Chapter 6

Management Implications of New Technologies

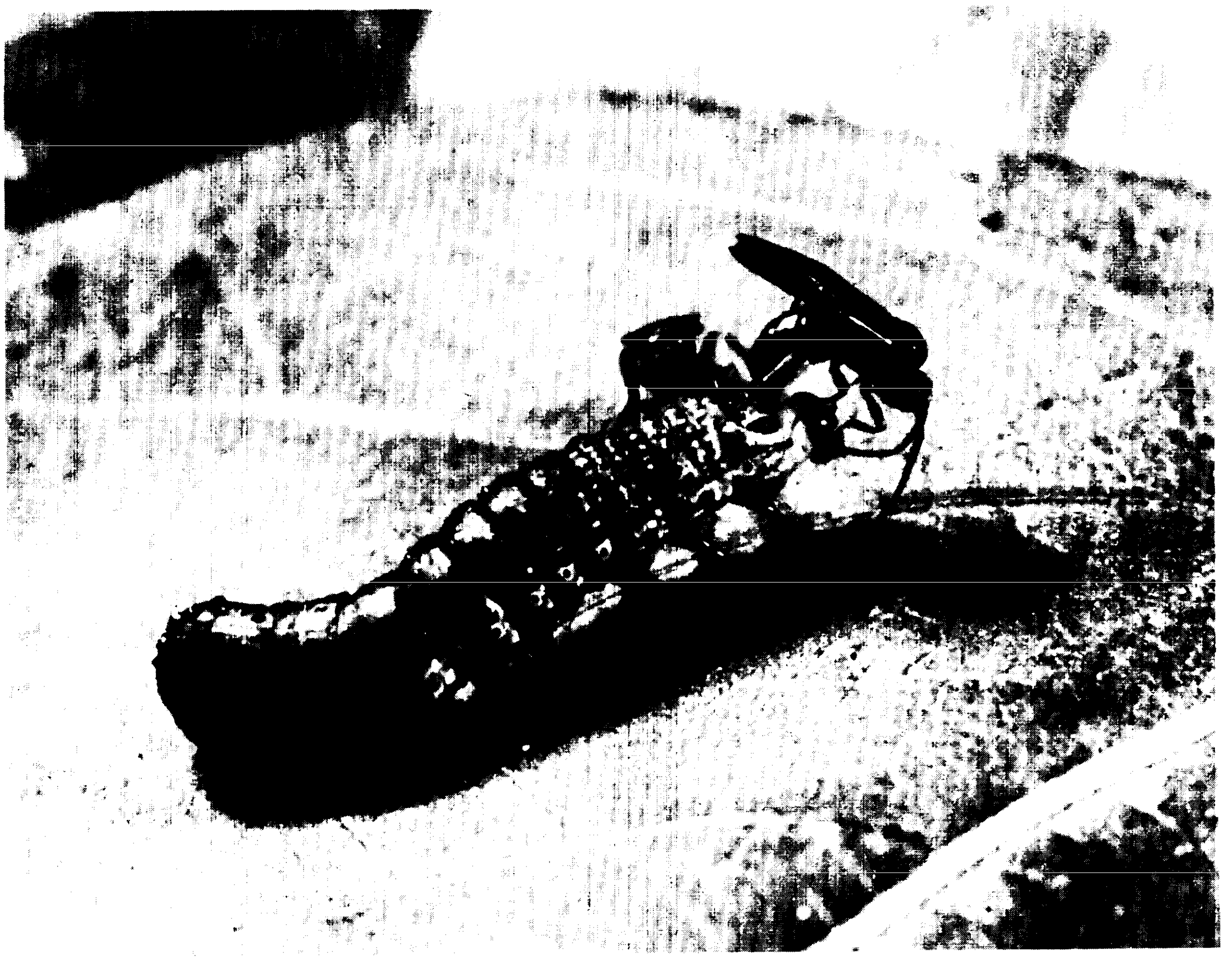

Photo credit: U.S. Department of Agriculture, Agricultural Research Service

Contents

Box

Figures

Chapter 6
Management Implications of New Technologies

Biotechnology holds great promise for American agriculture, but this promise may not be realized if the technologies are poorly managed. The new technologies will demand considerable management skills and a holistic or systems approach to management. Pest resistance to technologies that control pests exemplifies management problems in the past. Many chemical pesticides are ineffective today because of pest adaptation. Evidence suggests that pest adaptation could have been delayed and, in some cases, avoided if proper management strategies had been implemented. As products from the biotechnology era are used to control pests, management strategies for delaying or possibly avoiding pest adaptation need to be identified.

Good management will be of paramount importance for the effective use of new biotechnologies in animal agriculture. The new technologies are not magic bullets, and will not improve animal productivity without effective management. With or without biotechnology, a growing management issue in this decade is farm animal well-being. Little scientific evidence is available on farm animal well-being in the United States; much more is available in Europe. It is important that the American animal agricultural industries begin to focus more attention and resources on this growing issue and on the impact of new technologies on farm animal well-being.

This chapter focuses on these critical management issues. First, pest adaptation to various control technologies is explored for crop agriculture. Various management strategies for delaying pest adaptation are identified for the new technologies developed through biotechnology. Second, the importance of the farm animal well-being is discussed, areas of research are identified, and biotechnology's potential impacts on farm animal well-being are explored.

INTEGRATED PEST MANAGEMENT STRATEGIES FOR CROP AGRICULTURE

Pest infestation is a serious problem for agriculture and effective methods to control pests are needed. Of all crop pests, weeds boast the longest recorded history of adapting to agricultural practices. It is a history dotted with examples of one of nature's most interesting adaptive strategies: mimicry (35). By mimicing crop seed, weed seeds can lie hidden among crop seed stored for the next season's planting.

Successful mimicry of agricultural crops requires that weeds possess a number of important characteristics. Weed seeds must ripen by harvest time; remain on their stems during harvesting; and have a shape and density similar to that of the crop seed (35).

A surprising number of weeds have evolved all the characteristics required to become crop-seed mimics. An example comes from the mimicry of lentil seeds, Lens *culinuaris,* by the common vetch, *Vicia sativa.* The lentil seed has a convex shape. Normal seeds of the common vetch are much more rounded than lentil seeds (figure 6-1). Another example is one of rice's most serious rivals, barnyard grass. Barrett (1) discovered in weedy forms of barnyard grass so many rice-like traits that they found it more difficult to differentiate barnyard grass from rice than to distinguish two variants of barnyard grass from each other (figure 6-2).

In the mechanized farming systems dominant in the United States, hand weeding may be a thing of the past, but the battle between farmers and weeds continues. Chemical herbicides used to control weeds do not discriminate on the basis of appearance. The nature of the game has switched to biochemical mimicry. Agricultural chemical companies spend millions of dollars each year inventing chemical agents that kill weeds in cultivated fields without harming crops. This has put enormous selection pressure on weeds to biochemically mimic crops. It is estimated that there are at least 84 cases of weeds with resistance to at least one chemical herbicide (figure 6-3).

Like weed resistance to herbicides, the resistance of plant-pathogenic fungi to synthetic fungicides is a significant problem. By the mid- 1980s, more than 100 species were known to be resistant to at least one fungicide (figure 6-3). [1]

The real experts at resistance to synthetic chemical agents are insects. Resistance to DDT, detected shortly after its introduction as one of the first insecticides, is

[1] On the other hand, some pesticides have remained effective over the long term. For example, glyphosate has been used to control weeds for more that 17 years without any documented examples of resistance. Likewise there is no evidence of codling moths (pests of apples) developing resistance to organophosphates even though these pesticides were used intensely for 20 years to control the moth (34).

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frequently cited as a textbook case of rapid adaptation. Since DDT, insects have been most successful at adapting to almost all insecticides. More than 500 cases of insect adaptation to insecticides have been documented (figure 6-3).

Besides the growing problem of pest resistance to chemicals, there is much criticism of chemical pesticides because of their adverse environmental side effects (95). "Natural" control methods are often touted as safe and effective alternatives to chemical pesticides, but there is no guarantee that pests will not adapt to these methods as well. Indeed, numerous examples abound of pests overcoming a wide variety of control methods. Pests have adapted to cultivation methods as illustrated by wild vetch in lentils and barnyard grass in rice (34). Pests also have adapted to crops bred to be pest-resistant. For example, a random sample of 63 plants bred for resistance to viral pests indicated that pests had adapted in 28 cases. Only five cases showed no evidence of viral adaptation, and the rest were inconclusive (20). Insects also have adapted to crops bred for insect resistance. Hessian flies in wheat, green bugs in grain crops. and leafhoppers and planthoppers in rice are examples (22, 33). Other insects have adapted to biological control agents. For example, alfalfa weevils and the forest pest *Pristophora erichsonii* have adapted to parasitic enemies, and silkworms have adapted to fungal control methods (34). Some strains of insects, the diamond back moth, for example, have developed resistance to biological control with *Bacillus thuringiensis (56, 80, 91),* a bacterium that is toxic to many insect pests.

These examples lead to three basic conclusions:

1. pests have demonstrated tremendous ability to adapt to almost any control mechanism,
2. unilateral pest suppression tactics rapidly can be rendered ineffective due to evolutionary change in pests, and
3. the assumption that natural pest control tactics are superior to synthetic methods, at least in terms of limiting pest adaptation, is false.

Control of pests requires the use of many approaches, rather than reliance on one single method. A holistic program that considers all causes of plant stress—pathogens, weeds, insects and other arthropods, water and nutrient excesses and deficiencies, soil pH, salinity etc., is needed. However. developing such an integrated approach will require an enormous amount of information and an understanding of the interactions among different stress-reduction strategies. Much effort will also be needed to educate farmers in taking such a multifaceted approach to pest and other stress control.

Figure 6-l—Successful Seed Mimicry by Common Vetch Weed of Lentil

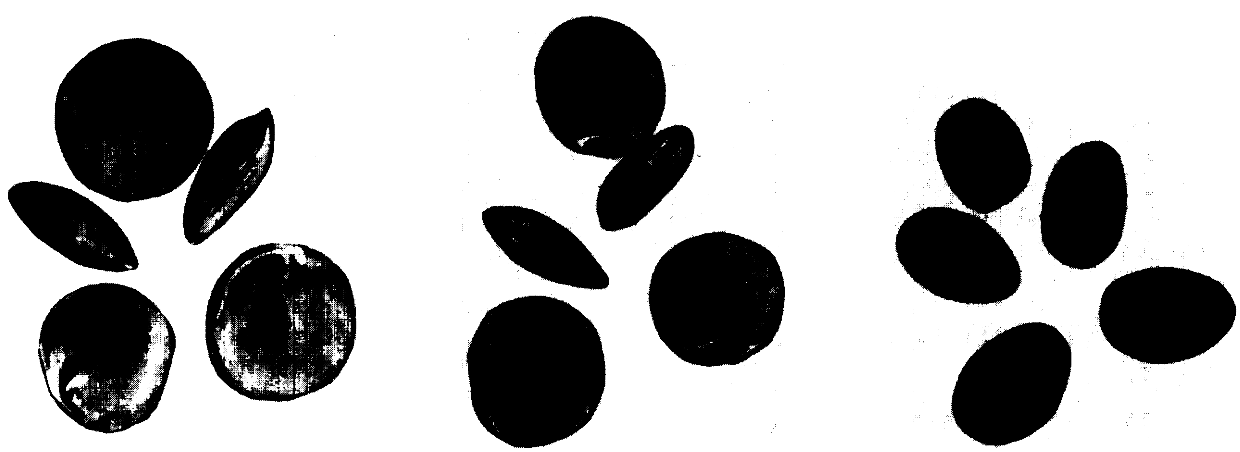


Photo credit: Virge Kask

Success at seed mimicry has given the common vetch the ability to contaminate lentil fields. At left is the typical seed shape of the common vetch, *Vicia sativa.* In a lentil field near Albion, Washington, plant pathologists recently found vetch seeds that had a distinctly different shape (center) that is quite similar to the flatter shape of the lentil, Les*culinaris* (right).

SOURCE: Richard M. Hannon, U.S. Department of Agriculture, Agricultural Research Service

Figure 6-2-Successful Mimicry of Barnyard-Grass Seedling for Cultivated-Rice Seedling

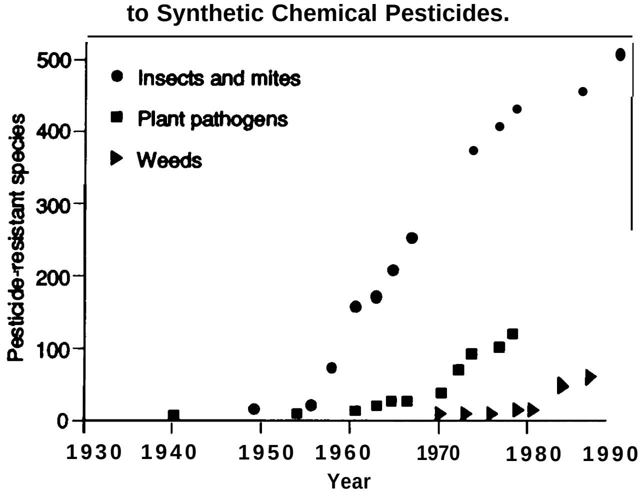
Photo credit: Beverly Benner

Survival in a hand-weeded field is easier for a weed that looks like a crop plant. A barnyard-grass seedling, a serious nuisance in rice fields, is easily mistaken for a cultivated-rice seedling. Left to right, the plants shown are cultivated rice, the ***oryzicola*** variety of barnyard grass, and another barnyard grass seedling.

SOURCE: Spencer C H Barrett, University of Toronto

Integrated Pest Management (1PM) represents an attempt at such an approach. 1PM strategies seek to create a crop management system that combines compatible production techniques and methods in a manner that maintains pest populations at levels below those causing economic crop injury. The 1PM approach is based on ecological principles and requires a solid understanding of the ecological system to be managed. Development and deployment of integrated strategies requires basic knowledge about target pest species and their interactions with other pest and beneficial species, as well as with the crops to be protected and other host plants (70). Knowledge of the direct and indirect effects of other crop production and protection inputs on nontarget pests and beneficial species is also essential. Because crop/pest interactions display tremendous geographical variation for the same crop and pest, pest management systems must be adapted to local conditions. The complexity of, and lack of adequate knowledge about, pest populations and agroecosystem dynamics make 1PM an unrealistic goal at this time.

Figure 6-3—Number of Crop-Pest Species Resistant to Synthetic Chemical Pesticides.



SOURCE: N.G Green, H.M. Lebaron, and WK. Moberg, Managing Resistance to Agrochemicals: From Fundamental Research to Practical Strategies (Washington, DC: American Chemical Society, 1990).

Limited 1PM strategies have been used in cotton and apples to control insects, rather than weeds or disease (2 I). Presently, 1PM efforts focus on integrating cultural controls (sanitation, crop rotation, appropriate selection of planting dates, irrigation regimes, planting densities, varietal selection); naturally occurring biological control; and the application of chemical controls when pest populations or damage to the crop reaches a threatening level. These action thresholds are based on the complex and dynamic relationship between crops and pests throughout a growing season (72).

Combinations of pest-control methods ideally should act synergistically to control pests; at least they should not counteract each other. Research shows that synergism exists between some moderately resistant plants and biological control agents; in other cases, such plants adversely affect the activities of naturally occurring biological control agents (32).

Compatibility with biological control agents must be a significant consideration when biotechnology is used to create resistant crop varieties and to extend the range of biological control agents. Some preliminary research involving tobacco that has been genetically engineered to produce low levels of *Bacillus thuringiensis* (Bt), indicates that Bt does not negatively affect natural enemies of tobacco budworm. It is possible that Bt enhances the effectiveness of the natural enemy by slowing budworm growth (34).

Crops that have low to moderate levels of pest resistance, generally have responded well to chemical controls. Several cases have been documented where pest suppression has improved following insecticide use on resistant crop varieties (48, 93). However, there are also examples of antagonistic interactions (53, 55).

Crop rotation has been employed effectively to decrease pest infestation. However, continuous cropping has also lead to a decline in incidence and severity of pest infestation by providing a more stable environment for the establishment of naturally occurring antagonistic agents. For example, the severity of take-all disease in wheat has naturally declined in fields that have been continuously planted to wheat for years. The decline is due to the establishment of a bacterium that controls the disease (97). Little is known about the compatibility of genetically engineered crops and cultural practices. Currently the use of constitutive genes (i. e., genes that are expressed in all tissues at all times in the plant) leave little room for temporal flexibility.

In the above examples, the compatibility of only two control mechanisms for one pest is considered. However, many other plants, animals, and microbes, some of which are beneficial and some harmful to crops, are also part of the agroecosystem. Most of these components are studied in isolation; in a truly integrated system, all control mechanisms used to control all pests should be compatible. For example, mite management of almonds cannot be discussed without considering how simultaneously to manage codling moth, navel orangeworm, and weeds (49, 101, 102). The information needed to do this currently is unavailable.

As practiced currently, 1PM strategies do not eliminate but strive to decrease chemical use by improving the timing of pesticide application to achieve pest suppression with minimal nontarget effects. Improved pesticide application technologies to minimize off-target drift could also decrease amounts of pesticides used. Pesticide delivery equipment designed to directly mix pesticides at the proper rate, eliminating the need for tank mixing, could increase the efficiency of pesticide application (78, 95).

Development of pest management technologies and programs does not automatically lead to their adoption. Many obstacles stand in the way of farmer acceptance of these programs. The complexity of the programs requires high levels of management skill and this is a significant deterrent to many farmers. Information and programs tailored to meet the local needs, perceptions, resources, constraints, and objectives of farmers is imperative. Many farmers will need considerable training to use these technologies. The lack of coordination among organizations, personnel. and disciplines involved in pest management at the local and regional levels inhibits educational efforts. Development of expert systems and other information technologies may help in training and in coordinating these efforts (see ch. 4) (34).

The failure of growers to perceive the long-term cost advantage of integrated pest management strategies is a significant deterrent to adoption. There is a general need to demonstrate how these management strategies might reduce production costs. For example, almond producers were generally skeptical of adopting an integrated mite management program, until it was shown that this program could be effective, was compatible with pest control tactics already being used, and could result in decreased production costs of $24 to $44 per acre (47). Developers of pest management technologies generally lack the social science training needed to demonstrate cost-effectiveness to farmers. Input from social scientists is needed to successfully develop and implement any new methods.

Management of pests will continue to be a major concern of agricultural producers. Successful development and adoption of more comprehensive pest management strategies will require extensive scientific research, as well as improved methods of providing readily usable information to agricultural producers. A better understanding of the interactions between crops and pests and of mechanisms of resistance development is needed. Changes in farm management practices also may be needed. The ongoing battle to stay one step ahead of pests, given their ability to adapt, will require the development of new biological control agents, improved chemical pesticides and wholly new technologies such as genetically engineered plants.

Biotechnology holds great promise for providing new ways to control plant diseases, insects, and weeds. The tools of biotechnology have created the possibility of selectively engineering plants for insect, disease, and weed resistance. In addition, these new tools are expanding the knowledge base of plant resistance and the interaction of plants and pests with the rest of the ecosystem. In particular, biotechnology will be very useful in detecting resistance by pests at a much earlier time than traditional technologies and in developing strategies to slow or alleviate pest resistance.

Molecular Genetics as a Tool for Detecting Resistance and Tracing its Origins

Until recently, pesticide resistance could be detected only after it became a problem in the field or through laboratory bioassays in which samples from a pest population are treated with predetermined doses of the pesticide in question. The number of samples that can be processed in this fashion is low, especially with insects and some weeds.

If an enzyme that leads to resistance has been identified. another approach to detecting resistance is development of monoclinal or polyclonal antibodies to that enzyme (see ch. 3 for explanation of how they work). Although there are certain drawbacks to this approach, there is a potential with this system to detect resistance at very low levels using kits that can be applied directly in the field.

With many pests, resistance develops in a number of localized geographic areas. It often is not clear whether these localized resistant populations arise independently or whether one population becomes resistant and rare migrants invade new areas and become the dominant form in the newly invaded area. It is important to know which of these two scenarios reflects the dynamics of resistance in order to limit further progression of the resistance problem.

If the resistance developed in one location and spread to another via migration, then the mutation(s) leading to resistance are probably rare. It may be advisable to attempt to quarantine the areas of resistance and to eradicate pests within these areas. On the other hand, if resistance arises independently in each area. then the mutation frequency is probably high and the above strategy would be useless. If the biological mechanisms of resistance in two areas are clearly different. it is safe to assume that resistance arose independently. However, when the mechanisms of resistance are similar it is possible that resistance had one origin.

Advances in molecular genetics have allowed scientists to clone the genes responsible for some kinds of pesticide resistance. By determining the point at which a mutation in the gene occurred in a number of different populations it will be possible to more precisely determine the number of origins of resistance. Work in this field is only beginning but progress in at least one case has been astonishing. A French molecular biology group working with a Culex mosquito species was able to demonstrate that a single, initial, mutation in an esterase locus (an enzyme that accelerates the synthesis of esters) is responsible for most of the organophosphate resistance in this species worldwide (76). Their molecular analysis demonstrated that the DNA sequences adjacent to the coding region of the gene were identical in all resistant populations.

The Influence of Genetically Engineered Crops on Pest Resistance

Two primary questions arise about pesticide resistant crops (and about herbicide tolerance in particular): whether the level and pattern of pesticide use will be altered by such crops; and/or whether crop production patterns will be changed. Impacts that might occur as a result of these changing patterns also need to be evaluated. Impacts include environmental and food and water safety issues and continuing or increased problems with resistance. No definitive data exists on these issues, only reasonable speculation on changing patterns (but not levels) of herbicide use that might occur. There is also reasonable speculation about changing crop patterns and pesticide use that might result from insect and disease resistance. However, more data is needed to assess environmental and food safety issues. Speculations about changing crop patterns combined with knowledge of how pest resistance develops does lead to some conclusions about the type of resistance problems that might arise. It also suggests some farm and industry management strategies that might be pursued to minimize resistance. These issues are discussed below (34).

Herbicide-Tolerant Crops and Weed Resistance to Herbicides

Today agriculture depends to a great extent on herbicides to control weeds. Herbicide use patterns (and related pest-resistance problems) are affected by many factors, including price, the spectrum of weeds controlled. residue effects, flexibility or timing of pre or postemergence treatments, marketing strategies, and ease of use. While biotechnology may contribute to pest resistance risks in some cropping situations, it is only one of the factors involved, and its application to American agriculture must be considered holistically.

Biotechnology-agrichernical companies. and seed companies as well as public universities and laboratories are using genetic engineering to develop crops resistant to herbicides. With herbicide-tolerant crops greater quantities of particular herbicides can be used to control weeds. As the name implies, herbicide-tolerant plants can grow in the presence of herbicides that harm or kill a nontolerant plant. Some plants naturally tolerate particular herbicides. Grasses, for example, naturally tolerate certain herbicides that kill broad-leaved plants. Despite this, use of herbicides to control agricultural weeds is often limited by the sensitivity of a cultivated crop to a herbicide or by the sensitivity of other crops that subsequently will be planted in the same field. Herbicide-tolerant crops remove this limitation. They are designed to tolerate higher levels or more potent doses of herbicides than non-tolerant crops. A concern is that herbicide-resistance weeds may be created by the transfer of herbicide-tolerance genes to weedy relatives of crop plants or by the change in patterns or levels of herbicide use. Herbicide-tolerant crops could lead to increased problems with weed resistance or diminish these problems depending on the types of herbicide-tolerant crops developed and the manner in which they are deployed (27, 28). We must proceed with caution in developing and deploying herbicide tolerant crops.

Resistance of weeds to herbicides is a recent problem that is predicted to worsen during the next decade. As herbicide use increases (a possible consequence of herbicide-tolerant crops) so does selection pressure for resistant weeds. Furthermore, gene mutation leading to resistance to some of the newer herbicides occurs at a reasonably high rate, leaving these herbicides in a vulnerable position.

Research has shown that a number of the new herbicides (e. g., sulfonylureas, imidazilinones, and triazolopyrimidines) have the same target site in the plant, the ALS enzyme (acetolactate synthase), which is essential for plant growth. These herbicides bind to a nonactive site of the ALS enzyme, change its confirmation, and thereby inactivate it. Resistance to herbicides that inhibit the ALS enzymes has been found in eight weed species, and primarily arises through a change in the nonactive site of the enzyme (57). The mutation rate for this change is quite high (1 in 1 million) and companies are well aware that this presents a problem. Adaptation of a weed to one herbicide moreover can render the weed resistant to a number of other herbicides, a phenomenon called cross resistance (75). Overuse of a single ALS inhibiting herbicide or a group of ALS inhibitors in one area thus could be problematic.

For example, continuous use of ALS inhibitors in soybeans and corn maybe ill advised in that it may accelerate development of resistance in target weeds. In 1991, two new herbicidal products, both ALS inhibitors, were labeled for use in corn. If these are used on a substantial crop area and other ALS inhibitors are also used on soybeans in the same area, risk of weed resistance will be significantly increased. Because the spectrum of weeds that a given herbicidal product can control is limited, a single product is rarely used everywhere or all the time. The higher the diversity of ALS inhibiting compounds, the greater the acreage that is likely to be treated with an ALS inhibitor.

Herbicide Use in Corn/Soybean Rotations—Many herbicides fall into two groups based on their spectrum of activity: broad-leaf herbicides; and grass herbicides. This dichotomy presents a short-term agricultural problem. Broad-leaf herbicides can be used in corn (which is a grass), but could be a problem in soybeans since it is a dicot (i. e., broad-leafed plant). Conversely, a number of herbicides that can be used in soybeans could be damaging to corn (e. g., Scepter).

Until this year, imidazilinone and sulfonyl urea herbicides were used only in the soybean component of corn/soybean rotations. Care had to be taken so that residues would not carry over to and damage the next year's corn crop.

Recently, collaborative work between American Cyanamid and Pioneer has lead to development of corn with tolerance of the imidazilinone products, Scepter and Pursuit, both ALS inhibitors. Scepter is currently used in southern areas on the soybean component of soybean/corn rotations and Pursuit is used similarly in more northernly areas. If corn cultivars with imidazilinone resistance were introduced to areas with corn/soybean rotations, the door would be opened for the use of more ALS inhibitors in these areas. Pioneer is currently planning to release imidazilinone-resistant corn cultivars in the early 1990s in areas that do not generally use soybean/corn rotations (17). Since these areas grow continuous corn this could mean continuous use of these ALS inhibitors. Such an introduction must therefore be considered carefully. If tolerant corn cultivars were also released in areas with soybean/corn rotations, more land would receive continuous control with ALS inhibitors.

Biotechnology could, on the other hand, be used to diminish risks of herbicide resistance in weeds. The ALS inhibitors are being relied on increasingly as they replace older herbicides with known environmental problems or high costs. Other types of herbicides are available that affect different target sites in weeds (e. g., glyphosate, glufosinate). Some of these compounds are limited in use because specific crops lack tolerance to them. If, for example, corn cultivars were developed with glufosinate or glyphosate tolerance, it might allow farmers to alternate use of ALS inhibitors and compounds with a different mode of action.

Monsanto is currently trying to develop soybeans with tolerance to glyphosate based herbicides (e.g., Roundup). If they are successful and such soybeans were introduced

Photo credit: Grant Heilman, Inc.

Research is ongoing to develop soybeans with tolerance to glyphosate based herbicides. if successful, the cycle of continuous use of ALS inhibitors could be broken, thus slowing the development of resistance to target weeds.

into corn/soybean rotations, the cycle of continuous use of ALS inhibitors could be broken.

Herbicide Use in Cotton—Although cotton is sometimes rotated with other crops such as soybeans and corn, in major cotton producing areas of Louisiana. Mississippi, and Arkansas 75 to 80 percent of the cotton lands are planted to cotton for 5 or more years in a row (6). While soybean and cotton may be grown on the same farms, the land with the highest yield potential generally is reserved for cotton. Only about 5 percent of the land in these areas is rotated between cotton and soybean.

Currently, mid-south cotton generally receives three herbicide applications, one pre-emergence and two post-emergence. The most commonly used post-emergence treatments involve mixtures of Monosodium Methane Arsenate (MSMA) and fluometuron (a substituted urea) for the first post-emergence treatment, and Disodium Methane Arsenate (DMSA) plus cyanazine or prometryn (triazine compounds) as the second treatment. To date, none of these has caused significant resistance in weeds or environmental problems (7), although DSMA- and MSMA-resistant cocklebur has been found in North and South Carolina (58). Some of the major weeds requiring control are the morningglories, cocklebur, prickly sida, and sicklepod, but the weed complex varies geographically, and from farm to farm.

At least two companies have been working on developing transgenic cotton with herbicide tolerance. Calgene has had success in engineering cotton with tolerance of bromoxynil (a benzonitrile compound), which controls broadleaf weeds (87). Bromoxynil is especially effective against lambsquarters and young morningglories but is less effective on some other weeds.

Monsanto has been attempting to develop cotton with tolerance to glyphosate. The company seems to have had some success but has altered its strategy because the original approach was not leading to sufficient tolerance levels. Monsanto has isolated what it considers promising genes to insert into cotton but has not yet tested them in any plants.

Even if a high-yielding cultivar of bromoxynil-tolerant cotton were readily available, it is not clear how much acreage would be treated. Bromoxynil has a limited spectrum of activity and it will probably be heavily used only when lambsquarters or morningglory is the dominant problem. Where lambsquarters is the major problem, bromoxynil could be used twice a year. Where morningglory is the problem, bromoxynil will probably only be used once, in a post-emergence spray since other compounds can be used more effectively later in the season.

Adding bromoxynil to the cotton system could result in use of more diverse classes of herbicides (and mechanisms of weed toxicity) than are currently used in that system. Little concern exists that bromoxynil will decrease this diversity (7). Thus, transgenic cotton with Bromoxynil resistance is unlikely to present a problem in terms of fostering weed resistance.

If Monsanto succeeds in producing cotton with glyphosate tolerance, a very different situation may arise in cotton. Glyphosate is an effective broad-spectrum herbicide that can kill broad leaf weeds as well as grasses. If cotton were tolerant of glyphosate, this compound could replace the current post-emergence herbicides in a large portion of the cotton growing areas. While current post-emergence herbicides are generally effective, they could not match glyphosate for effectiveness nor for ease of use. Monsanto feels that two applications of glyphosate could replace current post-emergence combinations (14). Monsanto plans to lower the price of glyphosate to make it competitive with current practices (14). The U.S. use patent on glyphosate has been extended until the year 2000, but outside the United States this patent will expire soon if it has not already (26). A company in Canada is already gearing up to man-

Photo credit: Grant Heilman, Inc.

Scientists have had success in engineering cotton with tolerance to bromoxynil which controls broadleaf weeds. Adding bromoxynil to the cotton system could result in use of more diverse classes of herbicides and thus it is not likely to foster weed resistance.

ufacture a glyphosate-based herbicide. These changes offer incentives to reduce the price of the compound to gain market share. This price reduction would tend to make the compound appealing to farmers.

The potential, thus, exists for glyphosate to be used over a large area, two or more times each season. If this happens will there be a high risk of weed resistance developing'? Given the information we have to date there is no simple answer to this question. Box 6-A contains a review of some points made by scientists involved in the ongoing debate about this issue.

Most of the crops that have been targeted for herbicide tolerance research are large-herbicide-use crops (i.e., the money makers). Perhaps a more important need is for herbicide tolerance in limited acreage crops for which there are few herbicides available. Herbicide tolerance could open the door for use of safer herbicides in these crops. Additionally, with limited acreage crops the risk of weeds evolving herbicide resistance is probably lower than with major crops.

Crop-to-Weed GeneTransfer— Before the biotechnology era, resistance of weeds to herbicides evolved through mutations in the weed plant's own genetic material. The possibility that herbicide tolerance genes, engineered into crops, could find their way into weedy relatives of the crop has recently received considerable attention (e.g., Bioscience, June 1990).

What will be the fate of such transferred genes, and will they increase the risk of herbicide tolerance evolving in weeds? There is no answer to these questions yet but some general statements can be made. First, it is generally assumed that natural rates of mutation leading to resistant traits in weeds are one in a million or less. Thus, any introgression (the entry of a gene from one gene complex to another) between the crop and an important weed that increases this rate without lowering the fitness of the weed could be of importance.

If genes that reduce the fitness in the hybrid are tightly linked to the herbicide tolerant gene(s), the latter might not remain in the weed population long enough to cause a problem. Only empirical studies will determine the likelihood that a herbicide tolerance gene would free itself from fitness-reducing, or ''encumbering' genes and become a problem.

There are at least three things that could be done by genetic engineers to lower the risk of herbicide tolerance genes finding their way from crops to weeds, and leading to resistant weed strains. First, when developing transgenic crops containing the herbicide tolerance gene, molecular geneticists could determine if certain inserts map closely with specific crop traits that would tend to lower fitness of a weed. Second, when developing the initial constructs, a second gene could be inserted that would serve as a suicide gene if expressed in a weed seed (i. e., it would kill the whole weed).

A final strategy would involve engineering herbicide tolerance into plants that required two genes to be effective. If the two genes were placed on separate chromosomes the chance that both genes would segregate when they were at low frequency in the weed population would be minuscule in an outcrossing hybrid. This could dramatically slow the rate of increase in frequency of the tolerance trait. A similar result could be achieved if the tolerance trait was controlled by a single recessive gene.

Crops With Resistance to Pathogens

The only breakthroughs in genetic engineering that are likely to affect pathogen control practices in the near future involve virus resistance. Work on engineering plants to express viral coat protein genes and antisense genes has resulted in plants with significant protection against

Box 6-A—Glyphosate: A *Risk to Weed Resistance?*

History

Glyphosate hadbeen in widespread use for at least 17 years and no cases of resistance have been documented that could be directly traced to its use. However, due to its broad spectrum of activity, glyphosate has not been used on crop fields except in cases where weeds need to be controlled in fallow rotations. Most of the weeds that it has been used to control are perennials, and these weeds are less likely than annuals to evolve rapidly resistance. In at least one situation, however, glyphosphate has been used to control annual grasses in fallow rotations every other year for a long period of time with no sign of resistance. it has also been used on orchards **(14).**

Chemistry

Although glyphosate rapidly is degraded by some soil bacteria, plants apparently lack enzymes that can degrade this compound. in screening for resistance to glyphosate, Monsanto scientists have never found a plant enzyme that could degrade glyphosate. This further suggests that weeds are unlikely to mutate such that they become resistant to glyphosate (35).

Mode **of** Action

Unlike the sulfonyl ureas and imidazilinone herbicides that bind to an inactive site of a critical plant enzyme, glyphosate binds to the active site of an essential enzyme for synthesis of certain amino acids. Crop tolerance could be engineered by interfering with glyphosphate binding to this site. Any alteration in the active site that would inhibit glyphosate binding, however, potentially could also impair the binding of the enzyme to its target molecule and diminish the fitness of the plant. Monsanto's experience indicates that this is indeed the case. This has apparently been one of the factors that has made it difficult for them to engineer crops with glyphosate tolerance. While overproduction of a less efficient form of the enzyme is possible, it still could lead to decreased growth efficiency.

Lack of Persistence

One important characteristic of glyphosate is that it does not persist in the environment. Therefore, weed control exerted by this compound is restricted to those weeds that are actually sprayed.

Concision

Certainly the question of potential of weeds to adapt to glyphosate is not yet resolved. However, it seems clear that glyphosate poses less risk than some of the ALS inhibitors. The information to date would suggest proceeding with caution in developing and deploying glyphosate-tolerant cotton.

SOURCE: Office of Technology Assessment, 1992.

a number of viruses (2). Such plants could be used widely in developed and developing countries. They certainly have the potential to raise yields. The question is whether this increase of yield will be stable.

For 28 of 63 traditionally bred virus resistant crops examined, virus strains have been positively identified that could overcome the resistance (20). In only four cases was there good evidence that there had been no adaptation. Results were equivocal for the remaining cases. It is not clear whether or not we should expect the same track record from crops with genetically engineered resistance.

Only one short-term experiment attempted to look for genetic adaptation to engineered resistance. This experiment was reported on in an anecdotal fashion (2). He indicated that he had propagated a TMV virus to high levels in an attempt to induce systemic infection of resistant plants. He passed the virus through the resistant plant seven times, after which it was collected and tested for rate of disease development. This rate was unchanged.

This experiment was obviously a good first step in evaluating the potential of a virus to adapt to engineered resistance. Studies using a broader base of viral isolates and conducted over a longer period of time would be advisable and very useful before any engineered germplasm is relied on to increase yields in developing countries.

Engineered Plants With Insect Resistance

Background—There has been a great deal of interest on the part of industry in developing plants with resistance to insects. Although most of the traditionally-bred, resistant crop cultivars owe their resistance to secondary plant compounds (e.g., alkaloids, phenolics, terpenes) and changes in physical characteristics (e.g., spines, waxy leaves, solid stems) these traits are generally controlled by many genes and are not amenable to straightforward engineering approaches.

Molecular geneticists have instead taken the approach of 1) finding a protein from a bacterium, plant, or an animal that is toxic to insects (e. g., venoms, bacterial toxins), 2) finding the gene that codes directly for the protein, and 3) inserting that gene into a plant. Sometimes this approach works well as with the crystal protein toxins from *Bacillus thuringiensis* (Bt) (59). In other cases, this approach is only partially successful, probably because the proteins are digested in the insect gut before they reach their site of action. If it were simple to design toxic proteins that could withstand the gut enzymes, plants would probably do so themselves. Another successful approach to engineering insect resistance involves the proteinase inhibitors, whose site of action is the insect gut itself. Unfortunately, high levels of the proteinase inhibitors are usually needed to inhibit insect growth.

Of all the potential approaches to engineering insect resistant crops, those involving the Bt crystal proteins are farthest along. Crops that have been successfully engineered to produce insect-toxic proteins include tobacco, tomato, cotton, and potato. Other crops targeted for Bt crystal protein production include but are not limited to corn, rice, soybean, cucumber, and eggplant.

The mother bacteria for the Bt toxin has been used for many years as a biological insecticide by organic farmers and to a limited extent by others. Recently, there has been an increase in the use of these bacteria in conventional, production agriculture. This is in part due to increased pest resistance to conventional pesticides. For example, few insecticides are still effective against diamondback moth and the Colorado potato beetle (23). Other reasons for increased use of *Bacillus thuringiensis* include better formulations and increased toxicity. Both conventional breeding and genetic engineering have been used to improve the potency of the bacterium. The Mycogen company in California has taken the gene from a crystal protein and placed it in another bacterium. They have reported field results indicating that their product has slower decay in the field than normal Bt strains and therefore is more useful for the farmer (23). Ecogen, a company in Pennsylvania, has ''bred' a strain of Bt that produces two crystal proteins, one effective against lepidoptera (caterpillars), the other effective against beetle larvae. This product offers useful control of the Colorado potato beetle and the European corn borer when they infest potato.

There appear to be some good markets for Bt products, whether engineered in plants or used as biological insecticides. One very good thing about using Bt is that it is not likely to disrupt natural enemies of pests or hymenopteran pollinators found in the crop, because most natural enemies and bees are immune to the effects of Bt. This property should make the use of Bt or Bt genes compatible with biological control.

Again, the major question is whether or not Bt will offer long-term solutions to pest problems or whether pest insects will adapt to Bts and nullify their utility. There has been much concern over this issue. In the mid 1980s, there was a feeling among some workers that insects would not adapt to Bt (8). Many early attempts to select for resistance failed or produced very low levels of tolerance (24). In 1985, however, McGaughey (65) found that Indian meal moths selected in the laboratory for Bt resistance became over 100-fold resistant.[2] Further work by McGaughey and his colleague led to a level of resistance in excess of 250 fold. McGaughey and Johnson (66) also found cross-resistance to a number of other Bt strains. This was considered by some scientists to be an exception, but in 1989 Monsanto scientists published work (89) indicating 20 fold resistance to a Bt toxin in one member of the cotton bollworm complex, a major target for Bt toxin production. Further work by the Monsanto group found up to 70 fold resistance of cotton bollworms to this toxin (60). Ongoing research has found resistance in this insect to a number of Bt toxins, to plants expressing the toxin, and to mixtures of Bt spores and crystals (36).

However, all of the above work was done in the laboratory, and field results do not always match laboratory findings. Nonetheless, in 1988 there was a report of field failure of Bt sprays in the Philippines due to resistance

[2] The meaning of this term involves a ratio. For example, if it takes 200 micrograms to kill a resistant pest compared to 2 micrograms to kill a susceptible pest, the pest has a 100-fold resistance (200 divided by 2).

Photo credit: Monsanto Co.

The large boll of cotton on the left is the product of a transgenic plant with Bt genes. The boll on the right was grown in the same field but comes from an unprotected, nontransgenic plant. However, resistance to Bt by bollworms is a very real possibility.

of the diamondback moth (56). in 1990 resistance was carefully documented in a crop field in Hawaii (9 1). The level of resistance in Hawaii was about 30 fold. Recent evidence of Bt resistance in Florida, Southeast Asia and Japan indicate levels as high as 400 fold in the diamondback moth (85). There is no longer any doubt that at least some insects are very capable of adapting to Bt and Bt toxins.

Recent work on the biochemistry of resistant Indian meal moths indicates that the difference between susceptible and resistant individuals involves a change in a receptor binding site in the midgut of the caterpillars. Interestingly, a change in the receptor that leads to resistance to one Bt toxin does not necessarily lead to resistance to other Bt toxins (96). For some insects (e. g., diamondback moth. cabbage worms), scientists have found two or more distinct groups of toxins with high activity. For species like the cotton bollworm. only one group of toxins offers high activity.

There is high risk of resistance to Bt in some cropping situations. If a crop or a set of crops is engineered to produce a Bt toxin and is planted widely, the potential for resistance must be considered.

Cotton—One of the first major crops in which Bt genes may be commercialized is cotton. Monsanto claims to have Bt toxin expression high enough to kill 100 percent of the insects placed on a cotton sample in the laboratory. Close to that level of success was achieved in the field. Monsanto intends to commercialize Bt-producing cotton in the early-to-mid 1990s.

In some areas of cotton production, cotton and soybeans are grown on the same farms although not rotated on the same field. This could be helpful in limiting selection pressure on bollworms to adapt to Bt-producing cotton because some of the insects (a refuge sub-population) will feed on soybeans. The effects of insects in refuges has been described earlier and can be quite important, especially if adaptive genes are recessive. Unfortunately, large tracts of cotton acreage are planted in solid blocks. Potential for resistance in these areas will be quite high. As long as the size of the bollworm populations is large there is likely to be sufficient genetic variation to lead to resistance. While it is impossible to say for sure that the bollworms will be able to adapt to Bt in the field, laboratory results certainly support this possibility.

Potato—Two types of Bt-toxin genes have been engineered into potato. Plant Genetic Systems in Belgium has engineered a Bt toxin into potato that is active against the potato tuberworm. Monsanto has engineered a beetle-specific Bt toxin into potato and reports to have achieved high levels of Colorado potato beetle mortality.

The Colorado potato beetle (CPB) is notorious for adapting to pesticides. One reason for this is that there are few refuges for this beetle. When potatoes have been heavily sprayed with insecticides. it has very few alternative plants on which to feed.

However, there is only one report of CPB resistance to Bt. which comes from a laboratory study in Michigan (68). Results of this study were only briefly described but seem to indicate approximately 30-fold resistance. No field resistance has been reported. It is difficult to assess the meaning of this since Bt sprays capable of controlling CPB have only recently come to market and have not been used widely.

If potato plants with Bt expression are introduced and used widely, the selection pressure for potato beetle adaptation is likely to be as strong as that exerted by insecticides.

Corn—Success with transgenic corn is very recent. Therefore, it is too early to know just what levels of Bt toxin expression will be obtainable in this crop. There is no doubt, however, that one of the goals of molecular geneticists in industry is development of corn with Bt toxin levels high enough to control European cornborer.

The European cornborer currently causes over 10 percent yield reduction in certain areas of the United States (54) but is rarely the target of chemical control measures. In general, chemical control is not economically profit-

Photo credit: Grant Heilman, Inc.

Molecular geneticists have had recent success in developing transgenic corn with Bt levels sufficiently high to control the European cornborer. In the corn belt, there would be few alternatives for cornborers so Bt resistance could be strong, especially if corn is planted in monoculture.

able because of the low value of the crop (on an acreage basis) and the difficulty of controlling this insect because of its habit of feeding in crevices and within plant tissue. Bt expression in corn would be a very desirable trait from the perspective of yield. If some farmers start to use it early on, they will have at least a temporary yield advantage over their neighbors. Certain areas of the United States where cornborers cause more yield loss than in other areas would gain an advantage. This would occur because their yield increase would be greater than in other areas (54).

It is possible that corn seed with Bt genes would be adopted widely if it were priced low enough. In the corn belt there would be few refuges for the cornborers, so selection pressure for Bt resistant strains would be strong. In other areas of the country where corn is not planted in huge monoculture and cornborers feed on other crops (e.g., potato, beans, cotton, peppers, etc.), selection pressure would not be as intense.

Strategies for Delaying Pest Adaptation

Need for a Comprehensive Approach—From the farmer's perspective, the history of pest control is the saga of a long struggle to stay a step ahead of pest adaptation. Some of the techniques used to combat pests have proved relatively resistance-proof, but these successes have been limited (34). The experience with synthetic chemical pesticides has been particularly disappointing.

There is growing recognition among scientists that they need to maintain an arsenal of pest-control tools in anticipation of pests' evolutionary responses. That arsenal contains some potentially powerful weapons, among them the novel approaches of biotechnology.

Much of the discussion of resistance management for at least the past decade has centered on ways to reduce the rate at which pests adapt to conventional pesticides. Yet pests adapt not only to pesticides but also to other agricultural pressures, and they interact with other parts of the environment in important ways.

Thus, management strategies must take into account the entire spectrum of pest adaptation. As discussed above, insect adaptation to Bt toxin genes is a problem today. The following discussion of management strategies to delay insect adaptation to Bt is an example of a comprehensive approach that needs to be implemented generically for pest resistance in general.

Case Example—Adaptation to Bt—There exist six basic strategies for delaying insect adaptation to plants expressing Bt toxin genes (31), each of which is appropriate in a different crop/pest system. The basic strategies are:

1. high expression of a Bt toxin gene with no refuges,
2. high expression of a Bt toxin gene with refuges,
3. high expression of two or more unrelated toxin genes with refuges,
4. low expression of a toxin gene to slow the growth and vigor of the pest to complement natural enemies of the pest,
5. expression of toxin genes only at times and in plant parts where protection from pest damage is required, and
6. restricting Bt use to minor crops.

These strategies for delaying adaptation to Bt are based on the same general principles of population genetics that apply to resistance to conventional pesticides. The important differences between strategies for delaying resistance to Bt toxins produced by plants, and to mechanically applied pesticides derive from inherent differences in these two toxin delivery systems.

The mechanical delivery systems for insecticides usually have considerable temporal flexibility. When a scout determines that the number of insect pests in a crop is reaching an economic threshold, the information can be relayed to the farmer or crop consultant who can make the decision to spray the field with the appropriate insecticide. The farmer or consultant may have a number of insecticides on hand to choose from or can purchase them quickly. The insecticide can be applied to the field within hours if weather is not a problem and equipment and labor are available. Even in problematic cases, the insecticide can generally be applied within a few days. While there is some spatial flexibility in mechanical application procedures, it is generally not feasible only, for example, to spray plants that have two or more insects cm them.

Mechanical application also permits flexibility in dosage applied. Dosage can easily be adjusted to field conditions and to the species and developmental stage of pest requiring control. The only lack of flexibility is in cost: the more you apply, the more it costs. Given insecticide decay rates in the field. doses will decrease after application and must be renewed at a cost. if needed.

When the plant's genetic system is used as the delivery system the situation is different. The genomes of plants and other organisms are set up to turn genes on and off as they are needed to produce specific proteins. It would not be useful for a plant to turn on a gene in a root cell if that gene was involved in producing the red pigment for flower petals. A lot of work has been conducted by molecular biologists' to learn how genes are turned on and off. An important component of these switches resides in DNA sequences that flank the sequences that actually code for protein production.

Some flanking sequences cause a gene to be expressed everywhere continuously; others turn the gene on only in certain plant parts; still others activate the gene only when the plant experiences a specific type of stress such as drought or attack by insects. Comments from industry (37) indicate that the first set of engineered plants to be commercialized will express Bt toxins by relying on "constitutive" promotors, that is, flanking sequences that activate genes under almost all conditions. This means that there will be little temporal flexibility regarding when and where a toxin is produced.

In contrast to traditional pesticides, which can be applied as soon as reports of insect abundance warrant, seeds with the Bt genes must be purchased weeks or months before planting. Thus, a farmer has to assess how intense pest problems will be before a crop is even in the ground. If there is even a small chance of a pest problem and Bt seed is not too expensive, the choice will not be too hard unless the farmer has an individual concern about resistant pests. Use of Bt plants thus is generally referred to as prophylactic pest control as opposed to responsive pest control where toxins are only delivered when a problem is detected.

Another difference between transgenic plants and conventional insecticide-based control programs is that the dose of a conventional pesticide can be adjusted based on need; with engineered plants the "dose" of Bt delivered is predetermined. Once the seed is in the field there is no flexibility.

However, there is room for spatial flexibility in the use of engineered Bt plants. One option that a farmer has with cultivars that produce Bt continuously is to mix seed from the Bt cultivar with that of a closely related cultivar that is not resistant to pests (Strategy 1 and 2). Under certain conditions such a mixture would inhibit a pest outbreak without producing strong selection for Bt resistance. A number of models have been developed to look at this resistance management strategy, and results indicate that resistance does develop more slowly, especially if the Bt genes are recessive (29, 30).

As indicated above, a number of forms of Bt toxins affect different insects. In cases where two or more distinct types of Bt toxin are available for use on one pest it is possible to have both expressed in the transgenic plant (Strategy 3). Theoretical models indicate that planting seed with two or more dissimilar toxins along with 20 to 50 percent seed that was entirely susceptible to the insect pest could preserve crop resistance 20 times longer than use of the single toxin strategy in some crop/pest systems (29, 30).

There has been a good deal of work done on how "partial" plant resistance to insect pests could "work with' natural enemies of the insect pest to deter an outbreak (Strategy 4) (38). Scientists have conducted field tests with engineered tobacco that produces a low level of Bt toxin that causes about 15 percent mortality of larvae and slows the growth of survivors. The Bt was found to have no negative effect on the natural enemies of the budworm and may indeed lead to more natural enemy-induced mortality of young budworms than would otherwise be the case. This may be the result of larvae growing slower or being more restless on the plant.

This low dose strategy may be a good one in some cases but not in others. Two problems that can arise are 1) natural enemies that cause indirect selection for adaptation to the Bt, and 2) pest genes that mediate adaptation to mild (not high) Bt stress. This later problem is considered important in the medical field where it is sometimes advised that if antibiotics are used they should be used at high levels (9, 44, 73). Rigorous testing of the basis for this advice seems to be lacking.

As indicated earlier, some genes in plants are only activated in certain plant parts at certain times (Strategy 5). Molecular geneticists have been able to move the gene activity promotors from one organism to another and basically get the same pattern of gene activation. For example a promotor region from soybeans that turns on a gene only if it is in the developing seed's cells was moved to tobacco and only turned on the gene in the tobacco's developing seed (3). Promotor sequences from tomato that only turn on adjacent genes when there is pathogen or insect stress have also been moved to tobacco and operate just as they did in the tomato (82).

In some crops only certain plant parts need protection from insect damage. For example, the buds of the tobacco plant must be protected against the tobacco budworm but this insect also feeds on leaves. If the buds were protected, the budworm might switch to feeding more on mature leaves. Studies indicate that the budworm is expected to develop Bt resistance more slowly if only some plant parts express the Bt genes (36).

In some crops the plants only need to be protected at certain times of the season (e. g., cotton). If Bt toxin genes were only turned on at specific times in the plants' developmental cycle, the insect would experience selection pressure in one instead of three generations a year. This also should slow the development of Bt resistance.

Since some plant genes are turned on only when there is tissue damage, it may be possible to find promotors that would operate like an automatic pest scout and turn on Bt genes only when a threshold of damage had occurred. Such a system would turn engineered plants from a prophylactic pest control tool into a responsive pest management tool. Such a change could significantly reduce selection for Bt resistance, especially with pests that only reach outbreak numbers once every few years.

As with engineering crops for herbicide tolerance, much of the work to develop insect-resistant transgenic plants has focused on the major cash crops. This makes sense because potential industry profits are higher from working with these crops than with minor crops. If profit were not the major concern, other issues might dominate the decisions about which crops to engineer. For example, pesticides protect many small-acreage vegetable crops from insect pests up to harvest. Pesticide residues in fruits are a concern. If Bt is indeed harmless to mammals it would be useful to replace the chemical pesticides with Bt. In many cases only a small percentage of an insect pest population feeds on these minor crops, so selection for resistance to Bt would be much lower than it is in cotton or corn. If use of Bt was restricted to such crops, it would be possible to achieve long-term environmentally sound pest control (Strategy 6).

Weediness of Crops With Pest Resistance

Most traditional crops such as corn and tobacco are unlikely to start reproducing like weeds (i. e., uncontrollably) solely because they have pest resistance. However, semi-domesticated crops are another matter. Poplars, pine trees, and many pasture grasses and legumes can already compete well in natural habitats. Pests help maintain a balance among plant species in a pasture or forest. In mixed hardwood/pine forests, insects and pathogens are important sources of tree mortality. If a gene for insect or pathogen resistance were placed in a stand of cultured pine trees, and pollen from these trees were to reach native pines there could be a problem. Or if pine trees became resistant to their insect or microbial pests but the hardwoods did not, it is reasonable to expect a significant shift in the balance of hardwoods to pines in forest. The practical and aesthetic impact of such a change in forests must be considered.

POLICY IMPLICATIONS REGARDING THE DEVELOPMENT AND DEPLOYMENT OF ENGINEERED CROPS

If we maintain a laissez-faire policy regarding pest control, it is likely that developed products will be those expected to sell best. For example. farmers who have not been specifically educated about Bt-producing plants are unlikely to buy seed that produces moderately resistant plants (with hopes that natural enemies can control the rest) if seed selling on the same shelf for an equivalent or lower price produce highly resistant plants.

Only if companies exert restraint in marketing their seed will there be any potential for a multifaceted approach to resistance management. For example, if only one company has a product (such as Bt in cotton) priced such that only 50 percent of the farmers in an area decide to use it, other approaches will be adopted. When two companies have the product this is less likely to happen. Even when one company controls the market, economic analyses may dictate going for the highest volume of sales.

In that Bt is a naturally occurring organism that has been used by organic farmers for many years, there may be potential for regulating the use of Bt products based on resistance risk, even though synthetic chemicals have not been regulated on that basis. If it can be shown that the traditional uses of Bt would not lead to evolution of resistance as rapidly as new biotechnology approaches using Bt toxins, there may be grounds for some regulation of use. This issue is not yet resolved and the Environmental Protection Agency (EPA) does not seem to be pursuing the issue.

Weed resistance problems may be somewhat different than insect resistance problems. In the case of most insects, resistance is an area-wide phenomenon—what one farmer does affects other farmers in the region. The stage is set for a tragedy of the commons with no farmer willing to comply with practices that would help others who may be cheating. Weed seed and pollen do not move as far as most insects, so resistance can become a single-farm or even a single-field phenomenon. If one farmer overuses a herbicide and winds up with a resistance problem, other farmers who hear about it may be cautious about using that herbicide too frequently, even if it is inexpensive. If glyphosate use leads to resistance in one area of the mid-south, farmers in other areas may respond by becoming more cautious in decisions to use the product. Educational programs to point out risks to farmers would be very appropriate, and could be very effective in this case, but much research is needed to bolster the information content of such educational programs.

Overall, we already have enough information to formulate general policies that prescribe judicious use of engineered crops with insect and pathogen resistance and herbicide tolerance. However, if we are to make detailed rulings about the development and use of specific products of biotechnology, we will need to generate a body of empirical knowledge relevant to these products. And, we will need an educational program designed to bring these results to the farmer and the public.

A NEW ISSUE IN ANIMAL AGRICULTURE MANAGEMENT

The use of new animal technologies will place a premium on the management capabilities of livestock producers. Research results clearly show the extent of response achieved depends heavily on the management capability of the producer. Use of somatotropins, for example, may require altering the animals' diets. Growing pigs receiving somatotropin will require diets high in protein, and with adequate levels of the necessary amino acid, lysine. Administration of somatotropin to lactating cows may require extending the reproductive cycle to 14 months instead of using the current 12-month cycle. The availability of many different types of growth promotants may result in the use of more than one at the same time. Compatibility of these promotants will be an important management issue. Thus, producer management skills are critical to the optimal use of these technologies.

As important as these management issues are, a more pressing management issue is that of animal welfare—with or without biotechnology as a complicating factor. Society has focused on many of the resulting impacts of technologies such as environmental quality, food safety, and decline of the small farm and rural communities. Farm animal well-being is the most recent concern to receive attention. Much of the success in increased productivity in agriculture has been the result of lowered costs through the use of confinement systems—which some have coined factory farming. The question from an animal welfare perspective is whether we have gone too far.

Farm Animal Well-Being

In the decade of the nineties, the advance of new animal technologies will coincide with increasing interest in farm animal well-being. This interest is not new. It nucleated in England at the turn of the 19th Century with the formation of the Royal Society for the Prevention of Cruelty to Animals. This in turn led to the organizing of more radical groups. In America, the American Society for the Prevention of Cruelty to Animals was formed in the 1860s by a Special Act of the New York State Legislature. However, it was not until the late 1970s and early 1980s that the majority of animal welfare/rights organizations were formed. Although no specific records are kept, estimates indicate that today there are a total of 7,000 animal welfare/rights groups in the United States with a combined total budget of $50 million (81).

Widespread public concern for farm animals began to develop in 1963 with the publication of *Animal Machines.* This book by Ruth Harrison (46) chronicled the problems in farm animal well-being in the United Kingdom that led to the Brambell commission and its report enunciating the famous ‘‘Five Freedoms’ ‘—to lie down. stand up, turn around, stretch, and groom.

Concern built steadily in Europe, and in 1979 the first European meeting on farm animal welfare was held. European governments have allocated significant public funds to research on alternative farm systems and the European

Community (EC) has supported numerous symposia on the well-being of various farm animals. Legal protection for farm animals includes far-reaching laws in Sweden and Switzerland.

In the United States the level of concern has grown more slowly. However, in the past few years the pressure on farmers and animal scientists to address the issue of farm animal welfare has increased steadily. The issue of farm animal welfare has provided important impetus to a movement that may eventually be considered as significant by policy makers as that for environmental and food safety concerns. Today, the issues of animal welfare/rights foster well-entrenched polar positions. The polarity between the agricultural establishment and animal well-being advocates has highlighted the extremes of each group's position. Economics, values, and institutions determine care and treatment of farm animals. These factors divide into two animal welfare paradigms: the traditional and the alternative. Which paradigm will dominate future public policy for animal welfare remains to be seen (94).

The Traditional Paradigm

Those who hold the traditional paradigm of animal welfare draw on the market model of free enterprise, and on Judeo-Christian ethics.

The Market Model—Advocates of the market model argue that farm animals subject to cruelty and neglect give fewer eggs and less milk, meat, or wool than well-treated and properly cared for animals. Why not, they ask, depend on profits to ensure farm animal welfare?

Quantifiable variables such as feeding efficiency, rate of growth or productivity, morbidity, and mortality rates can provide proxy measures of animal welfare. Favorable values for those objective measures of humane treatment for the most part are consistent with good management and high profits.

Advocates of the market model further argue that confinement systems improve some dimensions of animal welfare. Temperature, disease, and pest control are improved. Predators are kept away. Nutrition is enhanced. Modern farming systems have lowered costs and expanded utilization, allowing more animals to exist.

The Judeo-Christian Ethic—Advocates of the traditional paradigm hold the Judeo-Christian ethic that God created man in his own image, that man is unique in having a soul, that man has dominion over animals, and that man as husbandman and steward of God's kingdom is not to practice cruelty to or neglect animals (77, 86). Many advocates of this position hold that no element of society has more compassion for poultry and livestock than does the farmer (45). Other than laws protecting animals from cruelty and neglect, advocates of this view consider laws, rules, and regulation on care and treatment of farm animals to be unwarranted infringement on free enterprise. This creed holds that 1) proprietors deserve the right to prescribe rules under which they operate; and 2) a prime function of government is to prevent anyone, including the government, from infringing on the managerial freedom of proprietors (5).

Some traditionalists will admit that, despite market incentives, cruelty-neglect laws, and producers with the Judeo-Christian ethic, animal welfare falls short of the ideal. But they contend that ''Big Brother' intrusions of an expensive and often incompetent bureaucracy into managerial prerogatives of farmers would entail more social cost than the abuses government is attempting to correct. They favor minimal policy intervention consistent with the traditional paradigm as the lesser of two evils.

Alternative Paradigm

An increasing number of people reject the Judeo-Christian ethic and market paradigm in favor of an alternative paradigm emphasizing animal rights or much enhanced animal welfare. As with the traditional paradigm, the alternative has economic and ethical dimensions.

Market Failure—Animal welfare has public goods properties, implying that the market alone will not bring the proper level of animal welfare. Externalities are apparent: all the public benefits from seeing livestock freely grazing in a meadow. Animal rights activists contend that the market results in confinement cages allowing too little space per animal for laying hens, sows, and veal calves. The drive to reduce costs and cater to consumer demand has kept veal calves isolated, in the dark, and on low iron diets; has disfigured animals, by encouraging practices such as trimming chickens' combs and beaks and pigs' and lambs' tails. According to activists, animals are not allowed their "natures' '—socialization, sex, exercise, nest building, nurturing of offspring, the outdoors, and a full life.

However. the role of markets in shaping the way farm animals are raised cannot be denied. Market forces have raised real prices of land and labor, and reduced the relative price of capital. Rising labor and land prices have placed a premium on labor-saving and land-saving methods of production. Gains in income and population along with changes in production technologies, including disease control, have interacted with prices to create economies of size and to make confinement systems feasible. Small may be beautiful but it is frequently not competitive. The small-scale poultry operator is nearly extinct; the small Wisconsin dairy has difficulty competing with the large industrial-type California dairy farm; and the family hog farm in Iowa has difficulty competing with the large confinement operations in Arkansas. Animal welfare enthusiasts view these outcomes of market forces as a disaster to farm livestock and to traditional farmers, rather than as a means toward cheaper food. more land for urban use, and higher income for the Nation.

Ethics—The alternative paradigm views man as an evolutionary product of a holistic Nature. Man is one with nature and must live in harmony with plants and animals. If he has primacy, it is to be used to ensure the rights of the rest of nature.

Philosopher Jeremy Bentham's (4) much-quoted comment summarizes the basis for the ethical treatment of animals under the alternative paradigm: ''The question is not Can they reason'? nor, Can they talk'? but, Can they suffer'?'

Animals that are sentient (can experience pleasure or pain) are to be afforded rights given to people. Killing an animal is murder and eating its flesh is cannibalism. Hard-core animal rights adherents have little alternative to vegetarianism. Other advocates do not go that far but insist on improving animal welfare through provision for each species' nature.

Animal suffering and pain is probably the most powerful rationale for the public's concern over farm animal welfare. This concern must be addressed by objective research.

Research Needed

To understand and fulfill agricultural animals' needs, more must be learned about their fundamental psychological and behavioral processes. Researchers must be able to elucidate farm animals' cognitive and motivational processes before it is possible to begin to answer such rudimentary and obvious questions about their well-being such as: How does this animal feel in one environment versus another? Is the animal suffering—and if so. how much? For example, when the animal's farm environment is devoid of a particular feature that would characterize its natural environment, does the animal suffer—and if so, how much (11, 12)?

The scientific community generally has been slow to accept the notion of animal awareness and only recently has such recognition been forthcoming. Many in agriculture now acknowledge that animals are aware of themselves and their surroundings, and thus scientists are beginning to give attention to animals' conscious sensations of well-being. Only recently have factors that affect conscious well-being been considered logical criteria for the design of animal accommodations. However, there exists little hard data on which to base such a design strategy.

How an animal feels, some assume, depends largely on how it expects to feel. How it expects to feel in turn depends on how it thinks, remembers, and imagines. How an animal feels also depends on factors such as the predictability and controllability of its environment (100).

Feeling, thinking, remembering, and imagining are cognitive processes. To the extent that feeling and thus, thinking, remembering, and imagining affect an animal's overall well-being, and therefore its health and productivity, these cognitive processes are factors to be considered in the economic and humane production of agricultural animals.

There is reason to believe that when an animal experiences a feeling of malaise, its productivity is reduced, if only slightly. However, such decrements are cumulative; and together they can reduce productivity significantly. In the chicken, for example, there is recent evidence that as many as six stressors—ammonia, beak trimming, coccidiosis, electric shock, heat, and noise—can combine in additive fashion to affect feed intake, growth, and several important physiological and pathological traits (64). In addition, stressors and combinations of stressors occurring in various sequences affect productive performance of chickens in predictable, repeatable ways (52). This linear additivity of stressor effects on such a variety of traits suggests that some single phenomenon is governing the animals' overall response. This could be psychological stress. The following discussion depicts some of the production practices that animals encounter and areas of research that are needed (12).

Thermal Comfort— Little is known about the perception of thermal comfort by farm animals (10). Animals do respond to changing conditions in their thermal environment with different thermoregulatory behaviors. But the degree to which animals suffer when experiencing heat stress or cold stress is not known. One experiment to find the answer to cold stress of farm animals is cur-

Photo credit: University of Illinois

An example of a thermal comfort experiment involving pigs operating a heat switch. The sitting pig—presumably because it felt the environment was too cool—has just operated the switch in the panel to engage the heater.

rently underway involving pigs operating a heat switch when they feel cold.

Another thermoregulatory behavior response is wallowing by swine under heat stress. Wallowing in mud compensates for the pig's absence of thermal sweating. Research has shown that sows wallow only when environmental temperature exceeds some threshold (e.g., 12 "C for sows in one experiment) (83). This limited research suggests that swine wallow only to achieve thermal comfort, not because they need to wallow or enjoy wallowing as play. If the thermal environment is maintained below 12 "C all the time, sows never take advantage of a mud wallow even if it is provided.

Quality of Space-The richness of an environment is somehow perceived by animals because it affects how they behave and function. The behavior repertory of swine in natural settings is larger than it is in typical production environments (88).

When contemporary production environments are furnished with enriching features, pigs readily make use of these features and thereby expand their behavior repertories. Nehring (71) built a maze in a pig pen. McGlone and Curtis (67) provided pigs hiding places for their heads allowing them to submit to and subsequently avoid an aggressive pen mate. Fraser provided pigs a mezzanine for use in getting away from group mates (19, 74). Grandin (40) enriched pig environments with suspended manipulanda (pig toys). Pigs reared in enriched environments proved easier to be moved about than pigs in traditional production environments (43). Pigs residing in pens equipped with suspended manipulanda fouled their feeder markedly less often than did those in a relatively barren environment (92).

From the above, it might be inferred that animals in richer natural or artificial environments behave differently and experience an enhanced sense of well-being compared to those in more barren surroundings. But this has not been determined scientifically to be the case, and many questions persist. For example, do pigs enjoy a higher sense of well-being when able to use enriched features'? Are they starved for stimulation in less rich environments'? If so, does this lead to a craving for stimulation'?

Commercial gilts and sows often reside during pregnancy in rectangular crates that prevent them from turning around. When living in a crate shaped so as to permit her to turn around, a pregnant gilt will turn around approximately 13 times daily in a crate 61 cm wide, but only 9 times daily in a 56 cm wide crate (in which it is more difficult for the gilt to turn around) (63). Little is known about what motivates a gilt to turn around. Does she need to turn around'? Does this need affect her productive performance'?

How an animal perceives its living space may be crucial to its sense of well-being. Sometimes space can be modified physically or rearranged so as to make it more accommodating to the animal. For example, animals in pens have a propensity to keep their heads at or to lie around the perimeter of a pen instead of in the middle (39, 90). A triangle has 28 percent more perimeter and a square 13 percent more than a circle of equal area. Thus, of the three, triangular pens maximize the ratio of perimeter to area. Should animal facilities be built with triangular pens and cages instead of rectangular ones to enhance the animals' comfort'? Is it necessary to have more space in a rectangular pen to engender the same feeling of well-being that an animal would experience in a square pen of equivalent perimeter'?

Learned Helplessness— Animals often encounter frustrating situations and presumably these may decrease their well-being. For example, when anything gets in the way of an animal on its way to the feeder to eat, that animal becomes frustrated. Frustration is one of the prepathological states indicative of stress (69). Frustrating situations generally are stressful, as indicated by various physiological indicators (13).

Farm animals may be frustrated when engaged in any strongly motivated behavior pattern, whether eating, nesting, and engaging in sexual activities, among others. Depending on the circumstances, for example, frustrated hens may show displacement behavior—behavior patterns that occur out of context with preceding and succeeding behavior (16).

In other settings, an animal may find that it can neither control its environment nor predict what its environment will be, and the animal may learn to act in a helpless manner. In a state of learned helplessness, an animal stops initiating behavior aimed at controlling or making use of environmental features because it has learned to expect that these features are uncontrollable and that these attempts would be futile (84).

Animals residing in certain intensive production systems might well learn to expect that they have little or no control over their surroundings. It is possible that agricultural animals living in certain housing systems may develop learned helplessness (14, 61. 62). Learned helplessness would be another of the prepathological states indicative of stress (69).

Nestbuilding—Females of all domestic avian species build nests in which they lay their eggs. The domestic hen will engage in nest-building every day, even when a previous nest exists. It seems that the performance of nest-building is itself positively reinforcing to the hen (50).

Most sows attempt to construct a farrowing nest beginning 12 to 16 hours prior to delivering the first pig, regardless of where they are (51). In many modern farrowing environments, there is neither the space in which to conduct nest-building behavior nor the material with which to build a nest. Sows nevertheless direct substantial amounts of time toward small amounts of material even though a nest may not result. This suggests that for the sow, as for the hen, nest-building behavior in itself is rewarding (99). Research is needed to answer such questions as: Do hens and sows need to build nests'? How much frustration do they experience when they either cannot move enough material to nest-build or cannot find nesting material? How do they feel when they cannot build a nest? Does this feeling in sows result in hormonal changes that are an anathema to oxytocin's actions in birth and lactation'?

Electro-Immobilization— Animal may find certain procedures routinely performed in agricultural production to be uncomfortable or even painful. When an animal actively avoids a procedure it is presumably revealing negative feelings about the procedure. Ewes having experienced restraint by electro-immobilization and by a squeeze-tilt table, when given the choice between the two in a Y-maze avoid-avoid test, chose the squeeze-tilt table 79 percent of the time, and the electro-immobilizer 13 percent (42). Questions that need answers include: What was the ewe thinking as she hesitated at the decision point, indicating by her head movements that she is vacillating? Was she actually imagining the feeling she experienced during electro-immobilization earlier'? Based on the ewe's reactions, when should the electro-immobilizer not be used? What behavior indicators identify the point beyond which it would be inhumane to continue subjecting the ewe to the procedure?

Photo credit: University of Illinois

The sow—in anticipation of delivering a litter of piglets within a few hours—is building a maternal nest to protect the piglets from cold and predators.

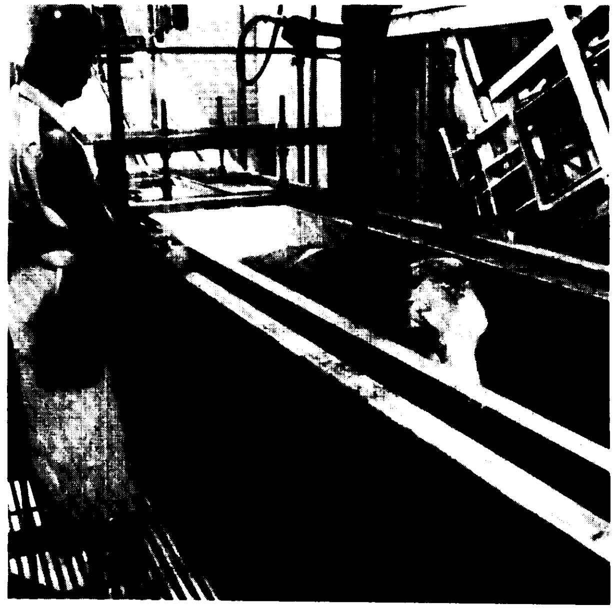
Chicken-Harvesting Machine— Animals can adapt in a matter of seconds to machines with which they are forced to interact, provided that the machines are designed with the animal's nature in mind. Take, for example, the chicken harvesting machine developed in the United Kingdom. The harvesting of birds from growing houses is a monumental task. Moreover, considerable losses are incurred in the process of harvesting and transportation, especially in the hand-catching and hand-crating processes (25).

A prototype chicken-harvesting machine has been evaluated in terms of the stressfulness of the harvesting process (15). By means of electrocardiograms and immobility tests, it has been found that the stress from harvesting could be reduced by catching and picking up broiler chickens with a carefully designed machine, rather than by hand. Heart rate dropped back to normal more quickly and duration of tonic immobility (a phenomenon that increases with fear) was much shorter in machine-harvested birds than in those caught by hand. Research questions include: What is a chicken thinking when it is manually caught by one leg and carried upside down to the crate in which it will be transported to the processing plant'? How does this contrast to what it is experiencing when it is caught by the long rubber fingers of a chicken-harvesting machine, moving it onto a moderately inclined conveyer belt, which it rides to the gathering stage'?

Double-Rail Restrainer Conveyor **System—Means** of rapidly moving large numbers of animals of all kinds are needed in the production and processing industries. The V-restrainer, in which animals are moved along and wedged between two v-angled conveyor belts, with their legs dangling, is a vast improvement over driving animals through a chute, but it gives rise to additional problems.

A prototype of this system was developed in the late 1970s, and it caused little premortem stress in animals when used in a processing plant (98). The system was further developed for applications ranging from veal, lamb, and swine slaughter lines to feedlot cattle processing. When designed specifically for the species and size range to be handled, the animals apparently find the conveyer belt comfortable to ride. Adjustable sides prevent the animal from leaning sideways which is important because tilting sideways seems to frighten the animal.

As the above discussion illustrates, there are many questions to be answered regarding animal welfare. Of particular importance is the effect of animal well-being on the animal's performance. Some research seems to indicate that the amount of psychological stress an animal experiences determines how the pituitary-adrenal axis responds. In other words, psychological stress may be reducing the animal's performance as well as the animal's well-being. Much more research is needed to understand such relationships. To date, little research has been done in the United States on animal well-being.



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Biotechnology and Farm Animal Well-Being

In the past few years, animal protection groups have begun to voice concerns about biotechnology. Their concerns are rather diffuse and it is difficult to determine precisely what could be done to address those concerns. The new techniques for manipulating genetic material strike at some deep-seated fears amongst animal protection groups. While there are few concise papers explaining animal protection concerns, a reading of the relevant literature leads to the identification of the following issues:

- reinforcing notions of animals as mere property to be manipulated at the whim of human owners, and
- animal well-being issues (81).

Manipulation of Property

Genetic engineering conjures up images by some in the animal protection movement of animal machines being reconstructed by ingenious scientists to meet human needs. The push to be allowed to patent animals (discussed in ch. 15) merely reinforces the idea of animals as patentable machines. At a time when the animal movement is pushing to increase the moral status of animals to, at the very least, something between persons and property, the biotechnology era and patenting seem to be a major step backwards.

Animal Well-Being Issues

The impact of biotechnology on animal well-being is probably the most challenging issue genetic engineering raises. The technology is most likely impact-neutral in that one could use biotechnology to improve animal well-being (e.g., engineer disease resistance, eliminate detrimental genes from a population) as well as compromise it. The clearest example of compromised well-being is the "Beltsville pig" (discussed in ch. 3). This pig is the result of research at the U.S. Department of Agriculture (USDA) in Beltsville that involved the insertion of extra growth hormone genes. When the extra genes were expressed, the animal grew fast but, as it gained weight, it became lame and lethargic and suffered from degenerative joint disease and a variety of other disorders (41). There is little doubt that the animal was under stress as a result of the genetic manipulation. Questions also have been raised about the quality of life for the "oncomouse' and some of the other mice that have been developed to shorten the time of standard carcinogen and mutagen tests.

It is also possible, however, that some genetically engineered animals might reduce the need for research animals and hence qualify as alternatives. Among farm animals, moreover. it may be possible to use genetic engineering to eliminate the horn gene in cattle, thereby removing the welfare problems associated with dehorning (4 1). While some object strongly to the proposal that farmers should create breeds of microcephalic (small brained) farm animals that are quite content in close confinement (41), others say that as long as the animal is in a state of positive well-being, such a creation would not be morally objectionable though there may be some esthetic problems with such creatures (79). To date, there has been little discussion or debate of these questions. and about the most that can be concluded at this stage is that careful monitoring of transgenic animals to determine their state of well-being is essential. As more experience and research with transgenic animals takes place, it will be possible to develop more sensible guidelines and conclusions.

Biotechnology is a *priori* neither good nor bad for animals. Its impact depends on what is done and its effect. If it is used judiciously to benefit humans and animals, with foreseeable risks controlled, and the welfare of the animals is kept in mind, it is morally defensible and can provide great benefits.

CHAPTER 6 REFERENCES

1. Barrett, S., "Crop Mimicry in Weeds, " *Economic Botany* 37:255–282, 1983.
2. Beachy, R.N. et al., "Genetic Engineering of Plants for Protection Against Virus Diseases, " *Plant Resistance to Viruses.* D. Ever and S. Harnett (eds.) (New York, NY: Wiley & Sons, 1990), pp. 151-158.
3. Benfey, P.N. and Chua, N. H., "Regulated Genes in Transgenic Plants. ' *Science* 244: *1* 74– 181, 1989.
4. Bentham, J., *The Works of Jeremy Bentham*, J. Bowring (cd.), vol. I (New York, NY: Russell and Russell, 1962). pp. 142-143.
5. Brewster, J.. ''Societ y Values and Goals in Respect to Agriculture, ' Chapter 6 in *Goals and Values in Agricultural Policy* (Ames. IA: Iowa State University Press, 1961).
6. Burch, T., Professor, Cooperative Extension Program, Louisiana State University. Baton Rouge, LA, personal communication, Dec. 20, 1990.
7. Coble, H., Professor, Crop Science Department, North Carolina State University, Raleigh, NC, personal communication, Dec. 18 and 20, 1990.
8. Comai, L. and Stalker, D. M., ''Impact of Genetic Engineering on Crop Protection, " *Crop Pro?.* 3:399–408, 1984.
9. Curtis, C.F. and Otoo, L. N., "A Simple Model of the Build-Up of Resistance to Mixtures of Anti-Malarial Drugs, " *Trans. Roy. Soc. Trop. Med. & Hyg.* 80:889–892, 1986.
10. Curtis, S.E. "Perception of Thermal Comfort by Farm Animal s,' *Farm Animal Welfare and Housing*, *S.* H. Baxter, M.R. Baxter, and J. A.D. MacCormack (eds.) (Boston. MA: Martinus Nijhoff, 1983), pp. 59-66.
11. Curtis, S., ''Environment and Animal Behavior, ' commissioned background paper prepared for the Office of Technology Assessment, 1991.
12. Curtis, S. and Stricklin, R., "The Importance of Animal Cognition in Agricultural Animal Production Systems: An Overview, ' a paper presented at the symposium, Cognition and Awareness of Animals: Do Farm Animals' Perceptions Affect Their Production or Well-Being'? 1991.
13. Dantzer, R. and Mormede, P., "Can Physiological Criteria be Used to Assess Welfare in Pigs?" *The Welfare of Pigs*, W. Sybesma (cd.) (Boston. MA: Martinus Nijhoff, 1981), pp. 53–73.
14. Deaton, R., Monsanto Agriculture Co., St. Louis. MO, personal communication, Dec. 18, 1990.
15. Duncan, I.J. H. et al., "Comparison of the Stressfulness of Harvesting Broiler Chickens by Machine and by Hand,'' *Br. Poultr. Sci.* 27: 109, 1986.
16. Duncan, 1. J. H., "The Welfare of Farm Animals: An Ethnological Approach," *Sci. Prog.* 71:317, 1987.
17. Fincher, R., Pioneer, personal communication. Dec. 21, 1990.

18. Fox, M. W., "Farm Animals: Husbandry, Behavior, and Veterinary Practice' (Baltimore, MD: University Park Press, 1984), pp. 237–249.
19. Fraser, D., Phillips, P. A., and Thompson, B. K., "A Test of a Free-Access Two-Level Pen for Fattening Pigs," *Anim. Prod.* 42:269, *1986.*
20. Fraser, R. S. S., "Genetics of Plant Resistance to Viruses, " *Plant Resistance to Viruses, Ciba Found. Symposium 133*, D. Evered and S. Harnett (eds.) (New York, NY: Wiley & Sons, 1990), pp. 6-15.
21. Frisbee, R.E. et al., "Implementing 1PM in Cotton, ' *Integrated Pest Management Systems and Cotton Production*, R.E. Frisbee, K.M. El-Zik, and L.T. Wilson (eds.) (New York, NY: J. Wiley & Sons, 1989), pp. 389-412.
22. Gallun, R. L., "Genetic Basis of Hessian Fly Epidemics," *Ann. N.Y. Acad. Sci.* 287:223–229, *1977.*
23. Gelernter, W. D., "Targeting Insecticide-Resistant Markets, " *Managing Resistance to Agrochemicals, ACS Symposium Series 421*, M. B. Green, H.M. LeBaron, and W.K. Moberg (eds.), Am. Chem. Soc., Washington, DC, 1990, pp. 105-117.
24. Georghiou, G. P., ''Overview of Insecticide Resistance, *Managing Resistance to Agrochemicals, ACS Symposium Series 421,* M.B. Green, H.M. LeBaron, and W.K. Moberg (eds.), Am. Chem. Soc., Washington, DC, 1990, pp. 18-41.
25. Gerrits, A. R., de Koning, K., and Migchels, A., "Catching Broilers, " *Poultry* 1(5):20, *1985.*
26. Goldberg, R., Environmental Defense Fund, New York, NY, personal communication, December 1990.
27. Goldberg, R. et al., "Biotechnology's Bitter Harvest, " Biotech. Work. Group, Rural Advancement Fund International, Pittsboro, NC, 1990.
28. Goodman, R. M., "Future Potential, Problems, and Practicalities of Herbicide-Tolerant Crops from Genetic Engineering, " *Weed Sci.* 35:28–31, 1987.
29. Gould, F. "Simulation Models for Predicting Durability of Insect-Resistant Germ Plasm: A Deterministic Diploid, Two-Locus Model, " *Environ. Entomol. 15:* 1– 10, 1986a.
30. Gould, F., "Simulation Models for Predicting Durability of Insect-Resistant Germ Plasm: Hessian Fly (Diptera: Cecidomyiidae)-Resistant Winter Wheat, *Environ. Entomol. 15:* 11–23, 1986b.
31. Gould, F., "Evolutionary Biology and Genetically Engineered Crops, " *Bioscience* 38:26–33, 1988.
32. Gould, F., "Managing Pest Adaptation to Genetically Engineered Crops, ' pp. 80–86, in National 1PM Coordinating Committee, 1989, Proceedings National Integrated Pest Management Symposium/ Workshop, Las Vegas, Nevada, Apr. 25-28, 1989, Communications Service, NY AES, Cornell Univ., Geneva, NY., 1989, 276 p.
33. Gould, F., "Ecological Genetics and Integrated Pest Management, " *Agroecology*, C.R. Carroll, J.H. Vandermeer, and P.M. Rosset (eds.) (New York, NY: McGraw-Hill Publishing Co., 1990), pp. 441-458.
34. Gould, F., ''Evolution of Resistance to Toxic Compounds by Arthropods, Weeds and Pathogens, " commissioned background paper prepared for the Office of Technology Assessment, 1991.
35. Gould, F., "The Evolutionary Potential of Crop Pests, *American Scientist*, vol. 79, November/ December, 1991.
36. Gould, F. and Anderson, A., "Effects of *Bacillus thuringiensis* and HD-73 Delta-Endotoxin on Growth, Behavior, and Fitness of Susceptible and Toxin-Adapted *Heliothis virescens* (*Lepidoptera: Noctui-&e)* Strains," *Environ. Entomol.* 20:30–38, *1991.*
37. Gould, F. and Weissinger, A., "Roles for Public and Private Sector Scientists in Developing Pest-Resistant Crops, " New *Directions in Biocontrol*, P. Dunn and R. Baker (eds.), Proc. Univ. California Los Angeles Molecular Biology Symposium, 1990, pp. 641-648.
38. Gould, F. et al., "Feeding Behavior and Growth of *Heliothis virescens* Larvae (*Lepidoptera: Noctuidae*) on Diets Containing *Bacillus thuringiensis* Formulations or Endotoxins,'' *Entomol. Exp. Appl.* 58:199–210, *1991.*
39. Grandin, T., "Livestock Behavior as Related to Handling Facilities Design, " *Int. J. Stud. Anim. Prob.* 1 :33, 1980.
40. Grandin, T., '*Double Rail Restrainer Conveyor for Livestock Handling, " *J. Agric. Eng. Res.* 41:327, *1988,*
41. Grandin, T., "Biotechnology and Animal Welfare, " *Animal Biotechnology?* and Quality of Meat Production*, L.O. Fiems, B.G. Cottyn, and D.I. Demeyer (eds.) (Amsterdam: Elsevier, 1991), pp. 145-157.
42. Grandin, T. et al., "Electro-immobilization versus Mechanical Restraint in an Avoid-Avoid Choice Test for Ewes, " *J. Anim. Sci.* 62: *1469, 1986.*
43. Grandin, T. et al., ''Richness of Pig's Environment Affects Handling in Chute," *J. Anim. Sci. 63(* Suppl. 1): 161 (Abstr.), 1986.
44 Grogl, M. et al., ''*Leishmania* spp.: Development of Pentostam-Resistant Clones in vitro by Discontinuous Drug Exposure, " *Exp. Parasite/.* 69:78–*90, 1989.*
45. Guither, H. and Curtis, S., "Changing Attitudes Toward Animal Welfare and Animal Rights, " FS8, *The Farm and Food System in Transition* (East Lansing, Ml: Cooperative Extension Service, Michigan State University, 1983).
46. Harrison, R., *Animal Machines* (London, England: Stuart, 1964).

47. Headley, J.C. and Hey, M. A., "Benefit/Cost Analysis of an Integrated Mite Management Program for Almonds," *J. Econ. Entomol. 80:555-559, 1987.*

48. Heinricks, E.A. et al., "Susceptibility of Rice Plant Hoppers, *Nilaparvata lugens* and *Sogatella furcifera* (Homoptera: Delphacidae) to Insecticide as Influenced by Level of Resistance in the Host Plant." *Environ. Entomol.* 19:455–458, 1984.

49. Hey, M. A., "Almonds (California): Integrated Mite Management for California Almond Orchards." *Spider Mites, Their Biology, Natural Enemies and Control,* W. Helle and M.W. Sabelis (eds.) (Amsterdam: Elsevier, 1985), pp. 299–3 10.

50. Hughes, B. O., Duncan, I. J. H., and Brown, M. F., "The Performance of Nest Building by Domestic Hens: 1s It More Important Than the Construction of a Nest'?' *Anim. Behav.* 37:2 *10,* 1989.

51. Hurnik, J. F., "A Review of Periparturient Behavior in Swine," Can. *J. Anim. Sci.* 65:777, 1985.

52. Johnson, R. W., Curtis, S. E., and Shanks, R. D., "Effects on Chick Performance of Ammonia and Heat Stressors in Various Combination Sequences," *Poult. Sci. 70: 1132, 1991.*

53. Kennedy, G., "2-Trldecanone, Tomatoes and *Heliothis zea*: Potential Incompatibility of Plant Antibiosis with Insecticidal Contro l," *Entomol. Exp. & Appl.* 35:305–3 *I I*, 1984.

54. **Kennedy, G., Department of Entomology.** North Carolina State University, Raleigh. NC, personal communication, August 1990 and October 1990.

55. Kennedy, G. G.. Farrar, R. R., and Riskallah, M. R., "Induced Tolerance of Neonate *Heliothis zea* to Host Plant Allelochemicals and Carbaryl Following Incubation of eggs on Foliage of *Lycopersicon hirsutum* f. *glabratum*," *Oecologia* 73:615–620, *1987.*

56. Kirsch, K. and Schmutterer, J.. "Low Efficacy of a *Bacillus thuringiensis* (Ber.) Formulation in Controlling the Diamondback Moth, *Plutella xylostella* (L.), in the Philippines," J. *Appl. Entomol. 105:249-255, 1988.*

57. LeBaron, H.M. and McFarland, J., "Herbicide Resistance in Weeds and Crops," Managing *Resistance to Agrochemicals, ACS Symposium Series 42/,* M.B. Green, H.M. LeBaron, and W.K. Moberg (eds.), Am. Chem. Soc., Washington, DC., 1990, pp. 336-352.

58. LeBaron, H., Ciba Geigy Corp., Greensboro, NC, personal communication, March 1991.

59. Leemans, J. et al., "Insecticidal Crystal Proteins from *Bacillus thuringiensis* and Their Use in Transgenic Crops," *New Directions in Biological Control,* R.R. Baker and P.E. Dunn (eds.), Proceedings of Univ. California Los Angeles Molecular Biology Symposia, 1990, pp. 573-588.

60. Marrone, P.G. et al., "Discovery of M icrobial Natural Products as Sources of Insecticidal Genes, Novel Synthetic Chemistry. or Fermentation Products." *Biotechnology, Biological Pesticides and Novel Plant-Pest Resistance for Insect Pest Management,* D.W. Roberts and R.R. Granados (eds.), Boyce Thompson Inst.. Cornell Univ., Ithaca, NY, 1989, pp. 1 12– 114.

61. McBride, G., "Feral Animal Studies in Animal Science: The Uses and Limitations of Feral Animal Studies to Contemporary Animal Science," *J. Anim. Sci.* 58:474, *1984.*

62. McBride. G. and Craig. J. V., "Environmental Design and Its Evaluation for Intensively Housed Animals, *Appl. Anim. Behav. Sci.* 14:21 *I , 1985.*

63. McFarlane, J. M., Bee. K. E., and Curtis. S. E., "Turning and Walking by Gilts in Modified Gestation Crates, *J. Anim. Sci.* 66:326, 1988.

64. McFarlane, J.M. et al., "Multiple Concurrent Stressors in Chicks. 1. Effect on Weight Gain, Feed Intake, and Behavior," *Poult. Sci.* 68:501. 1989.

65. McGaughey, W. H., "Insect Resistance to the Biological Insecticide *Bacillus thuringiensis*," *Science 229: 193– 195, 1985.*

66. McGaughey, W.H. and Johnson, D. E.. "Toxicity of Different Serotypes and Toxins of *Bacillus thuringiensis* to Resistant and Susceptible Indianmeal Moths (Lepidoptera: Pyralidae)," *J. Econ. Entomo/. 80: 11 22– 1126, 1987.*

67. McGlone, J.J. and Curtis, S. E., "Behavior and Performance of Weanling Pigs in Pens Equipped with Hide Areas," *J. Anim. Sci.* 60:20, 1985.

68. Miller, D. L., Rahardja, U., and Whalen, M. E., "Development of a Strain of Colorado Potato Beetle Resistant to Bt," *Pesticide Resistance Newsletter* 2(2):25, *1990.*

69. Moberg, G. P., "A Model for Assessing the Impact of Behavioral Stress on Domestic Animals. *J. Anim. Sci. 65: 1228, 1987.*

70. National 1PM Coordinating Committee, Proceedings National Integrated Pest Management Symposium/Workshop, Las Vegas, Nevada, Apr. 25-28, 1989, Communications Services, NY AES, Cornell Univ., Geneva, NY, 1989, 276 p.

71. Nehring, A., "One Answer to the Confinement Pig Problem," *Int. J. Stud. Anim. Prob.* 2:256, *1981.*

72. Pedigo, L. P., *Entomology>* and Pest Management (New* York. NY: MacMillan Publishing Co., 1989).

73. Peters, W., "The Problem of Drug Resistance in Malaria," *Parasitology 90:705-715, 1985.*

74. Phillips, P. A., Thompson, B. K., and Fraser, D., "Preference Tests of Ramp Design for Young Pigs," *Can. J. Anim. Sci. 68:41, 1988.*

75. Powles, S.B. and Howat, P. D., "Herbicide-Resistant Weeds in Australia," *Weed Technol. 4: 178-185, 1990.*

76. Raymond, M. et al., *Nature* 350: 15 1–153, 1991.
77. Regan, T. and Singer, P., *Animal Rights and Human Obligations* (Englewood Cliffs, NJ: Prentice Hall, 1989).
78. Reichard, D.L. and Ladd, Jr., T. L., "Pesticide Injection and Transfer Systems for Field Sprayers, *Trans ASAE, 1983, 26* p.
79. Rollin, B. E., ''The Frankenstein Thing: The Moral Impact of Genetic Engineering of Agricultural Animals on Society and Future Science, *Genetic Engineering of Animals: An Agricultural Perspective,* J.W. Evans and A. Hollaender (eds.) (New York, NY: Plenum Press, 1986), pp. 285-297.
80. Roush, R.T. and McKenzie, J. A., "Ecological Genetics of Insecticide and Acaricide Resistance, * *Annu. Rev. Entomol.* 32:361–380, *1987.*
81. Rowan, A., "Agricultural Animal Welfare Issues, commissioned background paper prepared for the Office of Technology Assessment, 1991.
82. Ryan, A., ''Proteinase Inhibitor Gene Families: Strategies for Transformation to Improve Plant Defenses Against Herbivores, " *BioEssays* 10:20–23, *1989.*
83. Sambraus, H. H., "Das Suhlen von Sauen, " Deutsches Tieraerztliche Wochenschrift 88:65, 1981.
84. Seligman, M. E. P., *Helplessness* (San Francisco, CA: W.H. Freeman, 1975).
85. Shelton, A., New York State Agriculture Experiment Station, Geneva, NY, personal communication, Dec. 21, 1990.
86. Singer P., *Animal Liberation (New* York, NY: Avon Books, 1975).
87. Stalker, D. M., McBride, K. E., and Malyj, L. D., "Herbicide Resistance in Transgenic Plants Expressing a Bacterial Detoxification Gene, ' *Science* 242:419–423, 1988.
88. Stolba, A., "A Family System in Enriched Pens as a Novel Method of Pig Housing, " in *Alternatives to Intensive Husbandry Systems*, Univ. Fed. for Animal Welfare, Potters Bar, UK, 1981. pp. 52–67.
89. Stone, T. B., Sims, S. R., and Marrone, P. G., "Selection of Tobacco Budworm for Resistance to a Genetically Engineered *Pseudomonas fluorescens* Containing the Delta-Endotoxin of *Bacillus thuringiensis* subsp. *kurstaki*,'' *J. Invert. Pathol. 53:228-234, 1989.*
90. Stricklin, W. R., Graves, H. B., and Wilson, L. L., "Some Theoretical and Observed Relationships of Fixed and Portable Spacing Behavior of Animals, ' *Appl. Anim. Ethel. 5:201, 1979.*
91. Tabashnik, B. E., Finson, N., and Johnson, M. W., "Managing Resistance to *Bacillus thuringiensis*: Lessons from the Diamondback Moth (Lepidoptera: Plutellidae), " *J. Econ. Entomol.*, 1990.
92. Taylor, 1. A., Grandin, T., and Curtis, S. E., "Pig Toys: Effects on Feeder-Fouling and Dunging Pattern, *J. Anim. Sci. 63(* Suppl. 1): 161 (Abstr.), 1986.
93. Teetes, G. L., Becerra, M.1., and Peterson, G. C., "Sorghum Midge (Diptera: Cecidormyiidae) Management with Resistant Sorghum and Insecticide, ' *J. Econ. Entomol. 79: 109 I- 1095, 1986.*
94. Tweeten, Luther, "public Policy Decisions for Farm Animal Welfare, ' paper presented to *International Conference on Farm Animal Welfare*, June 1991.
95. U.S. Congress, Office of Technology Assessment, *Beneath the Bottom Line: Agricultural Approaches to Reduce Agrichemical Contamination of Groundwater, OTA-F-417* (U.S. Government Printing Office, Washington, DC: May 1990).
96. Van Rie, J. et al.. "Mechanism of Insect Resistance to the Microbial Insecticide, ' *Bacillus thuringiensis, Science* 247:72–74, *1990.*
97. Weller, D. M., "Biological Control of Soilborne Plant Pathogens in the Rhizosphere with Bacteria, ' *Ann. Rev. Phytopathol.* 26:379–407, 1988.
98. Westervelt, R.G. et al., ● 'Physiological Stress Measurement During Slaughter in Calves and Lambs, " *J. Anim. Sci. 42:831, 1976.*
99. Widowski, T.M. and Curtis, S. E., "The Influence of Straw, Cloth Tassel, or Both on the Prepartum Behavior of Sows," *Appl. Anim. Behav. Sci.* 27:53, *1990.*
100. Wiepkema, P. R., ''Behavioral Aspects of Stress, in P.R. Wiepkema and P.W. M. Adrichem (eds.), *Biology of Stress in Farm Animals: An Integrative Approach* (Boston, MA: Martinus Nijhoff, 1987). pp. 113-133.
101. Wilson, L. T., "Estimating the Abundance and Impact of Arthropod Natural Enemies in 1PM Systems, *Biological Control in Agricultural IPM Systems*, M.A. Hoy and D.C. Herzog (eds.) (Orlando, FL: Academic Press, 1985), pp. 303-322.
102. Zalom, F.G. et al., *Sampling Mites in Almonds: 11. Presence-Absence Sequential Sampling for Tetranychus Mite Species* 52:14–24, 1984.