Intl. Weed Control Cong., Copenhagen. pp.415-420.

33. Wrubel, R.P. and Gressel, J. 1994. Weed Technol. 8:635-648.