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Fifty Years Since *Silent Spring*

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Abstract

Rachel Carson's 1962 *Silent Spring* exposed both observed and potential environmental and health externalities of the increasing organochlorine and organophosphate insecticide use in the United States post–World War II. *Silent Spring* was a critical component in a popular movement that resulted in increased regulation and the development of safer pesticides. Most changes in pesticide use in the global north have involved pesticide substitutions, although riskier pesticides remain in use. Many ideas in *Silent Spring* are compatible with the theory of integrated pest management (IPM), and IPM has been broadly embraced in the United States and internationally as a strategy for achieving least-use and/or least-risk pesticide use in agriculture. IPM is a politically feasible policy that purports to reduce pesticide use and/or risk in agriculture but often does not, except in extreme cases of pesticide overuse that result in negative agricultural/economic consequences for growers.

CARSON'S *SILENT SPRING* AND ITS LEGACY

Rachel Carson published *Silent Spring* in 1962 as a reaction to the increased use of insecticides in the United States, primarily organochlorines, such as DDT, and organophosphates (OPs) (22). In *Silent Spring*, Carson states,

> It is not my contention that chemical insecticides must never be used. I do contend that we have put poisonous and biologically potent chemicals indiscriminately into the hands of persons largely or wholly ignorant of their potentials for harm.... If we are going to live so intimately with these chemicals ... eating and drinking them ... we had better know something about their nature and power.

Figure 1 shows an advertisement for DDT in *Time Magazine* in 1947. With regard to the use of DDT to control malaria and other insect-transmitted diseases, Carson states,

> No responsible person contends that insect-borne disease should be ignored. The question that has now urgently presented itself is whether it is either wise or responsible to attack the problem by methods that are rapidly making it worse. The world has heard much of the triumphant war against disease through the control of insect vectors of infection, but it has heard little of the other side of the story—the defeats, the short-lived triumphs that now strongly support the alarming view that the insect enemy has been made actually stronger by our efforts.... The list of resistant species now includes practically all of the insect groups of medical importance.... Malaria programs are threatened by resistance among mosquitoes.... Practical advice should be "Spray as little as you possibly can" rather than "Spray to the limit of your capacity ...." Pressure on the pest population should always be as slight as possible.

Many of the claims in *Silent Spring* are in keeping with the essence of Stern et al.'s (147) classic work on integrated control and what was later termed integrated pest management (IPM). However, Carson's editors encouraged her to avoid technical terminology, and *Silent Spring* is written in a polemic ("As crude a weapon as the cave man's club, the chemical barrage has been hurled against the fabric of life.... ") rather than in a scientific style (118).

Many agriculturalists, who were delighted by the yield increases associated with pesticide and fertilizer use (123), rejected the claims in *Silent Spring*. Norman Borlaug, the key wheat breeder in the green revolution, stated "We're having troubles now feeding this hungry world.... If you remove DDT with the hysteria that is present in the USA, the US will be importing food, only there won't be any place from where to import it" (121). The pesticide industry ridiculed Carson and denied the validity of virtually all of her claims (118). Pesticide companies tried to stop the *Silent Spring* message; before *Silent Spring* was published, pesticide manufacturers threatened lawsuits against the New Yorker and Audubon magazines for printing chapters. In many ways, the gulf between pesticide enthusiasts and pesticide skeptics has remained for the past 50 years. For example, DDT is inexpensive and persistent, and the benefits versus the harms for continued use in control of malaria and other insect-borne diseases remain controversial (93). Pimentel (127) estimated that in the United States $10 billion per year for pesticides resulted in $40 billion in benefits, which are distributed to growers and pesticide companies as profits and to the public as lower food costs and plentiful food. However, Pimentel (132) also estimated $12 billion per year in quantifiable negative externalities, such as water pollution (122) and health impacts, which are primarily paid for by the public. It is notoriously difficult to estimate the costs of negative externalities (162), particularly for major ecosystem services that can be adversely impacted by pesticides; Gallai et al. (56) estimated that beneficial insect pollinators worldwide provide a value of $206 billion per year.

The great expectations held for DDT have been realized. During 1946, exhaustive scientific tests have shown that, when properly used, DDT kills a host of destructive insect pests, and is a benefactor of all humanity.

Pennsalt produces DDT and its products in all standard forms and is now one of the country's largest producers of this amazing insecticide. Today, everyone can enjoy added comfort, health and safety through the insect-killing powers of Pennsalt DDT products . . . and DDT is only one of Pennsalt's many chemical products which benefit industry, farm and home.

GOOD FOR STEERS—Beef grows meatier nowadays . . . for it's a scientific fact that—compared to untreated cattle—beef-steers gain up to 50 pounds extra when protected from horn flies and many other pests with DDT insecticides.

Knox Out FOR THE HOME—helps to make healthier, more comfortable homes . . . protects your family from dangerous insect pests. Use Knox-Out DDT Powders and Sprays as directed . . . then watch the bugs "bite the dust"!

Knox Out FOR DAIRIES—Up to 20% more milk . . . more butter . . . more cheese . . . tests prove greater milk production when dairy cows are protected from the annoyance of many insects with DDT insecticides like Knox-Out Stock and Barn Spray.

GOOD FOR FRUITS—Bigger apples, juicier fruits that are free from unsightly worms . . . all benefits resulting from DDT dusts and sprays.

GOOD FOR ROW CROPS—*25 more barrels of potatoes per acre* . . . actual DDT tests have shown crop increases like this! DDT dusts and sprays help truck farmers pass these gains along to you.

Knox Out FOR INDUSTRY—Food processing plants, laundries, dry cleaning plants, hotels . . . dozens of industries gain effective bug control, more pleasant work conditions with Pennsalt DDT products.

PENN SALT
CHEMICALS
97 Years' Service to Industry • Farm • Home

PENNSYLVANIA SALT MANUFACTURING COMPANY
WIDENER BUILDING, PHILADELPHIA 7, PA.

Figure 1

"DDT is good for me." An advertisement for widespread farm, home, and food-processing use of Pennsalt's DDT from the June 30, 1947 issue of Time magazine.

Evidence of increasing air and water pollution in the United States, such as the 1952 Cuyahoga River fire, primed the *Silent Spring*–era public for a message that at least some industrial chemicals had negative health and environmental consequences. President John F. Kennedy acknowledged *Silent Spring* and initiated a review of its claims. Tait (152) contends that the agrochemical industry's denial that organochlorine insecticides damaged wildlife caused a decline in the public's trust in the industry that has yet to be rectified. One scandal in the United States dealing with pesticide manufacturer veracity and pesticide safety involved fraudulent toxicology results; fabricated results from the Industrial Bio-Test Laboratories (IBT) between 1953 and 1983 resulted in uncertainty about the data for 200 registered pesticides (102). US Environmental Protection Agency (EPA) cancellations of pesticide registrations for safety issues also may trigger public concern. For example, after the discovery that exposure to high concentrations of the fumigant and nematicide 1,2-dibromo-3-chloropropane (DBCP) caused human sterility, DBCP was banned by the EPA in 1979. However, its water solubility and persistence have resulted in groundwater contamination. In 1990, the city of Fresno, California filed a $650 million lawsuit against three DBCP manufacturers.

Sachs et al. (137) indicate that consumer concern about pesticides increased between 1965 and 1984. In an ABC News poll in 2001 (1), 52% of US consumers that were asked, "If you saw a label on food at your market saying it had been grown or raised organically, without the use of pesticides, chemical fertilizers or feed additives, would you be more likely to buy it, less likely to buy it, or would it make no difference in your buying decision?" answered more likely, only 10% answered less likely, and 36% said that it made no difference. Largely due to consumer concerns about pesticide residues, organic food sales in the United States increased from $11 billion to $25 billion from 2004 to 2011, although this only accounted for 3.5% of food sales in 2011 (120).

Negative impacts of pesticides continue to become apparent. Although the mechanism of honeybee decline is unclear, pesticides appear to have a role (96, 111). There is the greatest evidence for the involvement of neonicotinoid insecticides, which can suppress immune function at sublethal concentrations and are systemic in plants (33, 67, 74, 139, 164). In terms of public health, in addition to acute pesticide poisonings, which are particularly prevalent in the global south (126), more subtle pesticide effects have become apparent. Space limits us to just three examples: Multiple studies have demonstrated brain anomalies and compromised cognitive development in children that were exposed prenatally to organophosphate insecticides (15, 36, 131, 132); selection pressure from applications of triazol agricultural fungicides in the field appears to have resulted in multidrug resistance of the human pathogenic fungus *Aspergillus fumigatus* (146, 161); and the majority of studies on organochlorine, OP, and pyrethroids have concluded that occupational and environmental exposures can result in decreased sperm concentration in men (103).

TRENDS IN PESTICIDE USE WITH AN EMPHASIS ON US AGRICULTURE, 1962–2012

Despite large increases in pesticide use since the 1960s, the percentage of crop loss has remained relatively constant (115). On the basis of the Crop Protection Compendium (**http://www.cabi.org/cpc**), Oerke (115) estimated that weeds, animal pests, and pathogens in six major crops in 2001 to 2003 collectively accounted for losses of approximately 26% to 40% of the crop, depending on the crop; pathogens alone accounted for 7% to 15%, with viruses accounting for 0.7% to 7%. However, in the absence of current management practices (including but not limited to pesticides), losses would account for 50% to 82% of the crop; pathogens alone would account for 8% to 21%, with viruses accounting for 0.8% to 8%. Indeed, the agricultural environments that allow the highest yields are also the most favorable for the highest losses. Thus, efficacious pathogen and pest control remain critical for providing an adequate food supply (116).

Mass of total pesticides applied is a poor measure of pesticide use partly because newer pesticides are typically used in lower concentrations (i.e., with greater toxicity per gram of mass) than older materials and partly because there is a poor correlation between mass of active ingredients applied and environmental risk. Nonetheless, in the United States, pesticide use increased from the 1960s to the early 1980s (119). The highly persistent organochlorines, such as DDT, dominated the insecticide market until they were replaced in the 1970s and 1980s by the OPs and carbamates. In 1972, the EPA revoked approval for the use of DDT on food. Pyrethroids, which have lower mammalian toxicity but high aquatic toxicity, were introduced in the early 1980s and partly replaced the OPs and carbamates. Neonicotinoids were introduced in the 1990s and also partly replaced the older materials. In 2000, OPs accounted for 72% by mass of the insecticides used in the United States. In 2007, OPs accounted for 35% of the insecticides (70).

Several classes of organic fungicides that have multiple biochemical sites of action were introduced between 1940 and 1970, including the dithiocarbamates maneb in 1955 and mancozeb in 1961, the phthalimide captan in 1952, and the pthalonitrile chlorothalonil in 1964 (110). Starting in the 1970s, fungicides that have a single site of action were introduced, including the triazole sterol biosynthesis inhibitors, which accounted for approximately 30% of the world fungicide market in 2010; and the strobilurin cytochrome bc1 inhibitors, which were released starting in 1996 and accounted for approximately 20% of the world fungicide market in 2010 (153). Other fungicides with single sites of inhibition but smaller market shares include β-tubulin inhibitors and succinate dehydrogenase inhibitors as well as many others. The economic success of the sterol demethylase and cytochrome inhibitors is probably partly due to their inhibition of cytochrome P_{450} and cytochrome reductase enzymes, respectively, in the plant, which can confer horticultural benefits, such as delayed senescence, stress resistance, and increased yield (153, 169, 172). Wise & Mueller (169) attributed increased use of foliar fungicides on corn in the Midwestern United States in 2007 to an increased market price in corn, some increases in foliar disease in portions of the United States, new fungicide registrations, and fungicide manufacturer marketing. Primarily using the pesticide-industry supported CropLife data, it was found that agricultural fungicide use in the United States cost growers $0.9 billion and resulted in a yield benefit to growers of $12.8 billion (128).

In the 1980s, based on mass, pesticide use declined somewhat because of the scaling back of pesticide overuse and the introduction of compounds that are used at lower concentrations (23). For example, the OP-chlorinated hydrocarbon chlorpyrifos, which was introduced in 1965, is typically applied in orange orchards at 2.9 kg active ingredient (a.i.)/ha. The neonicotinoid imidacloprid, introduced in the United States in 1994, is typically applied in orange orchards at 15% of the mass of chlorpyrifos (0.45 kg a.i./ha). Similarly, the fungicide captan, which was introduced in 1952, is typically applied in almond orchards at 3.3 kg a.i./ha, whereas the strobilurin fungicide azoxystrobin, which was introduced 1996, is typically applied in almond orchards at 7% of the mass of captan (0.22 kg a.i./ha). Despite the decrease in the concentration of active ingredients in newer pesticides and the adoption of newer pesticides, there is no compelling evidence of an overall decline in current pesticide use in the United States (119). Regardless, the California Department of Pesticide Regulation (DPR) typically concludes in individual years with lower use that we are "moving in the right direction" and in years with higher use that there was "higher pest pressure." More realistically, pest pressure is only one factor that drives pesticide use (17).

As a percentage of farm production costs in the United States, pesticides are relatively inexpensive and only accounted for 0.9% of the costs in 1951, 1.3% in 1964, 5.0% in 1998, and 3.9% in 2010 (35). Since the 1980s, the prices paid by agricultural producers for fuel, seed, fertilizer, and labor increased roughly twice as fast as the prices paid for pesticides. During the 1996 to 2007 period, US agricultural producers spent 63% of their pesticide expenditures on herbicides and plant growth regulators, 21% on insecticides, 10% on fungicides, and 7% on other chemicals (including nematicides, fumigants, and rodenticides). In 2007 in the United States, farmers spent $7.9 billion on agricultural pesticides: They used 200 million kg of herbicides and plant growth regulators, 29 million kg of insecticides, 20 million kg of fungicides, 60 million kg primarily of fumigants and nematicides, and 88 million kg of sulfur and other miscellaneous pesticides (70).

In terms of mass, in 2007 in the United States, the most-used pesticide (excluding sulfur and oils) was the herbicide glyphosate; the herbicides atrazine, metolachlor, acetochlor, and 2,4-D were ranked 2, 4, 5, and 7, respectively (70). The fumigants metam sodium, dichloropropene, methyl bromide (MB), chloropicrin, and metam potassium were ranked 3, 6, 8, 9, and 13, respectively. The fungicides applied agriculturally in the greatest quantity in the United States in 2007 were chlorothalonil (3.6 million kg), and mancozeb (2.3 million kg). The insecticides used in the greatest quantity were the OP chlorpyrifos (3.6 million kg), the carbamate aldicarb (1.6 million kg) and the OP acephate (1.4 million kg).

Following passage of the Food Quality Protection Act (FQPA) in 1996, the United States decreased its reliance on OPs and carbamates. There are 22 FQPA-targeted pesticides that were used in California fields in relatively large quantities (i.e., greater than 10,000 kg in either 1993 or 2010) (42). Of these, 19 declined in use an average of 69% between the pre-FQPA period of 1993 to 1995 and 2008 to 2010 (42). Three compounds (the new fungicide propamocarb, the insecticide bensulide, and the insecticide/nematicide oxamyl) increased in use. Despite the decreases, more than 100,000 kg were applied annually of each of seven of the compounds in California fields (the insecticides chlorpyrifos, dimethoate, malathion, and methomyl, the plant-growth regulator ethephon, and the herbicide thiobencarb) in the 2008 to 2010 period (42); applications of chlorpyrifos, a water pollutant (7) and human developmental toxin (131, 132), averaged 5.9×10^5 kg/year in California fields during the 2008 to 2010 period (43). Decreased use of OPs in agriculture throughout the United States (119) has been accompanied by a decrease in ingested OPs, as indicated by decreased OP metabolites in urine (27).

There are eight fungicides that were used in California at levels greater than 10,000 kg in either 1993 or 2010 that are on the California DPR's risk lists. The manufacturer of benomyl voluntarily requested that EPA cancel its registration, at least partly because benomyl was off-patent and the manufacturer faced lawsuits for environmental and health damages. On average, use of the seven compounds decreased an average of 39% between 1993 and 1995 and 2008 and 2010 (42). Nonetheless, more than 100,000 kg were applied annually of each of four of the compounds (captan, chlorothalonil, iprodione, and mancozeb) in the 2008 to 2010 period. All four either are listed as a US EPA B2 carcinogen or are on the California State Proposition 65 list as causing cancer; captan and mancozeb also are on the California DPR's toxic air contaminant list.

The acute toxicity and extensive use of soil fumigants in the United States have been relatively unchanged, in contrast to the case of the insecticides, herbicides, and fungicides, in which many of the older compounds with greater mammalian toxicity were at least partly replaced by compounds with less mammalian toxicity. Fumigants used in California agriculture between 1993 and 2010 are shown in **Figure 2** in millions of kilograms. These data show the common pattern of pesticide replacement (showing here a decline in MB use that was mandated by law) with fumigants that do not degrade the ozone layer but that are similarly acutely toxic: dichloropropene (which is listed by the EPA as a probable human carcinogen), chloropicrin, and metam potassium.

In 2007, the global crop pesticide market was $33 billion and European Union (EU) member states accounted for 31% of purchases. The EU is a comparatively large fungicide market, and in 2012 it accounted for 36% of world sales (2). Eighty percent of the worldwide cereal fungicide market is in the EU (64). Fungicides were introduced for European cereal crops in the latter 1960s

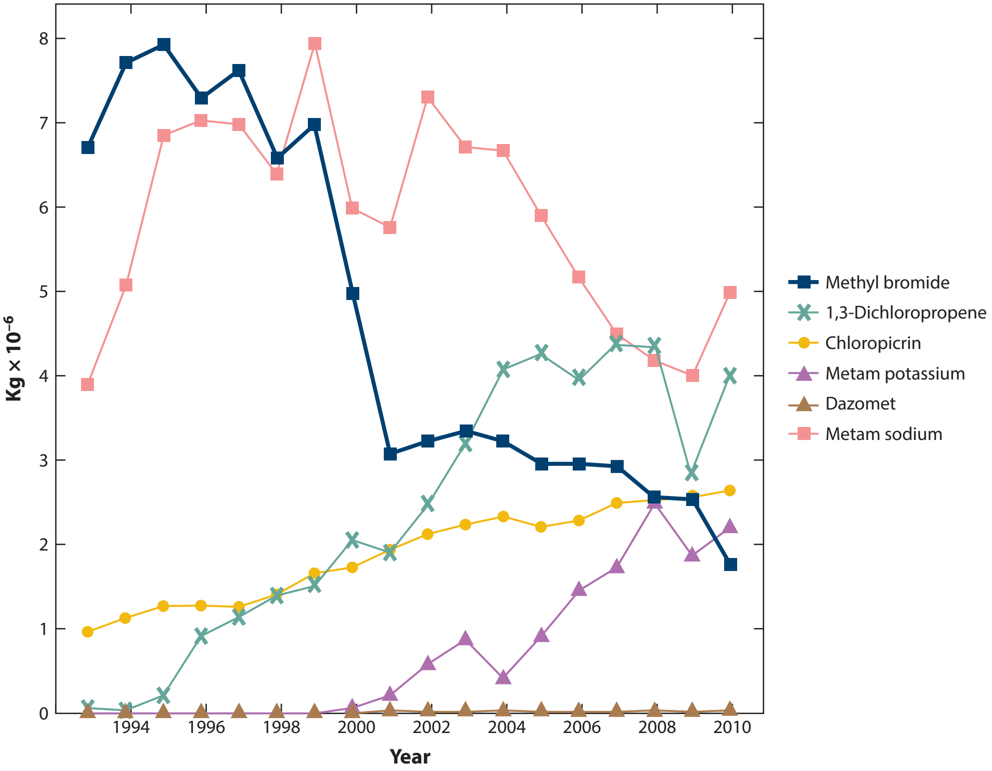

Figure 2

Mass in millions of kilograms of agricultural fumigants used in California fields between 1993 and 2010. These data show the mandated (partial) replacement of methyl bromide (*thicker dark blue line*) with 1,3-dichloropropene (*green Xs*), chloropicrin (*yellow circles*), metam potassium (potassium n-methyldithiocarbamate) (*purple triangles*), and dazomet (*brown triangles*); metam sodium (*pink squares*) has been used throughout the period. Data are from the California Pesticide Use Reports. The figure is modified with permission from Epstein & Zhang (42).

and then increased in use through the 1990s. Wheat is relatively highly subsidized in the EU, and fungicide treatments for *Septoria tritici* leaf blotch, caused by *Mycosphaerella graminicola*, allow yields of 6 metric tons/ha. Yield responses from fungicide treatments are often in the 0.5 metric tons/ha to 2.5 metric tons/ha range. Resistant varieties are available but have lower yields, and it is currently more profitable for growers to use susceptible varieties and apply fungicides than to use resistant varieties (77). Similarly, in a review of pesticide use and alternative options in maize production in the EU, Meissle et al. (107) indicate that pesticides are the predominant control method in maize and that "currently used pesticides are usually relatively cheap and efficient, supply chains exist, and growers are equipped to apply them."

There are numerous examples of chemical overuse, particularly in the United States in the 1970s and more recently in the global south (31, 126, 155). Overuse is often stimulated by various marketing practices, including an effective market infrastructure, bundling of pesticides with seeds and fertilizers, incentives for high-volume purchases, hyped results, and government subsidies in multiple forms, including pesticide tax breaks (99). The global south is increasingly facing a major problem in pesticide overuse because the nations often lack the infrastructure for farmer education on the proper use, containment, and disposal of pesticides (31, 126, 155).

Internationally, pesticide sales are projected to increase annually by 5.5% to a $68.5 billion market in 2017, with higher growth rates in countries in the global south, particularly where income is rising (63, 135). In the decade between 1989–1991 and 1998–2000, pesticide use increased most rapidly in Latin America from 0.9 kg a.i./ha to 2.2 kg a.i./ha. In East Asia, Southeast Asia, and China, use increased from 1.2 kg a.i./ha to 2.0 kg a.i./ha. In comparison, in the global north, mass of pesticide applied decreased from 1.8 kg a.i./ha to 1.6 kg a.i./ha, but the decrease is accounted for at least partly by substitution of materials that are toxic to the target organisms at lower concentration. However, many of the newer pesticides are also less toxic to nontarget organisms, although there are exceptions, such as with the toxicity of the neonicotinoid imidacloprid to honeybees and the toxicity of the herbicide paraquat (introduced in 1962) to mammals and birds (23). As a fungicide example, the older fungicide captan has a lethal dose to 50% of the population (LD_{50}) in fish of 0.034 to 0.3 ppm, whereas the newer strobilurin azoxystrobin has an LD_{50} of 0.47 to 1.6 ppm (156), i.e., azoxystrobin has greater selective toxicity but remains a potential threat to aquatic environments, particularly because it has a half-life in soil of 70 days, in comparison to 1 day for captan (133, 156). Toxicity is typically presented for nonformulated active ingredients but can be enhanced by the inert ingredients in the formulation (174).

KEY REGULATORY CHANGES REGARDING PESTICIDES, 1963–2013

In the United States, some contemporary pesticide law dates back to the Food Drug and Cosmetic Act of 1938 (108). In 1958, the Act was amended by the Delaney Clause, which states that "the Secretary of the Food and Drug Administration shall not approve for use in food any chemical additive found to induce cancer in man, or, after tests, found to induce cancer in animals." The Delaney Clause was invoked in a number of public health alerts and lawsuits by nonprofit consumer groups. As analytical techniques for pesticides became more sensitive, the Delany Clause became increasingly unpopular with both regulators and those in food production and processing because it did not differentiate between de minimis risk and higher risk. The EPA, which was formed by an executive order from President Richard Nixon in 1970, is responsible for registering all pesticides sold in the United States and enforcing relevant laws, including the Federal Insecticide Fungicide and Rodenticide Act (FIFRA) of 1947 and its amendments. In 1988, the EPA eased restrictions on several pesticides based on their de minimis risk. However, the EPA was sued by a coalition of environmental groups for failing to enforce the Delany Clause, and by 1996, the EPA was slated to ban 80 pesticides.

In 1993, the US National Academy of Sciences published the report "Pesticides in the Diets of Infants & Children" (114), which recommended establishing health-based standards for pesticides used on crops and to provide special protections for infants. These recommendations were enacted into US law in 1996 in the FQPA, which was passed unanimously by the Congress. The FQPA was backed by a coalition of groups promoting pesticide use, partly because it allowed the EPA to set pesticide residue tolerances without regard to the Delany Clause (108). The FQPA also expedited a streamlined approval process for safer pesticides. As a result of the FQPA, the EPA has focused on setting tolerances for pesticide residues that have a "reasonable certainty of no harm." Pesticides with the same biochemical basis for mammalian toxicity are considered as a group.

OPs, which are neurotoxic acetylcholinesterase inhibitors, have been the most affected by the FQPA. In 1996, 49 OPs were registered for use in pest control in the United States. As of October 2013, only 27 (55%) OPs were registered, and many of those have restricted use (160). Residential use of OPs has been mostly curtailed. A few other compounds have lost registration. In 1993, 14 to 16 million kg of the triazine herbicide cyanazine were used in the United States (4). In 1999, the manufacturer voluntarily canceled its registration following an EPA review of data that included evidence of fetal eye malformations after short-term exposure and cancer and reproductive toxicity after longer-term exposure. In response to the EPA's calculation of risk to children by the carbamate insecticide aldicarb, the manufacturer agreed to discontinue manufacturing by 2015, although it disagreed with the assessment (28).

As part of the FQPA and the Safe Water Drinking Act Amendments in 1996, the EPA was charged with assessing estrogenic and other endocrine-disrupting effects of pesticides. Pesticides were prioritized for review, but the EPA did not request manufacturers' data for this review until 2009. Eight fungicides are in review: the oomyceticidal RNA polymerase inhibitor metalaxyl; the sterol biosynthesis inhibitors propiconazole, tebuconazole, triadimefon, and myclobutanil; the signal transduction inhibitor iprodione; and the multisite inhibitors captan and folpet (**http://www.epa.gov/endo/**).

The EU has been more proactive about banning pesticides with potential health and environmental issues than the United States. In 2009, the EU adopted precautionary principle–based "rules for sustainable use of pesticides to reduce the risks and impacts of pesticide use on people's health and the environment." Acceptable pesticides must be scientifically proven to not harm human health, have no unacceptable effects on the environment, and be effective against the designated pest. As a result, 60% of active ingredients may be withdrawn (14). On the basis of the hazard criteria, Hillocks (75) considers that the EU is most likely to disallow the following fungicides: bitertanol, cyproconazole, epoxiconazole, flusilazole, fenbuconazole, metconazole, and tebuconazole, which are the triazole sterol biosynthesis inhibitors of demethylation; carbendazim, a β-tubulin inhibitor; dinocap, an uncoupler of oxidative phosphorylation; the MAP/histidine kinase in osmotic transduction inhibitor iprodione; quinoxyfen, another signal transduction inhibitor; and mancozeb and maneb, dithiocarbamates with multisite contact activity (55). The metam fumigants also may be eliminated as potential endocrine disrupters. Hillocks (75) speculates that loss of triazoles in the United Kingdom could allow *Septoria tritici* to reduce wheat yields 10% to 20% and could cause yield reductions in rapeseed oil due to *Leptosphaeria maculans* and *Pyrenopeziza brassicae.* If mancozeb is withdrawn, fungicide resistance deterrence strategies for potatoes and other minor crops could be adversely affected. A French study estimated that if pesticide use was reduced by 50% in arable crops, 21% in orchard crops, and 37% in viticulture, that yield decreases might be 12% in arable crops, 19% in orchards, and 24% in grapes (82). Whether the proposed reduction in the number of available fungicides will have impacts on food prices or quality, the incidence of fungicide resistance, disease incidence, the intensity of fungicide use, or environmental quality remains to be seen (76, 136). In order to reduce pesticide use, the EU is expected to implement a tax scheme, and member states will be expected to adopt reduction targets (142). Skevas et al. (142) summarized 27 studies from either the United States or the EU and concluded that pesticide demand is relatively inelastic in economic terms, meaning that pesticide use is relatively price-insensitive, and consequently proposed taxes likely would not have a major effect on pesticide use. They (143) conclude that pesticide quotas will be more effective in reducing pesticide use and decreasing adverse environmental consequences of pesticide use than taxes, even if they differentiate between high and low toxicity pesticides, price penalties on the environmental effects of pesticides, or subsidies on low-toxicity products.

Compared with the global north, the global south has less stringent and less enforced pesticide regulations (140). Pesticides in the economically developing countries have an annual market value of $900 million; Popp et al. (128) estimate that approximately 30% of the applications may not meet internationally accepted criteria for safe levels of pesticide residues. There have been two international agreements that have partly limited the use of the riskiest pesticides in the global south: the Rotterdam and Stockholm Conventions (57). In the 1980s, there was concern that as countries in the global north banned pesticides that were deemed hazardous for health and the environment, the banned pesticides would be aggressively marketed in the global south, where there was insufficient infrastructure to monitor the importation and use of the materials. The United Nation's Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade was first signed in 1998 and became effective in 2004, and has been signed by 153 nation states and the EU; as of 2013, it has not been signed by the United States (92). Named pesticides include approximately 30 older pesticides, primarily organochlorines, OPs, and carbamates. Named fungicides include captofol and certain formulations of benomyl and thiram. Signatories to the Rotterdam Convention may ban importation of the listed compounds and are entitled to receive information about chemical risks and safe handling of the listed compounds. The UN's Stockholm Convention on Persistent Organic Pollutants (POPs) was first signed in 2001 and became effective in 2004, and has been signed by 152 nation states and the EU but not by the United States. The Stockholm Convention has more extensive goals in eliminating or restricting the production and use of POPs, which include some of the pesticides included in the Rotterdam Convention. Regarding the pesticides, signatories agree to work toward eliminating production and use of 14 pesticides, with a few exemptions for agricultural use, and to limit the use of DDT to malaria control. The POPs slated for elimination include the organochlorine insecticides chlordane, chlordecone/kepone, dieldrin, endosulfan, endrin, heptachlor, hexachlorobenzene, α- and β-hexachlorocyclohexane, lindane, mirex, and toxaphene, and the carbamate insecticide aldrin. Safe disposal of current stocks of the banned materials in the global south is unresolved; the Food and Agriculture Organization (FAO) estimates there are a half-million metric tons of poorly stored obsolete pesticides in the global south (50, 128). Except for endosulfan, the United States has phased out these materials; the EPA action to phase out endosulfan was announced in 2010, several years after it was banned in numerous countries, including Colombia, Germany, the Netherlands, Singapore, Sweden, Syria, and the United Kingdom as well as the Indian state of Kerala (32).

The fumigant MB was slated internationally for discontinued use by 2005 by the Montreal Protocol and subsequent agreements because it is an ozone-depleting compound. Agricultural use of MB as a soil fumigant declined in California from 8 million kg in 1995 to 1.8 million kg in 2010 (**Figure 2**); the United States promoted provisions in the agreements that allowed exemptions for growers that would be economically impacted by MB loss. In California, most of the MB was used in strawberry fields, not only for control of pests, pathogens, and weeds but also for poorly understood growth promotion (89, 165). Despite predictions to the contrary (66), strawberry yields, acreage, exports, revenue, and market share increased during years of declining use of MB (105). Gareau & DuPuis (58) argue that US-backed policies of granting exemptions based on claimed economic losses to growers is in conflict with meeting a larger public health goal. Certainly, there are and will continue to be conflicts about pesticide use in relation to food production, health and environment protection, and grower/pesticide company financial interests.

Several conclusions about regulatory issues are germane to this review. First, there were 33 years between the publication of Carson's *Silent Spring*, which largely dealt with the problems of persistent organic pollutants such as DDT, aldrin, and dieldrin, and the start of the Stockholm Convention, and then another 9 years until full implementation by participating nations (32). Second, some of the riskiest materials are still used in relatively large quantities (42, 119). Third, some government policies encourage pesticide use (113). For example, in order to collect indemnities from federally subsidized crop insurance, farmers must follow "best management practices," which include pesticide applications; Horowitz & Lichtenberg (79) reported that corn growers in the Midwestern United States that purchased crop insurance spent 21% more on pesticides and treated 63% more acreage with insecticides than those without crop insurance (79).

INTEGRATED PEST MANAGEMENT AS A STRATEGY TO REDUCE PESTICIDE USE AND RISK

Integrated Pest Management in Theory and Practice

There are numerous examples of pesticide overuse in the United States in the latter 1950s through the 1970s (e.g., 72, 109) that resulted in less efficacious pest control because natural predators were killed or pesticide-resistant pests were selected. The United States started a national IPM program in 1971 (94). President Nixon characterized IPM as the "judicious use of selective chemical pesticides in combination with nonchemical agents and methods." IPM programs in the global south, in countries such as India, were started later and were initiated solely because of agricultural issues: an increase in percentage losses caused by insect pests because of changes in agricultural practices from the green revolution; changing insect pest scenarios in rice and cotton; and the development of resistance in insect pests to newly introduced pesticides (124).

The University of California Integrated Pest Management Program (159) states the following:

> Integrated pest management (IPM) is an ecosystem-based strategy that focuses on long-term prevention of pests or their damage through a combination of techniques such as biological control, habitat manipulation, modification of cultural practices, and use of resistant varieties. Pesticides are used only after monitoring indicates they are needed according to established guidelines, and treatments are made with the goal of removing only the target organism. Pest control materials are selected and applied in a manner that minimizes risks to human health, beneficial and nontarget organisms, and the environment.

IPM also has been adopted as a strategy for minimizing pesticide risk internationally. For example, the FAO "promotes IPM as the preferred approach to crop protection and regards it as a pillar of both sustainable intensification of crop production and pesticide risk reduction. As such, IPM is being mainstreamed in FAO activities involving crop production and protection" (51). Proponents of IPM stress that there is a continuum of IPM practices, from a "low IPM," which may include unnecessary chemical use, to a "full IPM," which minimizes pesticide use and/or risk.

IPM programs have often claimed that they are an effective strategy for reduction of pesticide use and risk. One of the major IPM programs in the 1970s, the Huffaker Project, had a goal of a "40–50% reduction in the use of the more environmentally polluting insecticides within a five-year period, and perhaps by 70–80% in 10 years" (94). Huffaker & Smith (80) considered the project partly successful—there were 30% to 50% or more reductions in insecticides and acaricides on some of the crops—but they railed against a "virtual army of insecticide salesmen . . . selling both insecticides and the advice to use them." Although public relations have continued to focus on reduction of pesticide use and risk, USDA (US Department of Agriculture) measures of IPM implementation are not based on changes in pesticide practice. In 2001, a US General Accounting Office report (158) concluded that the "USDA estimates that IPM has been implemented on about 70% of crop acreage . . . However, this implementation is not a good indicator of progress toward the originally intended purpose of IPM—reducing chemical pesticide use."

Despite the concern expressed here that IPM in the field is promoted to the public as focused on pesticide reduction but in practice is focused on either maximizing pest control or grower profits, there are documented cases of pesticide reductions via IPM (157, 163), albeit with some successes based primarily on substitutions of materials with toxicity in lower quantities (40, 41). Pretty et al. (130) reported that of 62 international IPM programs, three-fourths had declines in pesticide use, although Phalan et al. (125) note that there is selection bias in the study. Regardless, in the absence of rigorous IPM educational programs, pesticide overuse is common, particularly as nations try to increase agricultural production (31, 126, 140, 166). Grovermann et al. (69) estimate that 78% of pesticide use in Thailand is overuse; they attribute overuse to lack of knowledge about nonchemical alternatives, government policies (including tax-exemption and pesticide subsidies), and "lock in" to pesticide use. "Lock in" is a tendency to continue to follow the same or similar behavioral and/or technological paths; it occurs when farmers, for example, use pesticides because they have the equipment and know-how to apply them.

Several issues are relevant for this review. First, there are numerous circumstances in standard agricultural practice in the United States that are considered part of an IPM program but do not meet IPM guidelines. Indeed, the IPM criteria can be followed for control of many insects but generally not for control of either weeds or pathogens. In seed treatments and for many plant diseases, pesticides are applied prophylactically. Pre-plant fumigants are used annually for high-value crops, such as strawberries in California, regardless of previous history; the fumigants have been routinely used to assure maximum yield (89). In contrast, within the context of IPM, pesticides are supposed to be used only after a pest or pathogen has been quantified and an action threshold has been exceeded. Second, pesticide-use analysis can result in the conclusion that pesticides are underused from an economic perspective rather than overused. Skevas et al. (142) summarized seven studies in the United States and the Netherlands that examined the economics of pesticide use; overuse of pesticides was only clearly indicated in two of the studies, and of those, overuse was justified in one study (5) because apple fruits required prophylactic protection. Third, some US government policies, such as price supports for particular crops, can discourage more sustainable practices, such as crop rotation, that decrease pesticide reliance and use (113). Particularly in the case of commodity supports, farmers are financially rewarded with public funds for achieving the highest yields, often with increased inputs, even if those inputs would not be economical without subsidies. Fourth, many of the riskiest pesticides remain in relatively high usage because they are off-patent and economical for growers. Fifth, we are far from understanding all of the longer-term and region-wide agricultural and ecosystem impacts of the use of even softer pesticides (6). Repeated aerial applications of copper, largely used to control bacterial pathogens, accumulate in soil and are toxic to multiple microorganisms that are critical for soil function (38). Repeated sulfur applications used to control powdery mildew, particularly on grapevines, may be ultimately concentrated in aquatic ecosystems (78) and cause damage. Sixth, at least some pesticide-use decisions are made to satisfy market demands, such as cosmetic standards for consumers, food processor standards (152), and standards for a possible export market. Seventh, given the uncertainty about pathogen and pest populations, truly integrated pest management is extremely complex. For example, a relatively inexpensive pesticide application of a systemic neonicotinoid can significantly reduce grower risk of a viral disease (88), e.g., the control of *Tomato spotted wilt virus* spread via the control of the thrips vector (29), but can the insecticide be applied without adverse impact on pollinators? Eighth, apart from legal and customer constraints, farmers typically make their pesticide-use decisions based on their own needs (17, 170), often for a single growing season. Gent et al. (61) showed that Washington and Oregon grape growers ranked "environmental impacts" and "cost of chemicals" among the factors that were least likely to influence their decision about a pesticide application. A pesticide application may or may not result in an increase in yield or quality and a consequent profit in a given growing season. More importantly, pesticides provide growers with insurance that maximizes their chances of selling their crop; typically, crop losses or injury from pests and pathogens are borne by the grower, whereas benefits from not using a pesticide provide benefits to the broader community. Thus, in theory, IPM could be used to provide growers with knowledge that would allow them to reduce pesticide use and risk for the broader community. However, in practice in the United States, IPM rarely helps in this manner, partly because growers directly benefit from reduction in pesticides only when pesticide overuse causes obvious negative consequences for themselves. Jacquet et al. (85) argue that pesticide use could be reduced by 30% in France without reducing farmer income using a combination of a pesticide tax with subsidies for low-input techniques. Praneetvatakul et al. (129) suggest similar measures for Thailand but also emphasize the need for extensive education about nonchemical alternatives.

Specific Integrated Pest Management Strategies that have been Suggested as Methods for Reducing Reliance on Chemical Control of Plant Diseases

Two technological strategies (improved disease forecasting and more biological control products) are often suggested as means to reduce current fungicide use. Here, we argue that these strategies are unlikely to do so.

Disease forecasting. Since the mid-1980s, many disease-forecasting/decision-support systems have been developed (61, 141). Funding for system development is often obtained with the justification that implementation of the system will result in a reduction in pesticide use. However, there are few examples of sustained use of a forecasting system (61, 141), even when data indicate that use of the forecaster would save the farmer money from reduced pesticide applications. Gent et al. (61) suggest that this is at least partly because growers apply pesticides as insurance against crop failure. We note that there have been other suggestions, such as "lock in," about why growers do not adopt IPM measures that would save them money (167); for example, once farmers become insecticide reliant, natural predators are killed and it is simpler to continue to use insecticides than to try to restore an ecological balance. The rapid adoption of genetically engineered (GE) herbicide tolerance is evidence that farmers embrace easily implemented and flexible technology.

Epstein & Bassein (39) used the California Pesticide Use Report data (37) from individual applicators to examine the projected impact on fungicide use of a forecasting model for powdery mildew control on grapevines (71) as compared with a historically recommended weather-independent calendar-spray fungicide program. The study period from 1993 to 2000 included multiple years before the introduction of a temperature-driven algorithm that extended the recommended interval between applications when temperatures were suboptimal for the pathogen (71). Although there were some growers who appeared to use the calendar spray model, and consequently, could have reduced their fungicide use, the majority of growers appeared to have a schedule that was less than would be recommended by the temperature-driven model (39). Although these growers might have better disease control if they adopted the environmentally driven model, if all growers adopted the environmentally driven model, there would have been a net increase of fungicide use in California grapevines. Although many IPM programs promote themselves as a mechanism to reduce pesticide overuse, the argument can be made that there are many circumstances of pesticide underuse (142), particularly in the global south, where increased pesticide use would result in increased yield and/or farmer profits (62).

Biological control. The agricultural database AGRICOLA had 8,249 citations in English with the keyword "pesticide" for the ten-year period from 2004 to 2013 and slightly more citations (8,587) for the keyword "biological control." Biological control generally includes an array of organisms and targets. There are a comparatively large number of success stories for controlling insects in the field with management of populations of predatory insects and parasitoids, with or without applications of the control agents (47, 68, 97). Within the context of organic agriculture, Crowder et al. (30) used in-field enclosures to demonstrate that organically managed potato fields had a greater biodiversity of predators and pathogens of the potato beetle pest than conventionally managed fields; the increased evenness of the potato beetle enemies (primarily two predatory bugs, two predatory beetles, two insectivorous nematodes, and an insectivorous fungus) were associated with 18% lower pest densities and 35% larger plants in the organic versus conventional fields. There is also a history of successful use in the field of application of the toxin-producing bacterium *Bacillus thuringiensis* (10) to control specific insects (39, 42). However, except for *B. thuringiensis*, attempts to develop microbial agents for the control of insects, weeds, and pathogens have been less successful, despite considerable public sector research. Analysis of the California Pesticide Use Report records indicate that growers in California tried commercially available microbial biological control products but, with the exception of *B. thuringiensis*, abandoned their use (39, 42), presumably due to poor efficacy. Epstein & Bassein (39) examined the assumption that growers that adopted use of a biological control agent reduce their pesticide use. This was not true in the case of *Pseudomonas fluorescens* A506 on pear, in which the most intensive antibiotic users were most likely to try *P. fluorescens* but used it in addition to the antibiotic, not as a replacement.

ALTERNATIVES TO PESTICIDE-DEPENDENT PRACTICE FOR REDUCING PESTICIDE USE AND RISK: DURABLE HOST RESISTANCE

In practice, IPM often focuses on chemical and/or cultural control and not on selecting/breeding or genetic engineering for plant host resistance. Although there are some IPM programs that include arthropod resistance (e.g., on rice and sorghum in Asia, Australia, and North America), there is an urgent need for greater integration of IPM programs and breeding for disease and pest resistance (20, 145). Selection of genes with durable resistance requires a greater knowledge about types of resistance genes that have been effective over time (e.g., 19, 54, 95) and aspects of pathogen biology that predict durable resistance (98). Some resistance genes, such as *mlo* in barley, have a fitness cost (18). The University of California strawberry breeding program, for example, has been primarily conducted in fumigated soil. When breeding programs use pesticides to control pests and pathogens, and yield and horticultural features are the primary criteria for selection, particularly if genes for pest and pathogen resistance have a metabolic cost, effective alleles that could have provided sustainable resistance are likely to be selected against (106, 151).

Although we advocate here for breeding for resistance, it is important to note that for sustainable agriculture, breeding should be coupled with maintenance of diversity, at least on a regional scale. Zeller et al. (171) demonstrated that multilines of experimental transgenic wheat with powdery mildew resistance were more productive than monocultures of the transgenics. Zhu et al. (173) demonstrated area-wide control of rice blast in China using an intercrop of resistant and susceptible rice varieties. For truly sustainable food production, we advocate for a return to the original intent of IPM, which includes cultural controls such as crop rotation and intercropping (16).

TWENTY-FIRST CENTURY PERSPECTIVES ON MANAGING PESTICIDE USE AND RISK

Challenges in Globalized, Industrial Agriculture

Clearly, sustainable agriculture for the twenty-first century requires pest control without the current fossil fuel dependence and, preferably, with less environmental impact. Jaggard et al. (86) argue that global warming will result in more rapid multiplication rates in soilborne pathogens. On the basis of historical databases, Bebber et al. (9) estimated that, presumably due to global warming, fungal and oomycete plant pathogens are advancing seven and six kilometers poleward per year, respectively; both are largely controlled by pesticides. Globalization will continue to facilitate the introduction of pests and pathogens that are subsequently controlled with pesticides. California grape growers and state officials are currently primarily using insecticides, and primarily the neonicotinoid imidacloprid to limit the spread of the glassy-winged sharpshooter, which transmits the bacterium *Xylella fastidiosa*, causal agent of Pierce's disease. The glassy-winged sharpshooter is native to the southeastern United States, and its egg masses were presumably introduced into California on either ornamental or crop foliage in the early 1990s. California citrus growers have increased insecticide use to control the spread of the Asian citrus psyllids, which transmit the bacterium *Candidatus liberibacter*, causal agent of the devastating disease huanglongbing (HLB), also known as citrus greening. Both the pathogen and vector are native to Asia; the vector and pathogen were first observed in Florida in 1998 and 2005, respectively. Current control recommendations for Florida citrus growers are to apply at least eight broad-spectrum insecticide applications per year to reduce Asian citrus psyllids to slow the spread of HLB. Both the vector and pathogen have been established in Mexico and were first observed in California in 2008 and 2012, respectively. The California Department of Food and Agriculture is supervising a program involving surveillance, quarantine zones, and application of insecticides and biological control agents.

We can speculate about agricultural issues for the twenty-first century. First, increases in monoculture will continue to increase selection pressure on pathogens and pests to overcome any constraints on their replication and survival. Second, overreliance on pesticides, promoted by pesticide marketing and in some cases government policy, has historically led to negative agricultural consequences, including pesticide resistance, and the emergence of secondary insect pests. Many of the current weed problems, for example, are a consequence of intense herbicide (148), and sometimes fertilizer, use. Chen et al. (25) conclude that fertilizer and herbicide applications are a major factor in increased problems with invasive weeds. Third, unless there are major changes in pesticide policy, growers' pesticide costs will not include the full costs of negative agricultural (25, 52), health (8, 90, 103, 104, 126, 134), and environmental consequences (11, 48). Fourth, our current agriculture systems and crop genotypes have been selected for, in some cases, in fields with intensive pesticide use instead of in fields with minimal pesticide use. If there is a fitness cost for maintenance of genes for pest resistance, then, in the presence of intensive pesticide use, the cultivars with the highest yields will have the fewest functional resistance genes.

The Methyl Bromide Transitions Experience

Historically, approximately three-quarters of the world's MB use has been for soil fumigation for horticultural crops (117). Recommendations for MB soil fumigant use, generally in combination with chloropicrin, were developed at the University of California in the 1960s. Fumigation effectively kills nematodes, pathogens, weed seeds, and insects and promotes plant growth (89, 165), i.e., economically, MB is a superb risk-reducing input (99). Fumigation also allows year-after-year production without rotation. Between 1972, when strawberry fruit yields were 38 metric tons per hectare, and 2010, new higher yielding cultivars, changes in horticultural practices, and increased amounts of energy-requiring inputs, including fertilizers and fumigants and other pesticides, increased California strawberry yields to 150 metric tons per hectare. Although the Montreal Protocol and subsequent agreements to control ozone depletion in the upper atmosphere planned for a 2005 phaseout, "critical use exemptions" were granted when "(i) . . . lack of availability of methyl bromide . . . would result in a significant market disruption; and (ii) there are no technically and economically feasible alternatives or substitutes available to the user that are acceptable from the standpoint of environment and public health and are suitable to the crops and circumstances of the nomination." Worldwide annual MB use dropped from 64 million kg during the 1995 to 1998 period to only 7 million kg in 2010 (due partly to the critical use exemptions), of which 2.7 million kg (39%) were used in the United States, with 1.8 million kg in California; 0.98 million kg were applied as preplant soil fumigants in strawberry fields (21). Although the allowed applications of MB will continue to decrease, the point here is that there is a conflict between the horticultural practice of assuring maximal yield and plant disease control and international public health.

The USDA has sponsored MB transitions programs. Much of the research has focused on alternative fumigants, either singly or in combination: primarily, 1,3-dichloropropene (1,3-D); chloropicrin; methyl iodide (iodomethane); dimethyl disulfide; and the isothiocyanate generators metam sodium, metam potassium, and dazomet. Using a meta-analysis, Belova et al. (12) concluded that a 65:35 1,3-D:chloropicrin formulation was as effective as MB with chloropicrin. As a result of a combination of US and state regulations, and violations of the US Clean Air Act in California, 1,3-D and chloropicrin have some specific restrictions on use; virtually impermeable tarps reduce volatile release (3) and may result in relaxed restrictions. Methyl iodide is effective, does not affect ozone in the upper atmosphere, and was registered by the EPA in 2007 and by the California DPR in 2010. However, there is no scientific consensus that it can be used without risk to the public or farmworkers; the DPR's own scientific review did not support registration, and the external scientific review committee supported the DPR's scientific assessment (53). After the DPR registered methyl iodide, environmental and farmworker-rights groups sued the state of California, and the manufacturer subsequently removed MB from the US market and revoked its request for registration in California.

Some nonfumigation methods appear promising. Anaerobic soil disinfestation, also called biosolarization, involves addition of a carbon source, soil saturation, and then application of a plastic tarp in order to help generate higher temperatures, temporary anaerobiosis, and microbial production of fungitoxic compounds. Biosolarization of strawberry soil reduces pathogens and can result in strawberry yields similar to fumigated treatments but is not as effective for weed control as MB (34, 44). Steam is as effective as fumigation but is currently very energy intensive (138). Although rotation is the classic method to control plant disease and is used in organic strawberry production, because land costs are high and operating profit margins on strawberries are estimated currently at 17% (**http://www.epa.gov/ozone/mbr/CUN2014/2014CUNStrawberryFruit.pdf**), conventional strawberry growers in California will not adopt rotation at this time.

Genetically Engineered Crops

Between 1996 and 2013, two GE pest management traits were widely adopted into US agriculture, primarily on field corn, cotton, and soybeans: herbicide tolerance and resistance to insects via the *B. thuringiensis* (Bt) toxin. By 2012, there were 170 million hectares of GE crops, with over half in the global south (87). Although proponents of GE often claim that GE reduces pesticide use, this is only dramatically true for Bt cotton. The benefit of herbicide tolerance for farmers is largely that a grower has flexibility in timing herbicide applications (45), not in using less herbicide (24). More herbicide can be used in herbicide tolerant crops, particularly on soybeans (13, 46). Herbicide tolerance also facilitates use of reduced-till and no-till farming, which have environmental benefits that include reduced soil erosion and run-off as well as lower fossil fuel usage. In addition, glyphosate tolerance allows utilization of the least environmentally problematic herbicide. However, increased use of glyphosate has resulted in the emergence of glyphosate-resistant weeds. The next generation of herbicide-tolerant GE crops includes older herbicides, such as 2,4D, which have more environmental impacts than glyphosate (84).

The impact of the Bt toxin on pesticide use is more crop dependent. Bt corn has not had a significant effect on insecticide use on corn in the United States (46), perhaps because insecticides were not used to control the European corn borer. Nonetheless, Bt corn provided economic benefits to both Bt and non-Bt growers by area-wide suppression of the European corn borer in the Midwestern United States (81). In addition, compared with non-Bt corn, Bt corn has less *Fusarium* ear rot, less symptomless infection by *Fusarium verticillioides* (112), and lower concentrations of the mycotoxin fumonisin (73). Bt cotton has reduced pesticide use in multiple countries, including the United States, Australia, China, and India (24, 91, 168). Lu et al. (100) demonstrated that in China, decreases in insecticide use were associated with area-wide increases in predatory insects that controlled aphids. In contrast to herbicide tolerance, in which there has not been a plan for reducing the likelihood of resistance, Bt toxin transgenes were deployed with mandated (but not enforced) areas of nontransgenic refuges so that any insect survivors from transgenic fields would mate with Bt toxin–sensitive insects and their progeny would remain toxin sensitive. Regardless, in China and Australia, adoption of Bt cotton was followed by the emergence of pests that were not controlled by the Bt toxin (60, 101, 168). Indeed, Bt resistance in the Western corn rootworm can confer resistance against two of the three available Bt toxins in corn (59).

Thus, the data indicate that (*a*) IPM programs need to incorporate, but not be limited to, GE crops (83) and (*b*) that GE crops can be useful in reducing pesticide use and risk, as with Bt cotton, but that simply introducing GE crops—even with traits for pest control and, particularly, herbicide tolerance—does not necessarily result in a reduction in pesticide use and risk. We note that GE papaya engineered with the *Papaya ringspot virus* coat protein has been highly successful in control of *Papaya ringspot virus* in Hawaii (65); however, because insecticides were not used previously to control the vector, it did not decrease insecticide use. Nonetheless, transgenic strategies offer opportunities for disease control, particularly in the near term with viruses, and for reduction of insecticide use in those cases in which insecticides are used to reduce the population of virus vectors. Monsanto commercially developed two NewLeaf™ potatoes with virus resistance in the late 1990s, using either the coat protein of *Potato virus Y* or the putative replicase and helicase domains of the *Potato leaf roll virus* (154). Although the virus-resistant potatoes were approved by the regulatory process in the United States, McDonald's and other fast food restaurants responded to US consumers' concern about GE and refused to purchase GE potatoes; Monsanto discontinued the GE potato lines. A few other GE crops developed for disease control were also approved. In the 1990s, Seminis and Monsanto received authorization in the United States for coat protein–mediated virus (e.g., *Cucumber mosaic virus cucumovirus*, *Zucchini yellow mosaic potyvirus*, and *Watermelon mosaic potyvirus 2*) resistance in squash, and Beijing University registered coat protein–mediated *Cucumber mosaic virus* resistance in tomato and sweet pepper in China (84). The USDA registered a plum with coat protein–mediated resistance to plum pox in 2009. Brazil authorized a Brazilian-developed common bean with an RNAi-based resistance to *Bean golden mosaic virus* in 2011.

Compared with the identified transgenes for virus control in plants, there are fewer vector-ready transgenes for fungal disease control that could be immediately deployed in crop plants. BASF has bred a potato cultivar, Fortuna, that has two transgenes, *Rpi-blb1* and *Rpi-blb2*, from the wild potato *Solanum bulbocastanum* that confer economical resistance in the field to *Phytophthora infestans* (150); large quantities of oomyceticides are used to control the pathogen. Owing to undesirable linked genes in *S. bulbocastanum*, commercial cultivars with *Rpi-blb1* and *Rpi-blb2* could not be produced by conventional breeding. BASF plans to continue regulatory approval but has discontinued cultivar research and development because of the lack of market acceptance of GE in Europe.

China's experience as a producer of GE crops (26) offers an interesting example of GE that is less encumbered by intellectual property fees (149) than in the global north; GE seeds in China are not subject to high royalty fees (144) because some GE cultivars are developed by the state (49). The Chinese regulatory process for genetic engineering is also faster (26) than in the global north (43). China is the world's leader in the development of Bt rice (26) and has made progress in incorporating the Bt toxin into locally adapted cotton cultivars (49); in 2006, approximately 70% of the cotton produced in China was transgenic for Bt toxin (49). In 1998, 74% of the Bt-cotton seed in China was from Monsanto, but the percentage declined yearly until 2006, and there was a corresponding increase in diversity of cotton cultivars, with less than 8% from US multinational companies (49). During the 1999 to 2007 period, 436 cotton cultivars with the Bt toxin were registered in China.

CONCLUDING COMMENTS

Fifty years after *Silent Spring*, pesticides have been increasingly regulated, safety standards for new pesticides have been improved, and many but not all of the pesticides of concern in *Silent Spring* have been replaced. Global food production has increased, and food insecurity, malnutrition, and hunger are caused more by poverty than by an insufficient food supply. However, our agriculture has become more pesticide dependent and consequently more vulnerable to both severe crop loss and to pollution from pesticides. Many questions remain: How can we better understand, predict, and mitigate the negative agricultural, environmental, and health externalities of pesticide use? How can we as a civil society best regulate pesticide use so that the benefits for the public are maximized and the harms are minimized? And finally, how can we help develop the information and materials for an IPM within the context of sustainable and nutritious agricultural production?

SUMMARY POINTS

1. The agrochemical industry and many agriculturalists and pest managers disparaged the arguments in Rachel Carson's *Silent Spring*. With a few exceptions, history has demonstrated that Carson was correct about the negative agricultural, health, and environmental impacts of the increased use post–World War II of organochlorine and organophosphate pesticides.
2. Historically, introductions of large-scale pesticide use in the United States, starting in the 1950s and more recently found in the global south, have been characterized by pesticide overuse with resultant negative consequences, including pesticide-resistant pests and the resultant pesticide treadmill.
3. Increased regulation in conjunction with patent protection has encouraged pesticide manufacturers to introduce new classes of pesticides with fewer negative health, environmental, and agricultural impacts.
4. There have been reductions in the mass of compounds targeted by the FQPA.
5. IPM is typically presented to the public as an effective strategy for minimizing pesticide use and risk. It can be; however, in practice, IPM programs are often pesticide dependent, and pesticide decisions are often based on minimization of grower's income risk and/or maximization of profits. Growers often replace older pesticides with newer materials, but large quantities of older, more-hazardous materials are still used. Breeding can be an effective long-term strategy for sustainable agriculture and reduction in pesticide use, but IPM programs often fail to promote development of crops with durable resistance.

6. Transgenic cotton that produces the Bt toxin can be produced with fewer insecticide applications than nontransgenic cotton. Other transgenic crops in commercial production have had more limited impact on overall pesticide use.
7. The EU has followed the precautionary principle about pesticide registration to a greater extent than has the United States.

FUTURE ISSUES

1. In order to avoid negative externalities associated with overreliance on pesticides, we need more research and extension on a fully realized IPM that includes utilization of molecular and traditional breeding.
2. In the twenty-first century, multiple factors are likely to result in increased pesticide use, particularly in the global south: marketing capabilities of the major pesticide firms, the globalization of food markets, increasing acreage of monocultures with decreasing diversity of crop gene pools, and an increasing population that increasingly eats more meat.
3. We have yet to determine the full agricultural, health, and environmental costs of what are now considered appropriate levels of pesticide use. Critical current issues include the role of pesticides in the decline of pollinators and in water pollution, particularly by herbicides.
4. The genomic era offers unprecedented opportunities for the discovery of new pesticides with fewer negative externalities that specifically interfere with pathways specific to taxa of pests and pathogens. This will also require more public and private sector research.

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