Rounding up the costs and benefits of herbicide use

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In recent years, we have seen an exponential increase in the use of herbicides, such as RoundUp, that contain the active ingredient glyphosate (1). Glyphosate kills plants by inhibiting the production of aromatic amino acids in the shikimate pathway (2). This herbicide is popular because it works well and has been shown to be relatively ecologically "safe"; it has low toxicity to animals, including humans, and degrades rapidly upon contact with soil (3). Taking advantage of its efficacy and relative safety, biotechnology companies have been genetically engineering crops for resistance to glyphosate, which allows farmers to weed their fields by spraying herbicides that inhibit the weeds but not the crop. Although glyphosate is less ecologically damaging than some other herbicides, it may nonetheless come back to haunt us through the evolution of its target weeds. In a recent issue of PNAS, Baucom and Mauricio (1) showed that not only can herbicide use lead to evolution of resistance but also it results in the evolution of tolerance, the ability to compensate for damage. Importantly, they also suggested that there may be ways to halt or slow this evolutionary process because of the costs to evolving tolerance.

Human-caused evolution is becoming a dominant factor in biology (4). Not only do humans influence the ecology of every ecosystem, but also we change the survival and reproduction of organisms, leading to evolution (genetic change) in the survivors. For example, our preference for harvesting larger animals has imposed selection for reproduction at smaller sizes and has resulted in the evolution of smaller individuals in populations of game animals (5) and fish (6). Another way humans cause rapid evolutionary change is through the use of chemicals designed to kill other organisms (e.g., antibiotics, pesticides, herbicides). These compounds cause strong selection; when applied to populations of microbes, insects, or plants, most individuals die. However, any individual with a trait that allows them to survive and reproduce, despite the deadly onslaught, will pass on their genes to the next generation. Over time, survivors will increase in number, changing (evolving) the genetic composition of the population.

There are two ways organisms cope with damage: they can resist receiving it or tolerate it. Most of us are familiar with resistance, which occurs when traits are present that stop or decrease the activity of the pesticide (or pathogen or herbivore), allowing the organism to be relatively unaffected. Much less well understood are tolerance traits, which do not reduce or eliminate damage but instead allow the organism to survive and reproduce despite being damaged (Fig. 1). It was a breakthrough for ecologists when we finally realized that resistance and tolerance to pests were fundamentally different traits (7, 8) and that tolerance could only be measured by comparing the fitness of a genotype when it was damaged to that when it was undamaged. Tolerance to pests became operationally defined as a "norm of reaction" for fitness in which the slope of the line across the gradient of damaged to undamaged organisms defined tolerance and the intercept defined vigor (9). Baucom and Mauricio (1) have extended these conceptual developments to the study of pesticides.

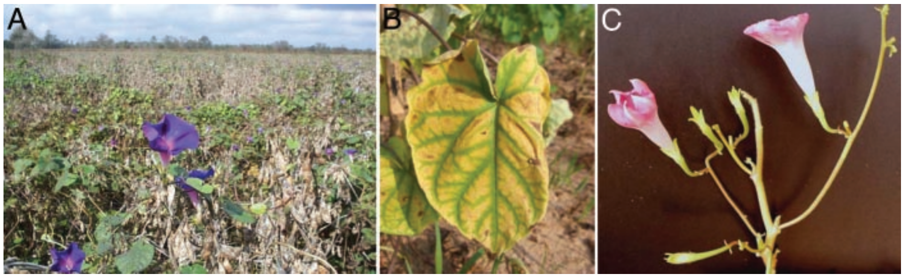

Fig. 1. Response of morning glories (*Ipomea purpurea*) to being sprayed by RoundUp. (*A*) Morning glories in a RoundUp Ready field of soybeans. The soybeans were genetically engineered to withstand application of the herbicide RoundUp, which has been sprayed on the field. The morning glory weeds are flowering despite being sprayed by the herbicide because they have evolved tolerance. The vegetation on the soybeans is brown because they are nearly ready to harvest; earlier in the year they were green. (*B*) A tolerant morning glory showing that tolerant plants are not resistant to herbicide damage. After contacting RoundUp, the leaves exhibit chlorosis and die. Tolerant plants later regrow (as in *C*) but remain stunted. (*C*) Stunted leaves on a glyphosate-tolerant morning glory. Both resistance and tolerance can improve the ability of individuals to survive and reproduce under assault by herbicides. Resistance does so by reducing damage, whereas tolerance does so by reducing the fitness loss despite damage. Photographs courtesy of Regina Baucom (*A* and *C*) and R. Scott Cornman (*B*).

Herbicide use results in the evolution of tolerance, the ability to compensate for damage.

Unfortunately, the terms resistance and tolerance have been in use for a long time but are not always rigorously defined, leading to the two terms being used interchangeably. For example, genetically engineered RoundUp Ready Soybeans, which are undamaged by the application of RoundUp and are thus resistant to it, are referred to as being "herbicide tolerant" by some (e.g., ref. 10) and "herbicide resistant" by others (e.g., ref. 11). Baucom and Mauricio (1) show that it is possible to differentiate herbicide tolerance from herbicide resistance. It is desirable to do so because the mechanisms behind the traits are likely to be different, and they will evolve differently.

Tolerance often involves some degree of compensation for damage. For example, plants can tolerate damage by pathogens or herbivores in several different ways, by delaying the senescence of infected tissue or by increasing chlorophyll concentration and leaf size (12, 13). Similar mechanisms are likely to be found for tolerating herbicides. Importantly, because both tolerance and resistance require reallocation of host resources, they are likely to be physiologically costly (14, 15). Baucom and Mauricio (1) found a high cost of tolerance for morning glories; in the absence

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of glyphosate, tolerant genotypes produced far fewer seeds than intolerant genotypes. Finding a high cost is important because it suggests that we may be able to delay the evolution of tolerant genotypes by altering our patterns of herbicide usage. Intolerant genotypes will be favored and will increase in the population when we stop using herbicides or, potentially, if we rotate several kinds with different physiological activity. We must learn how to slow down the rate of evolution of resistance and tolerance to herbicides if herbicides are going to continue being used. Otherwise we are creating even larger problems for ourselves than we had before.

Baucom and Mauricio (1) show that there is genetic variation in morning glories in response to a novel selective agent, glyphosate. This compound has not been a natural part of the ecology of morning glories, yet they have been able to evolve rapidly (within less than two decades) because they had preexisting genetic variation in traits that allowed them to compensate for damage. It will be interesting to follow the frequency of glyphosate tolerance in these populations over time because theory predicts that tolerance should become fixed within a small number of generations after it has arisen (16). Thus, genetic variation in this trait should diminish or even be eliminated over time. Whether or not fixation ultimately occurs, however, depends on the degree to which tolerance is genetically linked to resistance, pleiotropy, the cost of tolerance, and the strength and direction of selection (16, 17). Because morning glories are common weeds with a short life cycle and because their tolerance to herbivores (8, 18, 19) and now glyphosate have been well characterized, this system provides an exciting opportunity for following and documenting evolutionary change.

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