

Genetically Engineered Corn Rootworm Resistance: Potential for Reduction of Human Health Effects From Pesticides

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Objective and Methods Insecticide use, grower preferences regarding genetically engineered (GE) corn resistant to corn rootworm (CRW), and the health effects of using various CRW insecticides (organophosphates, pyrethroids, fipronil and carbamates) are reviewed for current and future farm practices. **Results** Pest damage to corn has been reduced only one-third by insecticide applications. Health costs from insecticide use appear significant, but costs attributable to CRW control are not quantifiable from available data. Methods reducing health-related costs of insecticide-based CRW control should be evaluated. As a first step, organophosphate insecticide use has been reduced as they have high acute toxicity and risk of long-term neurological consequences. A second step is to use agents which more specifically target the CRW. **Conclusion** Whereas current insecticides may be poisonous to many species of insects, birds, mammals and humans, a protein derived from *Bacillus thuringiensis* and produced in plants via genetic modification can target the specific insect of CRW (*Coleoptera*), sparing other insect and non-insect species from injury.

Key words: Genetically engineered corn; Corn rootworm resistance; Insecticide toxicity; Pest damage control; Health costs

INTRODUCTION

Loss of crops from pests such as corn rootworm (CRW) reduces corn yields significantly¹¹. CRW is considered a major pest, with over 80% of chemical insect control measures in corn being directed at CRW control in the United States (Steffen K: 2000. Research Communication, Agricultural Experiment Station and Cooperative Extension Service, Market Survey (corn) 1997, University of Illinois, Urbana, IL, August). Insecticides control pests, increase crop yields by reducing insect feeding, and increase grain quality, making it less likely to mold and to be deemed unsuitable for human or animal consumption. However, insecticides are generally toxic to a variety of species, kill insects regardless of whether these insects are beneficial (i.e. non-target) or harmful species, and may reduce biodiversity.

Human or animal exposure to high levels of insecticides can produce acute toxicity due to organophosphate, carbamate, or pyrethroid insecticides. In the last 10 years (1990-1999), the American Association of Poison Control Center data reported an average of 22 053 instances

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of organophosphate or carbamate insecticide exposure per year (ranging from 16 807 to 25 806). Of these exposures, an average of 5 586 or 25.3% received medical evaluation or treatment (ranging from 4 172 to 6 711), and there was a yearly average of 8.4 deaths (0.04%; ranging from 4 to 14) from organophosphate and/or carbamate exposures during the same 10-year period^[2-12]. No data are available to determine the number of insecticide exposures attributable, directly or indirectly, to CRW control.

The occurrence of adverse health effects and the continuing need for medical evaluation and treatment to limit morbidity and mortality highlights the risk involved with the use of insecticides. Despite educational efforts to inform insecticide users of necessary precautions, the rates of symptomatic organophosphate and carbamate insecticide exposure and resulting deaths have remained remarkably stable over the past 10 years.

Although existing data suffice to indicate a significant health impact, the adverse health effects of these insecticides remain potentially underreported^[13]. Reduction of insecticide use would benefit farmers and would lessen environmental release and impact of these agents^[14].

THE CURRENT PRACTICE OF CORN ROOTWORM CONTROL

Current Pesticide Usage (Acreage)

Approximately 78 million acres of corn were planted in the United States during the year 1999. Of this, 54 million acres (70%) were first-year corn (i.e. planted in a field that grew a different crop the previous year) and 23 million acres (30%) were planted as continuous corn (i.e. planted in a field where corn was grown the previous year.). In a smaller survey (Mulvaney, W. 2001 Foundation E.A.R.T.H. CRW impact survey, January 4), involving only a fraction of total corn acres, approximately the same distribution was found. When compared to continuous corn, CRW treatment was applied to a slightly lower percentage of first-year corn acres; the latter accounted for 8.2 million acres of treated first-year corn, or 60%, of the total 13.5 million CRW treated acres.

Grower's future preferences regarding use of a genetically engineered (GE) corn product incorporating CRW control were determined in a study by Foundation Earth in 2000 (Mulvaney, W. 2001 Foundation E.A.R.T.H. CRW impact survey, January 4). Three hundred farmers who had used insecticide for CRW control in 2000 were interviewed regarding their anticipated preferences for the 2001 growing season, assuming that a GE corn product incorporating CRW control would be available.

Table 1 presents the CRW treated acres by type of insecticide used based on various data sets for the 1997-2000 growing seasons (references in Table 1).

Table 2 indicates the percentage of farmers who indicated they were "very interested" or "somewhat interested" in various growing options ("Preference %"), including conventional treatment (non-GE corn plus insecticides for control), CRW corn with or without insecticide, and *Bacillus thuringiensis* (Bt) corn resistant to other corn pests (but not CRW) with or without insecticide. The Table also gives the percentage of the farmer's total acreage devoted to the 1st year or continuous corn.

Overall, 60% of corn farmers surveyed preferred to plant corn, whatever their CRW control choice (Mulvaney, W. 2001 Foundation E.A.R.T.H. CRW impact survey, January 4). When asked about their interest in planting a GE corn strain providing protection against the CRW pest and some secondary insects, 77% of farmers were "very" or "somewhat" interested. When asked about planting GE corn to resist CRW alone, 65% were "very" or "somewhat" interested.

TABLE 1

Current Pesticide Use (%) in 1st Year and Continuous Corn

	% Corn Acres Treated				1st Year Corn	Continuous Corn
<i>Organophosphate (OP)</i>						
Counter [®]	12				9	18
Counter ^{®b}	12				10	14
Lorsban [®]	12				12	12
Lorsban ^{®b}	26				29	22
Aztec [®] (OP + Pyrethroid)	10				6	16
Aztec [®] (OP + Pyrethroid) ^b	<u>14</u>				<u>12</u>	<u>15</u>
Total OP	37	45 ^b	50 ^c	72 ^d	35	39
<i>Pyrethroid</i>						
Force [®]	17				13	22
Force ^{®b}	20				18	21
Pounce ^{®b}	5				7	2
Warrior ^{®b}	<u>2</u>				<u>4</u>	<u>0</u>
Total Pyrethroid	32	38 ^b	37 ^c	20 ^c	31	31
<i>Fipronil</i>						
Regent [®]	13				5	22
Regent ^{®b}	<u>8</u>				<u>7</u>	<u>9</u>
Fipronil average	11	13 ^b	11 ^c	4 ^d	6	17
<i>Carbamate</i> ^b	3	4 ^a	3 ^d	4 ^c	2	3
Total insecticide use	83	100 ^c	101	100	76	92

Note. ^a Mulvaney W. 2001, Survey, Foundation E.A.R.T.H. 1/4/01. ^b Monsanto (Marketing Horizons Survey 2000, Corn Rootworm Mail Survey, prepared for Monsanto United States Ag Sector, April 19), 2000. ^c Wilde G: 2000. Research Communication: Corn Rootworm Insecticides; Insect management for field corn in 2000 (Entomology 120). Kansas State University Agricultural Experiment Station and Cooperative Extension Service, 1999, Market survey, August. ^d Steffen K: 2000. Research Communication, Agricultural Experiment Station and Cooperative Extension Service, Market Survey (corn) 1997, University of Illinois, Urbana, IL, August.

TABLE 2

Potential Use of Genetically Engineered (GE) Corn Root Worm (CRW) Seed and Reduction in Insecticide Use

Corn Treatment	Preference (%)	% Acres Committed to	
		1st Year Corn	Continuous Corn
Conventional treatment	82	25	31
GE CRW + 2 ^o insecticide	77	22	31
GE CRW (only)	65	20	30
GE CRW (only; limited survey)	84	24	48
Would use GE CRW + insecticide	--	77 ^a	92 ^a
<i>Bacillus thuringiensis</i> (Bt) Corn	63	21	32
Bt Corn + 2 ^o insecticide	62	19	25

Note. ^a This annotation indicates that for first year corn 77% of farmers who used genetically engineered CRW would prefer to use an additional insecticide to control CRW. With continuous corn, the number preferring to use an additional insecticide to control CRW increased to 92%.

Grower concerns regarding insecticide exposure were also determined in the

Foundation Earth Study (Mulvaney, W. 2001 Foundation E.A.R.T.H. CRW impact survey, January 4). Growers were asked to score their levels of concern regarding various exposures or operations related to CRW control, and to assess the degree of risk associated with these operations. Concern was rated on a scale of 1-10, while risk was assessed by the farmers as low, moderate, or high; with the latter characterized as reducing efficiency but not of high health concern. High concern was defined for study purposes as having a score of 8 or above for a particular exposure route or operation.

Table 3 documents grower rates of “high” health concern related to the various operations involved in the use of soil-applied insecticide for CRW control. When GE corn was considered as an alternative to insecticides, rates of high concern were reduced by 7-33%, with the greatest reductions seen among the perceived high-risk exposures.

TABLE 3

Concern for Amount of High or Moderate-exposure with Soil Applied Insecticide and Corn Root-worm (CRW) Modified Seed (%)

	Insecticide	CRW	Reduced Concern by Use of CRW
<i>Exposure Concerns (High Perceived Risk)</i>			
Filling Boxes	76	43	33
Family Exposure	<u>72</u>	<u>44</u>	<u>28</u>
$\bar{x} \pm s$	74 \pm 3	44 \pm 1	31 \pm 4
<i>Exposure Concerns (Moderate Perceived Risk)</i>			
Environmental Load	53	34	19
Livestock Exposure	47	32	15
Disposing Insecticide Containers	<u>41</u>	<u>29</u>	<u>12</u>
$\bar{x} \pm s$	47 \pm 6 ^a	32 \pm 3 ^a	15 \pm 4 ^a
<i>Efficiency-Performance Concerns</i>			
Clogged Insecticide Boxes Variable Performance	43	24	19
Planting Slowed to Fill Insecticide Boxes	<u>27</u>	<u>20</u>	<u>7</u>
$\bar{x} \pm s$	35 \pm 11	22 \pm 2 ^b	13 \pm 8

Note. ^a High exposure concerns > Moderate exposure concerns. ^b Moderate exposure concerns > Efficiency-performance concerns.

Estimated Reductions in Insecticides and Herbicides

One effect of the introduction of GE corn is an anticipated reduction in the use of current insecticides for CRW control. Genetically engineered corn use may allow avoidance of traditional chemical insecticides altogether, allow a reduced use of insecticides for residual CRW control and control of other pests, or perhaps allow a shift from the more acutely toxic agents needed for CRW control (organophosphates and carbamates) to less acutely toxic agents such as fipronil or pyrethroids to provide control of other pests not controlled by GE corn.

Kline and Company (at Linda_Dansbury@klinegroup.com) predict that by 2009 insecticide use will be reduced 70%. Reduction in insecticide use is expected to exceed 6 000 000 kg, with an even larger reduction occurring from herbicides-20 000 000 kg. The reduction in insecticide treated acres for CRW can be estimated using the Foundation Earth survey data (Mulvaney, W. 2001 Foundation E.A.R.T.H. CRW impact survey, January 4) in conjunction with available estimates of total corn acreage. The survey data (Fig. 1) indicate that, overall,

some 32% of growers would convert to the GE corn product, with slightly more interest in conversion in the continuous corn market, as would be expected due to greater pest pressure. Overall, of those corn acres that growers are willing to plant with the CRW corn seed, 82% would have been previously treated with an insecticide (Marketing Horizons Survey: 2000. Corn Rootworm Mail Survey, prepared for Monsanto United States Ag Sector, April 19). There is more tendency to use CRW corn seed for insect control on corn-on-corn acres (92%) versus first-year corn acres (71%).

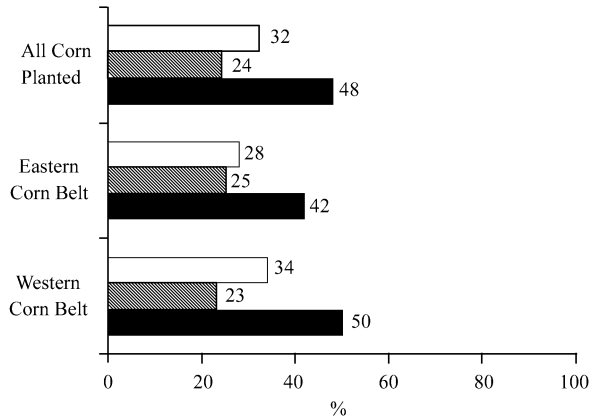


FIG. 1. Percent of corn acreage expected to be planted in corn root worm (CRW) seed. Base = 179 598 unweighted acres.

- % of all acres planted in corn that is planted in CRW seed.
- ▨ % of all acres planted in corn the 1st year that is planted in CRW seed.
- % of all acres continuously planted in corn that is planted in CRW seed.

Doane (Unpublished observations; 2000. Report on 1999 Corn Grown and Acres Treated for Corn Rootworm, Jim Johnson/Mike Hilton, Monsanto Chem Co, St Louis, MO. August) indicates that 10 346 635 corn acres in the eastern and western corn belt were treated for CRW in 1999. Applying the data from Mulvaney to the acreage figures of Doane, with adjustment for the different relative proportions of eastern and western corn borer acreage in the two surveys, results in a projected 44.2% decrease in total treated CRW acres. Thus, in the first year that CRW corn would be available there would be a potential reduction of 4 571 188 insecticide treated acres. At 0.5 pounds/acre average application rate, a use reduction of approximately 2 300 000 pounds of insecticide is projected (Steffen K: 2000. Research Communication, Agricultural Experiment Station and Cooperative Extension Service, Market Survey (corn) 1997, University of Illinois, Urbana, IL, August). Projections for the second year are higher, with the Foundation Earth survey indicating that an additional 19% increase in CRW use would occur if CRW corn performance was satisfactory (Mulvaney, W. 2001 Foundation E.A.R.T.H. CRW impact survey, January 4). With this additional increase in CRW corn planting, approximately 2 700 000 pounds less insecticide would be used in the second year following CRW corn introduction (Table 4).

Although the assumptions necessary to make these calculations may not reflect actual future field conditions, it is clear that the introduction of GE corn for CRW control has the potential to significantly reduce the amount of insecticide applied for CRW control.

TABLE 4

Acres of Corn Treated with Insecticide and Potential for Reduction

	Continuous Corn Treated	1st Year Corn Treated	Potential Reduction Corn Treated ^a (% Converted Acres ^a)
Eastern Corn Belt	2 360 000	3 320 000
Western Corn Belt	3 590 000	1 080 000
Total	5 950 000	4 400 000	4 570 000 (44.2% Converted Acres)

Note. ^a Converted acres: CRW acres that would have been treated with an insecticide.

HEALTH EFFECTS OF PESTICIDES CURRENTLY USED FOR CRW CONTROL

Organophosphates

Counter[®] and Lorsban[®] are the most popular organophosphate (OP) insecticides utilized for CRW control. Aztec[®], a combination of an OP and pyrethrin insecticide, is also utilized. Because of past reliability, these three agents are still the treatment of choice for continuous corn where CRW is most problematic. However, the use of these pesticides has decreased over the past three years from more than 2/3 of corn acres treated to slightly more than 1/3 of corn acres treated.

The principal route of OP environmental or work-related exposure is by oral ingestion. Some exposure also occurs via the dermal route. Inhalation is likely the least significant exposure route, as these agents are non-volatile and are not handled or applied in a readily respirable state.

Because breathing patterns, dermal absorption, ingestion, and metabolism vary, there is little correlation of exposure with reductions in serum acetylcholinesterase (AChE), a useful biomarker of OP exposure^[15,16]. No correlation has been shown between urinary concentrations of OP metabolites and exposure levels^[15,16].

Organophosphates were designed to inhibit AChE in the insect. Unfortunately, they also inhibit the AChE of humans and animals. Because inhibition of AChE by OP's is largely irreversible, new AChE must be synthesized to restore function. In humans, this occurs over a period of 1-3 weeks. During that time, considerable toxicity may occur. Treatment with atropine leads to physiological reversal of the acute non-muscular life-threatening signs, but will not reverse motor paralysis. Pralidoxime or other oximes, if given sufficiently early, reactivate AChE acting as an antidote. Supportive care helps the patient toward clinical recovery^[15-17].

Acutely poisoned adults develop muscle fasciculations and weakness, often requiring respiratory support. They may have tightness of the chest, wheezing, and a productive cough with evidence of pulmonary edema. Children more often presented with seizures (22-25%), mental changes, and lethargy-coma (54-96%), while only 2-3% of adults had convulsions^[16].

Organophosphate-induced delayed neuropathy (OPIDN) is associated with inhibition of neurotoxic esterase and is known to occur in humans. OPIDN causes weakness or paralysis and loss of sensation of the extremities, predominantly the legs^[18]. Some, but not all, OP's used as insecticides are implicated in causing delayed neuropathies in humans; and these occurrences are usually noted after acute and often massive OP exposures.

Intermediate syndrome is another neuromuscular presentation occurring 24-96 hours following OP exposure. There remains debate whether this syndrome is the result of

inadequate treatment of acute poisoning or represents a truly distinct clinical entity^[16].

Three case-control epidemiologic studies indicate that a proportion of patients acutely poisoned with OP may experience some long-term neuropsychiatric sequelae^[16,19–21]. In some cases, neurologic signs (neuromuscular fasciculations, generalized muscle weakness, and emotional lability with memory impairment) persisted well beyond the period when AChE had returned to normal levels^[15–17].

Early neurotoxic effects of acute OP intoxication have been well documented. Less understood is the potential development of chronic neuropsychological sequelae from exposures to insecticides^[21]. Residual, long-term, low level neurological damage, not following acute toxicity was associated with subtle changes in neuropsychological performance, manifested as slower reaction time in fruit tree farmers^[22]. The underlying mechanism, if any, is not clearly understood.

Chronic CNS effects expressed as deficits in auditory attention, visual memory, visual motor speed, sequencing, problem solving, reaction and dexterity have also been reported^[23,24]. The chronic psychiatric disorders following OP exposure in 146 farmer-sheep dippers relative to 143 controls appeared to occur independently of any symptoms that followed acute exposure^[23, 24]. Repeated exposures to OP-based pesticides were associated with subtle changes in the nervous system. The authors recommended minimizing exposure wherever possible^[25]. In follow-up study of 77 OP-exposed sheep dippers there were confirmations of exposures (urinary dialkyl-phosphate levels) but no evidence of any association between reported symptom levels and chronic neuropsychological effects. Although these sheep-dippers may have had higher levels of OP exposure than sheep-dippers in general, the neuropsychological effects occurred independently of previous OP exposure^[24].

The nature of these changes is unclear. However, Metcalf and Holmes and others^[25, 26] speculate that electroencephalographic analyses suggesting deep mid-brain lesions may have been associated with avoidance of problem-solving, oversimplified perceptual functioning, loss of ability to appreciate complex abstract relationships, and memory disturbances. Signs were often masked by adaptive tricks such as deliberately slowed responses, mnemonic aids and inappropriate “giving up”. The most severe effects were disturbed memory, difficulty in maintaining alertness, and appropriate focusing. These signs contrasted with controls whose errors were wrong answers, misinformation and inability to perform tasks^[25, 26]. Rabbits exposed to OP had subtle changes in complex behaviors detectable after AChE activity in blood and in the brain had returned to the normal level^[27]. A relationship between AChE inhibitors and aggression (homicide, antisocial behavior, schizophrenia) has been postulated^[28, 29].

Steenland *et al.*^[30] noted worsened mood scales and reduced visual attention as well as neurologic sequelae such as fatigue and abnormal pursuit aiming following OP exposure. Specifically, chlorpyrifos and dimethoate were associated with tension and fatigue, diazinon with tension, and mevinphos and demeton with worsened finger vibrotactile sensitivity. Deficits of sustained attention seemed correlated with “days off work”^[30].

Savage *et al.*^[31] reported differences in intellectual functioning, academic skills, abstraction, flexibility of thinking, and simple motor skills such as impaired hand-eye coordination. Twice as many exposed people (24) as control individuals (12) had Halstead-Reitan Battery scores in the range characteristic of individuals with cerebral damage-dysfunction. Patient by patient relative assessment of functioning revealed greater distress and complaints of disability in exposed individuals^[31]. Agricultural fieldworkers had poor compliance with the use of protective field clothing^[32]. Reviews suggested that little was known about connections of neuropsychological outcomes to dose, to indicators of dose, or to acute signs of OP poisoning^[15–17, 27]. Moreover, the ability of a second OP to inhibit the

breakdown of the first OP is not clearly understood; and further research is needed in this critical area. While the chronic neurotoxicity of the OP insecticides remains controversial, existing data do raise the possibility of persisting neurological effects even in the absence of apparent acute toxicity.

Although historically medical and veterinary medical personnel focused on acute symptoms, the medical community has recently come to recognize the potential importance of neurophysiological sequelae following lesser degrees of acute exposure. Although the data do not allow quantitative analysis, there is expected to be reduction in both acute and chronic sequelae resulting from the reduced use of OP if the use of GE corn displaces present insecticide use.

Pyrethrin(s)/Pyrethroid(s)

Pyrethrins and pyrethroid compounds are generally much less toxic than OP or carbamate insecticides. The pyrethrins currently represent 25% of total global insecticide use and a significant fraction of the chemicals used to control insects in crops, specifically corn. Their use, especially as a domestic insecticide, has been increasing^[33]. The most important pyrethrin/pyrethroid products used for CRW control are Aztec[®], a combination of OP (tebupirimphos) and pyrethrin/pyrethroids and Force[®] (telfluthrin), a pyrethrin/ pyrethroid. Pounce[®] (cyhalothrin) and Warrior[®] (permethrin) are less extensively used for CRW control.

Both dermal and gastrointestinal absorption of pyrethrins/pyrethroids are low in humans and other mammalian species. High local topical exposures to pyrethroids can induce paresthesia. Paresthesia is regarded as a local nuisance reaction and is not predictive of human toxicity^[34]. In practice, adverse effects in humans due to pyrethroid class insecticides are predominantly limited to irritant and allergic respiratory tract effects^[34]. The risk for toxic effects as assessed by systemic exposure during overuse conditions is projected to be 40 to 400 times lower for 5% permethrin cream than for 1% lindane lotion^[35].

When cypermethrin was given daily at levels of 300 mg/kg IP to rats and electroencephalographic analyses were conducted, paroxysmal epileptic activity appeared after the first bursts of epileptic activity^[36].

Neonatal exposures to pyrethrins or pyrethroids may induce toxic effects^[37]. The developing kidney was a target of the toxic action of cypermethrin. Specifically, it induced long-lasting impairment of renal dopamine D1-and D2-like receptors. Renal dopamine receptor changes caused by cypermethrin were consistent with possible alterations of renal tubular function and of sympathetic neuro-effector modulation^[37].

Estrogenic potential has been suggested for certain pyrethroid compounds in studies using the MCF human breast carcinoma cell line. Sumithrin or fenvalerate increased mRNA levels for tumor protein (pS2) slightly above basal levels^[38]. At micromolar concentrations, these two compounds induced pS2 to levels comparable to those elicited by 17-beta estradiol (five-fold) with an apparent dose-response. Neither permethrin nor d-trans allethrin induced pS2 expression. These findings suggest that pyrethroids, at sufficiently high concentrations, may have effects upon endocrine regulation; but the ability of pyrethroids to affect endocrine function in humans and wildlife requires further investigation.

Although pyrethrin/pyrethroids produce health effects, they are generally regarded as less toxic than OP or carbamate insecticides. The development of a less toxic alternative, which no longer necessitates the use of pyrethrin-pyrethroids, will likely lead to moderate reduction in health effects from these agents in the United States.

Fipronil (Phenylpyrazole)

There is a continuing need for novel and selective action on insect nerve cell targets. Fipronil's trifluoromethyl sulfinyl moiety, unique throughout agrichemicals, is considered important to its action, which involves interference with the gamma amino butyric acid (GABA) gated chloride channel. It is a potent convulsant, much like the cyclodiene insecticides, but much more insect specific^[39]. The combined action of the parent compound and its sulfone metabolite are responsible for its action on insects. The production of the sulfone does not occur in mouse studies, suggesting that this conversion is less significant for mammalian toxicology^[40]. Insect resistance which develops to fipronil is six- to >200-fold less than that in cyclodienes, pyrethroids or carbamates (49-fold resistance in fipronil compared to 290- to >10 000-fold in cyclodienes, pyrethroids or carbamates)^[41]. This insecticide would appear on the surface to be an ideal one for the control of CRW^[40, 41].

Clinical signs in animals exposed to fipronil were mostly neurotoxic. The LD₅₀ in mice for fipronil was >100-time that of insects as a whole body exposure. The receptor IC₅₀ was higher by a similar margin. Use of piperonyl butoxide increases this margin by seven-fold^[40]. Being new, fipronil's clinical properties are still being elucidated. For example, fipronil has not been tested for subtle, persisting neurotoxicities, such as those suggested with OP compounds. However, its intermediate clearance rate, and the persistence of higher bird densities when compared to OP compounds or carbamates is encouraging.

Predictions of improved health consequences are difficult with fipronil because no striking overt toxicities have been reported. The fact that mouse LD₅₀ concentrations were only two-fold higher than that of insects suggests that this compound was not without mammalian toxicity^[40]. However, if used properly, health related costs attributable to fipronil are likely to be minimal.

Carbamates

Carbamate usage for CRW is well established^[42]. Furadan is the major carbamate insecticide used to control CRW. Carbamates were used for three to four % of the acres on which insecticides were applied. Carbamates are rapidly absorbed and can cause rapid onset of toxicity. They are generally cleared from mammals within a few hours to one day^[43]. The mechanism of action of carbamates involves inhibition of AChE through binding of carbamates to the active site of the enzyme. Atropine will reverse the non-muscular effects caused by carbamates, with motor weakness fortunately being an uncommon effect of the carbamate insecticides.

Carbamate clinical toxicity in mammals is less persistent than is seen with OP's. Long-term neurological sequelae have not been reported with the carbamates, although it is not clear that the carbamates have been sufficiently investigated to exclude possible chronic effects.

Carbamates do have significant acute mammalian toxicity, suggesting that a reduction in their usage will benefit health care costs. Shifting from carbamates to fipronil, or the development of a GE plant resistant to CRW, would be expected to reduce health costs associated with carbamate control of CRW, although the effect cannot be quantified with existing data.

CONCLUSIONS

Despite the annual application of significant amounts of pesticides to corn, these agents have failed to halt yield reduction in corn crop amounting to approximately 1/3 of potential corn production in the United States^[1]. Human insecticide poisonings remain a health concern. Each year 18 000 to 26 000 cases of non-fatal poisonings are reported, with over 8 000 human patients requiring evaluation treatment for OP-carbamate poisoning^[2-12]. These data are potentially limited because they may be underreported^[13]. No data exist which would allow the enumeration of cases related specifically to CRW control. Although the impact cannot be quantified, CRW control using traditional pesticide-based approaches does impose health and environmental costs and may produce adverse health and environmental effects.

Bacillus thuringiensis endotoxins are useful for the control of insects that damage corn. This approach is more target-specific than the use of existing chemical insecticides. In this connection, plants genetically modified to produce Bt endotoxin and other toxins clearly have an important role to play. Projections based upon prospective determination of grower crop and CRW control preferences may not be closely predictive of actual future grower behavior. However, even allowing for substantial variability in outcomes, it is clear that the implementation of Bt control of CRW will result in substantial reduction in insecticide use.

An evaluation of presently available data regarding CRW corn, in conjunction with survey data regarding anticipated grower preferences, has been utilized to gain an understanding of the insecticide use-reduction benefits of genetically enhanced CRW resistant corn. Although we are not able to quantify the effects, qualitative analysis leads to the conclusion that the introduction of CRW corn will reduce insecticide use, allow growers to reduce their level of concern regarding exposure, and probably reduce insecticide associated health care costs.

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