Chapter 3
Acute Pesticide-Related Illness

Introduction
Acute effects are those that occur close in time to exposure, within a few minutes, a few hours, at the most a few days. The most important factor in pesticide toxicity is the amount it takes to poison, kill or do harm.

The EPA classifies all pesticides into one of four acute toxicity categories. Category I defines the most toxic, and Category IV the least toxic. The classification is based on how much of the chemical it takes to kill fifty percent of laboratory animals by feeding it to them, putting it on the skin, or inhaling it, called the oral, dermal, or inhalation LD_{50} (ell dee fifty).

Acute Health Effects of Pesticides

Irritation of the eyes, nose, and throat
Dermatitis
Systemic Poisoning
Death

The lower the LD_{50} the less of the pesticide it takes to poison the animals, and therefore the more toxic it is. For example, the oral LD_{50} of parathion is 4 m/kg and of malathion 1,000 mg/kg. This means that parathion is 250 times more toxic than malathion (or malathion is 250 times less toxic than parathion); that it would take 250 times more malathion to kill the animals than parathion (or 250 times less than parathion). See Appendix D for EPA classification criteria.

Acute Health Effects
Acute health effects range from burning, stinging and tearing of the eyes, to skin rashes, to serious poisoning and death. The best single source of information on acute pesticide poisoning is the fifth edition of the EPA's "Recognition and Management of Pesticide Poisoning", which is also available online[1].

Organophosphate (OP) insecticide toxicity is the leading cause of major morbidity and death in the insecticides class. The clinical syndrome of OP toxicity varies widely, ranging from the classic cholinergic syndrome to flaccid paralysis and intractable seizures. The mainstays of therapy for OP-poisoned patients are atropine, pralidoxime, and benzodiazepines. Tachycardia is not a contraindication to treatment with atropine in OP toxicity. Atropine should be administered to alleviate respiratory distress, symptomatic bradycardia, and as an adjunct to benzodiazepines to alleviate seizure activity. Atropine should not be administered systemically to alleviate miosis. In acute OP toxicity, a continuous pralidoxime infusion should be considered. Intermediate syndrome and OP-induced delayed neuropathy may occur in select patients with OP poisoning.

Irritant effects: The most common acute effect of pesticides is irritation of the eyes, nose, and throat. Of the 667 cases of pesticide related illness reported to the California Environmental Protection Agency in 2001, 21.6% were eye irritant effects, 11.1% to the skin[2]. The resulting tearing, stinging, burning, scratchiness and itching, can be from the active ingredient pesticide, an inert ingredient, or a combination[3,4,5,6].

Sulfur, a frequent source of eye and nose irritation, is essentially unreported by farm workers since it is so common. A study of apricot sulfurization found eye and nose irritation in 70% of the workers[7]. Eye irritation is on a frequently reported symptom in drift-related community exposures, including paraquat[8], metam sodium[9],[10] methyl isocyanate[11,12,13], and Mocap[14], methyl bromide and chloropicrin[15].

Effects on the Eye: Pesticides can cause chemical conjunctivitis that looks like pink eye. If pesticides splash directly into the eyes they can cause corneal abrasions or ulcers, damaging the layers of the cornea. With complete removal of the pesticide from the eye and proper treatment, the cornea should heal completely. If the pesticide or inert ingredient is corrosive and not thoroughly removed, permanent scarring can lead to blindness. Eyes symptoms often persist for some time after recovery from acute pesticide poisoning[16,17].

Transient ocular symptoms occurred in 70%, and temporary injury in 2% of 1,513 glyphosate (Roundup) related calls to a poison control center in the U.S. One injury took more than two weeks to resolve[18]. Topical irritation of the eyes was found in 49% of 815 glyphosate (Roundup) related reports from 1982-1997 to the pesticide surveillance

program of Cal-EPA[19]. Three outbreaks of conjunctivitis occurred in 35 workers in a California nut-packing facility from 1987 to 1988 . Phosphine gas was suspected, but ammonia gas, aluminum hydroxide dust, almond hulling dust, or propargite (Omite 6-E) could also have been responsible, or contributory[20]. Exposure-related conjunctivitis was found in 7% of agricultural pesticide applicators in Ecuador[21].

Paraquat, an epithelial toxin, is a frequent cause of eye lesions in agricultural workers[22], and can cause severe ocular damage from splashes, spills, and other occupational exposures[23,24,25,26].

Pesticide applicators in the Agricultural Health Study (AHS)[a] who reported retinal degeneration had a significant 180% increase in risk related to fungicide use. The risk increased with cumulative days of exposure and use of methods involving greater personal exposure . Organochlorine and carbamate insecticides were also related but the associations were less consistent [27].

Macular defects were found in pesticide applicators in India [28]. Optic neuritis associated with organophosphate exposure was found in several studies[29,30,31,32,33]. Opsoclonus (ocular bobbing) occurred in organophosphate poisoning[34,35,36,37] and in chlordecone (Kepone) poisoning[38]. Optic atrophy is rare and the cases reported were from methyl bromide exposure[39,40].

Cataracts have been related to ethylene oxide exposure[41,42,43], and methyl isocyanate in the Bhopal, India incident[13]. Organophosphate exposed farmers were found to have increased cortical wedging but no increase in cataracts[44].

Label Warning Statements that Indicate a Pesticide May Cause Allergic Dermatitis

This product is a skin sensitizer.

May cause skin reaction in rare cases.

May cause contact sensitization following repeated contact with skin of susceptible individuals. If sensitization reactions result, contact a physician

Frequent or repeated exposure to this product may cause allergic reactions in some people.

Reports from Japan of adverse ocular effects from organophosphate exposure, including myopia in adults and children have not been found in other countries[45,46,47].

A study of two organophosphate poisoned patients found that PET scanning (positron emission tomography) can confirm severe cortical visual loss even when standard eye exams and MRI (magnetic resonance imaging) examinations are normal[48].

Skin Effects

Pesticides can cause both irritant and allergic contact dermatitis; most are the irritant type. The immunologically based allergic response (sensitization) can be disabling or life threatening,. Pesticide manufacturers are required to put a warning on the label of commercial and over-the-counter products if the active ingredient is a skin sensitizer. Figure 2 shows some of these statements for some over-the-counter products.

Pesticide Associated Contact dermatitis

Most pesticide related dermatitis is the irritant type, and not an immunological sensitization or allergic reaction. Most reports of allergic contact dermatitis are anecdotal case reports, but some studies using patch testing have been done. More cases have been reported from fungicide exposure than other classes of pesticides (see Table 1).

There is an excellent review and discussion of skin reactions to pesticides[49]

Skin Reactions to Deet (Off): N,N-diethy-m-toluamide (deet, Off) is an insect repellent designed for use on human skin. A severe anaphylactic reaction occurred in a 42 year old woman with no prior history of allergy, who touched a companion who had just applied 52% deet. Rapid generalized pruritus progressed to angioedema, nausea, hypotension, and unconciousness[117]. Military personnel in south Vietnam who applied 50% deet, developed a burning sensation, erythema (redness), blisters, and a bullous eruption in the antecubital fossea which led to ulceration and scarring in some cases[50, 51]. Skin rash has been reported after topical application[52,53,54], and a

[a] A cohort study of licensed pesticide farmer applicators in Iowa and North Carolina begun in 1994, conducted by the National Cancer Institute Occupational Epidemiology Branch.

vesicobullous reaction from occupational exposure[55,56]. Applications of one to two milliliters of a 50% concentration for five days to the skin of volunteers produced paresthesia, blisters and local skin effects[57].

Table 1
Pesticides Related to Allergic Contact Dermatitis

Antimicrobials	Fentichlor[82,83]	Chloridazon[106]	d-Limonene[115, 116, 117]
Benzalkonium chloride[58,59]	Fluazinam[84]	Chlorpropham[54]	Methiocarb[118]
Chloramine[60]	Imazalil[71]	Dalapon[84]	Methomyl [119,120]
Fumigants	Maneb,Mancozeb[85,86,87,88,89,90,91,92,93]	Norflurazon[107]	Parathion[74]
Dazomet[61]	PCNB[94]	Paraquat [77,108]	Pyrethrum[121,122]
Ethylene oxide[62]	Propineb[95]	Phenmedipham[109]	**Inerts**
1,3-Dichloropropene[63,64, 65]	Thiabendazole[71,96]	Propachlor[110,111]	Ethylenediamine[123,124,125]
Fungicides	Thiram[97]	Trifluralin[96,99]	**Repellents**
Anilazine (Dyrene)[66]	Triforine[98]	**Insecticides**	Deet (Off [126,127]
Benomyl[67,68]	Zineb [82,84,99,100,101]	Barban[112]	
Captafol[69,70,71,72,73]	**Herbicides**	Dichlorvos[68,90]	
Captan[60,62,63,74,75]	Alachlor[102,103]	Dimethoate[113]	
Chlorothalonil[76,77,78,79,80,81]	Allidichlor[104]	Fenvalerate [114]	
Folpet [60,62,63]	Benefin[105]		

Other Skin Conditions (Table 2)

Pesticide exposure is linked to other skin disorders, including chloracne[128,129,130,131,132,133] ; dysesthesias[134,135,136,137,138]; pemphigus [139,140,141,142,143]; hypopigmentation[144,145,146,147]; vitiligo [148,149,150], ashy dermatitis[151]; nail damage (onchopathy)[152,153,154,155,156,157], and one report of localized scleroderma[158].

Omite-CR Reentry Poisoning

It is rare for a pesticide to cause skin poisoning of entire crews of farm workers, as occurred in California in 1986. Over a two week period, 114 of 198 orange pickers developed redness, itching, and chemical burns of the skin, resulting in small papules and vesicles (blisters), weeping, crusting, peeling, and hyperpigmentation[5,159].

It is also rare for an inert ingredient to be implicated in such a large outbreak. The cause of the episode was a reformulation of the widely used miticide propargite (Omite). The inert ingredient polyvinyl acetate was added to the new formulation, called Omite-CR, to prevent citrus leaf burn by delaying degradation on the leaves. That this would also prolong the length of time the pesticides stayed on the skin of the workers picked oranges sprayed with the new formulation was not considered.

The reentry interval (amount of time legally required after application of a pesticide before workers are allowed to reenter the treated field for cultivation or harvest activities) for propargite/Omite at the time of the poisoning was seven days. An emergency extension by Cal-EPA increased the reentry interval to 10 days, and then again to 14 days. Based on residue degradation studies of the Omite-CR, a final reentry interval of 42 days was enacted[160]. Omite-CR is no longer registered for use in California.

Table 2
Other Pesticide-Related Skin Conditions

Chloracne	
Methazole[a]	Manufacture contaminant
Pentachlorophenol	Manufacture, treated wood
Propanil	Manufacture
2,4,5-T[b]	Lawn sprayer, farm worker
Dysaesthesias	
λ-Cyhalothrin	Malaria wrkrs
Fenvalerate	Agric. applicator
Pyrethroids	Human study
Pemphigus	
DDT	Gardener
Diazinon	Sun exposure
Dichloropropene	Farmer
Pentachlorophenol	Non-occupational
Pigmentation Changes	
Alachlor (Lasso)	Hypopigmentation
Barban	Depigmentation[(c)]
Chlorothalonil	Ashy dermatitis[(d)]
Dinitrophenol	Vitiligo occupational
Dichloropropene[(36)]	Hypopigmentation
Mancozeb	Vitiligo
Methyl bromide	Hyperpigmentation
Paraquat	Hypopigmentation farmer[(e)]
Onchopathy (nail damage)	
DNOC	Agriculture
Mancozeb	Occupational
Paraquat	Reported with all sources of work exposure
Scleroderma (**Localized**)	
2,4,5-T	Lawn sprayer

(a) From contaminant 3,3',4,4'- tetrachloroazo-benzene **(b)** Also exposed to 2,4-D, bromofenoxin and picloram. **[c]** Partial repigmentation 6 wks later **(d)** Erythema dyschromicum persistans. In 70% lesions in sun exposed areas .**(e)** In black cocoa plantation workers.

Pesticide Poisoning: Organophosphates

Systemic poisoning occurs when pesticide enter the blood stream and spread throughout the body. The pesticides responsible for more occupational, accidental, and suicidal poisonings and deaths in the U.S. and throughout the world than any other, are the organophosphate insecticides. Similar to nerve gas, but less potent, they exert their toxic effect by interfering with a critical chemical in the nervous system called acetylcholine (ASS uh teel COAL een), which is essential for the transmission of nerve impulses. After acetylcholine is used to transmit nerve impulses across gaps (synapses) between nerve cells and receptors on muscles, glands, and other sites throughout the bod, it is no longer needed and must be deactivated until needed again.

Organophosphate Pesticides
Common Name (Brand Name)

Acephate (Orthene)	Isofenphos (Oftanol)
Azinphosmethyl (Guthion)	Malathion
Chlorpyrifos (Dursban, Lorsban)	Merphos (Folex)
DEF (tribufos)	Methamidophos (Monitor)
Demeton (Systox)	Methidathion
Diazinon	Methyl parathion
Dichlorvos/DDVP (Vapona)	Mevinphos (Phosdrin)
Dimethoate (Cygon)	Monocrotophos (Azodrin)
Disulfuton (Disyston)	Naled (Dibrom)
Ethion	Parathion (ethyl)
Ethoprop (Mocap)	Phorate (Thimet)
Fenamiphos (Nemacur)	Phosmet (Imidan)
Fensulfothion (Dasanit)	Terbuphos (Counter)
Fenthion	Tetrachlorvinphos (Gardona
Fonofos (Dyfonate)	

The enzyme responsible for deactivating acetylcholine is cholinesterase[b] (coal in ESTER ase). The organophosphate and N-methyl carbamate insecticides poison by binding (locking on) to cholinesterase and inhibiting its activity in the brain and peripheral nervous system. This allows acetylcholine to pile up at nerve junctions causing the signs and symptoms of poisoning.

Cholinesterase Activity

There are two type of cholinesterase affected by pesticides. Plasma or serum cholinesterase (pseudo-cholinesterase) is made in the liver. "True" cholinesterase is found in red blood cells (RBC).

In general plasma cholinesterase activity decreases more rapidly and regenerates more quickly, usually within a week to ten days after overexposure to organophosphates or N-methyl carbamates have lowered the activity level. After mild poisoning, sometimes a rebound effect occurs resulting in elevated levels. Plasma cholinesterase can be affected by liver disease, anemia, and other illnesses, and is not as reliable an indicator as RBC cholinesterase.

Label Statements Indicating a Product Contains an Organophosphate Insecticide

Atropine is an antidote

This product contains a cholinesterase inhibiting pesticide.

RBC cholinesterase activity decreases less rapidly and regenerates more slowly. It is more reflective of functional cholinesterase in the brain and nervous system and is biochemically the same enzyme. RBC cholinesterase regenerates at about 1% per day; therefore a 30% reduction in activity would take about a month to return to pre-exposure baseline levels. RBC cholinesterase has no known function and it is not known why how or why it cam to be present.

Potential chronic sequelae related to decreases in cholinesterase activity is discussed in Chapter 7.

California's Cholinesterase Monitoring Regulations

The State of California has required cholinesterase monitoring under medical supervision for workers who "regularly handle" Toxicity Categories I and II organophosphates or N-methyl carbamates since 1974[161]. "Regularly handle" means handling pesticides during any part of the day for more than six calendar days in any 30 day qualifying period beginning on the first day of handling.

The employer is required to arrange with a physician to obtain baselines pre-exposure plasma and RBC cholinesterase activity levels and interpret the results. This baseline value must be the average of two or more tests taken at least 72 hours but not more than 14 days apart at the same laboratory. One test is permissible under the regulations if two cannot be obtained. If two tests are done and the difference between them exceeds 15 percent, a

[b] Acetycholinesterase is commonly referred to as cholinesterase, and often abbreviated as AChe or Che.

third baseline test must be performed. The average of the two closest values should be considered the true value. Baselines must be measured before exposure begins and repeated at a minimum of every two years.

If plasma or RBC cholinesterase or RBC levels drops to 80% of baseline , that is a 20% reduction in activity, an investigation of work practices is required, including safety equipment use and condition, sanitation, and pesticide handling procedures

If plasma cholinesterase levels drops to 60% or less of baseline, that is a 40% reduction in activity, or RBC cholinesterase drops to 70% , a 30% reduction in activity from baseline, the employee must be removed from exposure, and may not be returned until cholinesterase activity reaches80% or more of their respective baseline values.The employer must maintain written records of any investigations, results, and recommendations, and the dates of removal and return to exposure; all values and reports must be available to the employee, and kept for a minimum of three years. See Appendix E for a summary of cholinesterase testing and how and when to do the test.

Table 3
Signs and Symptoms of Poisoning by Cholinesterase InIhibiting Pesticides
(Organophosphates, N–methyl Carbamates)

Mild Poisoning	
Headache	Blurry vision
Dizziness	Excess sweating
Fatigue	Salivation (drooling)
Nausea	Muscle pain, cramping
Vomiting	Abdominal pain
Chest pain	Diarrhea
Moderate Poisoning	
Severe weakness	Confusion
Difficulty walking	Difficulty concentrating
Difficulty talking	Small pupils (miosis)
Muscle twitching	
Severe Poisoning	
Loss of consciousness	Cyanosis (turns blue)
Marked miosis	Convulsions
Difficulty breathing	Coma
Involuntary urination	Death
Involuntary defecation	

Oxon Formation
Organophosphate insecticides that contain sulfur in a thion group (P=S) must undergo transformation in the liver before they can inhibit cholinesterase. Oxygen is substituted for the sulfur in the thion group to form an oxon (P=O), e.g. paraoxon from parathion, maloxon, from malathion, chlorpyrifos oxon from chlorpyrifos, and so on. Organophosphates without this thion group, such as mevinphos (Phosdrin) are direct inhibitors of cholinesterase.

The oxon is more toxic than the parent pesticide and is the actual cholinesterase inhibitor. The enzyme responsible for this conversion is called paraoxonase. Paraoxonase activity levels are genetically determined, and an individual's genotype and phenotype can affect their susceptibility to poisoning. Five polymorphisms are known to contribute to a 15-fold differences in plasma paraoxon levels among individuals. Newborn baby's levels are four times lower level than adult levels, which are reached around one year of age[162].

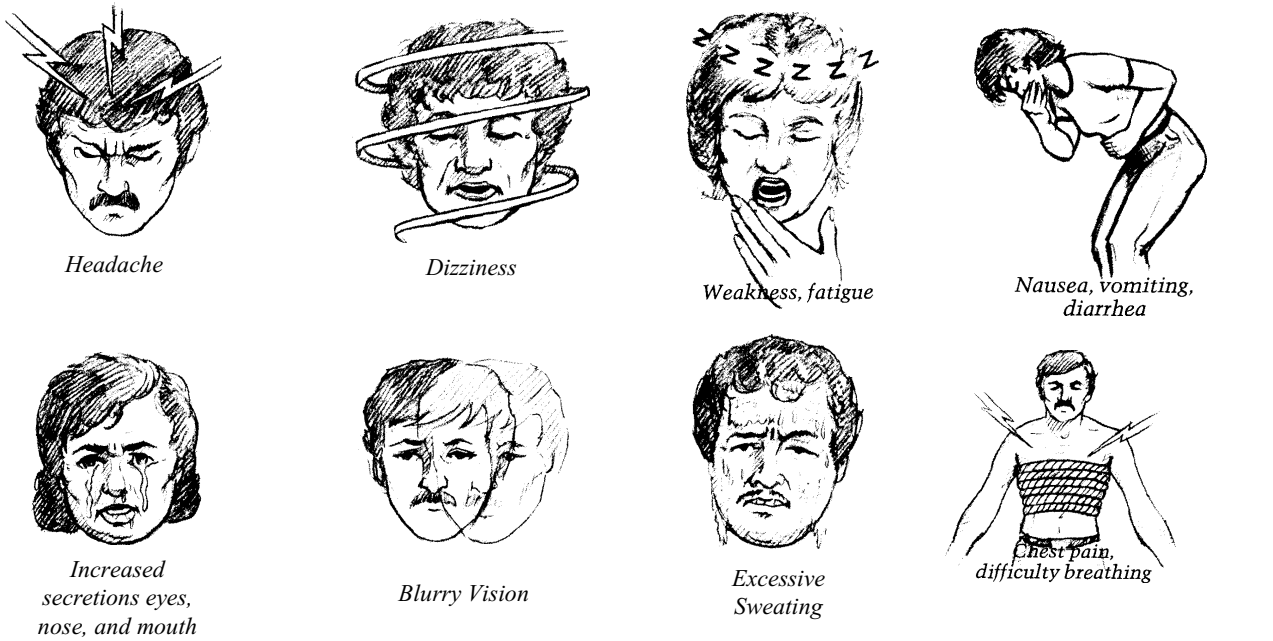
People with lower levels of paraoxonase may be less susceptible to poisoning since the oxon conversion will be slower. Those with higher levels may be more susceptible since the oxon conversion will be faster[163,164]. A worker in California poisoned by dialiflor (Torak), was found to have exposure to unexpectedly large amounts of dialifor oxon, which is twenty times more efficient in inhibiting cholinesterase than the parent chemical. Dialaflor is quite persistent compared to other organophosphate insecticides[165].

Animal studies have investigated whether gene therapy could prevent organophosphate poisoning[166]. Since paraoxonase is an HDL-associated enzyme, its role in cardiovascular diseases is an area of study[167], and as an "antioxidant" protein in certain neurodegenerative diseases including Parkinson's[168].

Signs and Symptoms of Poisoning (Table 3, Figure 1)
Poisoning by organophosphates and N-methyl carbamates (see discussion of N-methyl carbamate poisoning below) results in cholinergic effects at nerve junctions (muscarinic effects), at skeletal muscle (nicotinic effects), and in the brain. Death is usually from respiratory failure due to fluid in the lungs (pulmonary edema).

Atropine, the antidote for organophosphate poisoning, blocks the effects of acetylcholine, and must be given in much higher does than for other medical indications. Tolerance to high doses of atropine can be diagnostic of organophosphate poisoning. The oxime protopam (2-PAM) is another antidote which can reverse cholinesterase inhibition, but must be administered within 24 hours of poisoning.

Figure 1. Signs and Symptoms of Organophosphate and N-methyl Carbamate Insecticide Poisoning



Vincent Perez / Artist

Intermediate Syndrome

The intermediate syndrome appears one to four days after proper treatment and apparent improvement of organophosphate poisoning, and can last for several days or weeks. Prolonged cholinesterase inhibition results in respiratory paralysis, cranial motor nerve palsies, proximal limb muscle and neck flexor weakness, and depressed tendon reflexes. The condition is rare and relates to the to the severity of poisoning and not to the specific pesticide involved. Most cases are in severely poisoned patients who attempt suicide. Many countries have reported cases, including Belgium[169,170, 171,172], Canada[173], China[174,175], France[176], Germany[177], India [178,179,180,181,182,] Morocco[183], Poland [184,] South Africa [185], Sri Lanka[186,187,188], Turkey[189], Arkansas[190], the U.S.[191] , and Venezuela[192]. The pesticides involved were chlorpyrifos, dimethoate, fenitrothion, malathion, metasystox, methyl parathion, monocrotophos, omethoate, and parathion.

Farm Worker Crew Poisonings (Table 4)

Ever since the introduction of organophosphates in1943, farm workers have been at risk from toxic pesticide residues on the crops they cultivate and harvest. These dislodged foliar residues (DFR) are responsible for unknown thousands of poisonings. See Table 4 for reported incidents in California.

Cauliflower workers: mevinphos and phosphamidon

Sixteen farm workers in Monterey County, California were poisoned by mevinphos (phosdrin) and phosphamidon when they were sent into a cauliflower field that had been sprayed six hours earlier. State regulations required a 72 hour interval. Signs and symptoms of poisoning included blurred vision, dizziness, weakness, disorientation, headache, nausea, vomiting, and cramping. Plasma Che activity was inhibited by about 66% in eight workers receiving medical and red blood cell (RBC) activity by 33%. Eleven days after exposure, plasma and RBC cholinesterase were still decreased 34% and 39% respectively.

It took 57 days for plasma activity to return to 95% of normal, and 66 days for RBC. An important finding was that

symptoms of poisoning were more highly correlated with the rapidity of cholinesterase decline rather than the amount of reduction in activity[193].

Lettuce workers: mevinphos
Thirty-one of 44 farm workers and three agricultural officials were poisoned in Monterey, California after entering a field of iceberg lettuce that had been sprayed earlier that day with mevinphos. Signs and symptoms included dizziness, visual disturbances, headache, and nausea. Two workers were hospitalized; two had abnormal plasma ChE activity. Several workers were unable to return to work the next day because of continuing symptoms. ChE and AChE values increased significantly over the next 2 weeks. A retrospective evaluation based on the followup measurements indicated that during the acute stage of the incident plasma ChE and erythrocyte AChE had been decreased by a mean of 15.6 and 5.6%, respectively[194].

Grape pickers: dialifor and phosphalone
One of the first reported organophosphate crew poisoning of farm workers occurred in Madera, California in 1976, when 108 of 120 grape pickers became ill from exposure to dialifor (Torak) and phosphalone (Zolone). Eighty-five required medical attention and four were hospitalized. The average plasma and red cell cholinesterase activity was decreased by 60%. Workers had been sent into the vineyards before the required 30 day waiting period. Subsequent investigation found workers were exposed to foliage containing up to 57 ppm phosalone and up to 2.3 ppm of phosalone oxon. The estimated concentration of dialiflor in the fields was 100 ppm, a highly significant exposure level.

The growers' records of application date and amounts applied contained no indication that these residues could have been possible at the time of harvesting. A criminal complaint was filed against the grower, who was fined $1,750 for violations including the use of Torak without a valid permit and not maintaining record of use. The grower also paid substantial medical expenses, and lost heavily from grapes placed under quarantine A physician was also fined in this action for failure to report occupational injury to the Division of Labor Statistics and Research[195,196].

Grape pickers: phosalone
Thirty members of a crew of farm workers in Madera County, California became ill with weakness, dizziness, and gastrointestinal symptoms nine days after they began picking grapes. Ten were admitted to the hospital, and four had episodes of severe sinus bradycardia (slow heart rate) persisting for several days. Two workers developed a transient atrioventricular dissociation (abnormal heart rhythm) at the time of admission. Of 20 workers tested, all had moderate to severe inhibition of both plasma and RBC cholinesterase. Phosalone had been last applied to the vineyard 29 days earlier[197].

Apple orchard workers: mevinphos. An outbreak of mevinphos (Phosdrin) poisoning in 27 workers in 19 different apple orchards in Washington State occurred in the summer of 1993. Most cases (83%) were in airblast sprayer crews overexposed during mixing, loading, or application operations. The remaining cases were due to indirect contact, such as reentering recently treated orchards. All workers exposed during mixing, loading, or application sought treatment in emergency rooms. Seven required hospitalization, four in intensive care. Fourteen of 16 cases tested had cholinesterase depressions of 25% or more, and more than a 50% reduction. I

Subsequent investigations revealed failure to observe labeling requirements for protective equipment, lack of proper supervision, deficient hazard communication and training, and poor respirator maintenance. These incidents eventually led to suspension of mevinphos for use on apples and other tree fruits[198].

Emergency personnel. Three emergency room personnel were poisoned and required treatment after exposure to a contaminated patient[199]. Two emergency medicine personnel required hospitalization and treatment for organophosphate poisoning after giving mouth to mouth resuscitation to a suicide victim who later died[200].

Table 4
Reported Crop Residue Incidents of Group Poisonings from Re-entry or Drift
California - 1949 to 2000

Year	County	Number Ill	Crop	Pesticide(s)
1949	Yuba	10-25	Pears	Parathion
1951	Kern	16	Grapes	Parathion
1952	Riverside	1	Oranges	Parathion
1953	Riverside	7	Oranges	Parathion
1953	Riverside	-	Citrus	Parathion
1953	San Bernardino	-	Citrus	Parathion
1959	Various	275	Citrus	Parathion
1961	Tulare	10	Lemons	Parathion
1963	Stanislaus	94	Peaches	Parathion
1966	Tulare	18	Oranges	Parathion
1966	Los Angeles	11	Oranges	Parathion, Malathion
1966	Tulare	9	Oranges	Parathion, Ethion
1967	Stanislaus	24	Peaches	Guthion, Ethion
1967	Merced	3	Peaches	Guthion
1968	Tulare	19	Oranges	Parathion
1970	Tulare	3	Lemons	Dioxathion, Naled
1970	Tulare	2	Oranges	Parathion, Ethion
1970	Tulare	8-11	Oranges	Guthion, Ethion
1970	Kern	35	Oranges	Parathion
1970	Tulare	11	Oranges	Parathion, Malathion
1971	Fresno	8	Olives	Parathion
1972	Fresno	3	Oranges	Parathion
1972	Tulare	9	Oranges	Parathion
1972	Monterey	31	Lettuce	Parathion
1973	Fresno	27	Grapes	Phosalone, Dialifor
1974	Fresno	2	Grapes	Phosalone, Guthion
1975	Tulare	16	Oranges	Parathion
1976	Madera	118	Grapes	Phosalone, Dialifor
1977	Fresno	25	Oranges	Parathion
1978	Tulare	7	Grapes	Ethion
1980	Merced	6	Peaches	Guthion
1980	Monterey	22	Cauliflower	Phosdrin, Phosphamidon
1981	Monterey	41	Lettuce	Phosdrin
1982	Tulare	17	Oranges	Parathion
1982	Monterey	35	Cauliflower	Phosdrin, Metasystox-r
1983	Monterey	23	Cauliflower	Metasystox-r,dimethoate
1986	Tulare	121	Oranges	Propargite (Omite-cr)
1987	Fresno	35	Peaches	Guthion
1987	Madera	54	Grapes	Phosalone
1987	Fresno	24	Grapes	Phosalone
1993	All Counties	117	All Crops	Mixed
1994	All Counties	109	All Crops	Mixed
1997	Colusa	10	Rice	Methyl Bromide
1997	Imperial	10	Melons	Methomyl, Esfenvalerate,endosulfan
1997	Imperial	16	Melons	Benomyl, Triadimefon
1997	Riverside	31	Alfalfa	Inert Ingredient (Adjuvant)
1997	Tulare	12	Oranges	Not Listed
1997	Tulare	14	Grapes	Mixed
1998	Fresno	34	Cotton	Carbofuran
1998	Merced	12	Nectarines	Chlorpyrifos, Copper Sulfate
1998	Monterey	12	Apples	Diazinon, Fenarimol
1999	Fresno	13	Cotton	Chlorpyrifos, Naled
1999	Madera	10	Grapes	Chlorpyrifos, Lime-sulfur
1999	Tulare	171	Soil	Metam-sodium
2000	Kings	58	Eggs	Dimethoate
2000	Tulare	26	Almonds	Propargite, Chlorpyrifos
2000	Ventura	28	Lemons	Chlorpyrifos

N–Methyl Carbamates

N-methyl carbamates are cholinesterase inhibitors and share a common mechanism of action with the organophosphates. Unlike the organophosphates, the inhibition is rapidly reversible, and they do not form more toxic oxons. Signs and symptoms of poisoning in general appear earlier, are usually less severe and recovery is more rapid. The pesticide with the lowest oral LD_{50}, aldicarb (Temik), belongs to this class of pesticide.

N-Methyl Carbamate Insecticides

Aldicarb (Temik)	Methomyl (Lannate)
Aminocarb (Matacil)	Oxamyl (Vydate)
Bendiocarb (Ficam)	Pirimicarb
Bufencarb (Bux)	Promecarb
Carbaryl (Sevin)	Propoxur (Baygon)
Carbofuran (Furadan)	Thiodicarb (Larvin)
Fenoxycarb (Torus)	Trimethacarb (Landrin)
Methiocarb (Mesurol)	

Signs and symptoms of N-methyl carbamate poisoning are the same as with the organophosphates, as is the antidote, atropine. 2-PAM is usually contraindicated since it can worsen poisoning. Cholinesterase test is often not as useful because cholinesterase regenerates so readily, often in the test tube on the way to the laboratory.

There have been no reported occupational deaths from N-methyl carbamates in the U.S., although aldicarb (Temik) may have contributed to the death of a California farm worker in a tractor roll over accident[201]. An occupational fatality from methomyl was reported in a farmer from Greece working in an enclosed space without proper protection[202].

Farm Worker Crew Poisonings. Farm worker crew poisonings are unusual with N-methyl carbamates because of the quick reversibility of cholinesterase inhibition, and the rapid resolutions of signs and symptoms. Two reported incidents from California are described in which cholinesterase testing, which is usually not very helpful in carbamate poisoning, proved of value in diagnosing and managing the illnesses.

Grape girdlers: methomyl. Twelve members of a crew of 16 workers developed nausea, vomiting, dizziness, headache, and abdominal pain while girdling[c] grapes in Kern County, California. Depressed or low normal levels of both red blood cell and plasma cholinesterase were found in 12 of 13 workers tested. Four hospitalized workers, discharged within 24 hours, had a 20% increase in RBC cholinesterase activity compared to samples taken eight to 12 hours earlier in the emergency room. Four days later, all workers had complete recovery of cholinesterase activity, which is consistent with of N-methyl carbamate poisoning. Methomyl was found on clothing samples form the hospitalized workers. Samples of dislodgeable residues from the grape leaves in the field showed a mean methomyl level of 0.27 $\mu g/cm^2$ on the day of the poisoning.

In a study five days later, mean methomyl residues of 0.065 $\mu g/cm^2$ and a peak of 0.125 $\mu g/cm^2$ were found. None of the workers tested had significant cholinesterase depression. The previously estimated "safe" level of 1.5 $\mu g/cm^2$ was clearly too high, and illness and cholinesterase depression occurred at much lower levels[203].

Cotton weeders: carbofuran. Thirty four workers became ill after entering a cotton field two hours after it had been sprayed with carbofuran. This insecticide has a 48 hour restricted entry interval on cotton, and requires both posting of treated fields and oral notification of workers after application.– neither was done. The crew ranged in age from 13 to 64 years (median 31) . The symptoms most commonly reported were nausea in 97% headache in 94%, eye irritation in 85%, muscle weakness in 82%, tearing in 68%, vomiting in 79%, and salivation (drooling) in 56%. The most commonly observed signs were bradycardia (heart rate less than 60) in 21%, diaphoresis (excess sweating) in 15%, and miosis (small pupils) in 12%.

Twenty-nine workers were released after decontamination and evaluation; one was hospitalized with new-onset atrial fibrillation. Four workers went home, showered, and did not seek medical care until three to 17 days later. Twenty-eight workers (82%) lost at least one day of work.

Plasma and red blood cell cholinesterase samples from 29 workers were all within normal limits but had not been

[c] "Girdling" is done to prevent sugars being transported to vine roots. Workers kneel or squat beneath the canopy of each vine trunk and interrupt the phloem layer of the vine trunk by cutting a 2-4 mm deep and 3 mm wide band around its circumference using a special curved, double-bladed knife designed for the task.

placed on ice after collection. Ten workers who had proper collection of red blood cell samples three hours later were lower than laboratory reference normal values. Urinary metabolites of carbofuran were detected by in 18 (58%) of 31 samples up to 11 days following the exposure.

The California Department of Health investigators concluded that since reliance on control measures may be inadequate, the substitution of safer, less toxic alternative pesticides should be adopted when feasible[204]. The investigator from the Department of Pesticide Regulation Worker Health and Safety branch concluded that the incident could have been prevented with appropriate communication and adherence to existing regulations on restricted entry intervals and field posting[205]

Watermelon Poisoning. On July 4, 1985, the largest outbreak of pesticide related food-borne illness in North America, was traced to the illegal use of aldicarb (Temik) on watermelon by certain farmers in Kern County, California. Of the 1,376 cases reported in California , 77% were classified as being probable or possible aldicarb poisoning. Seventeen people were hospitalized, and two of 47 pregnant women reported subsequent stillbirths, although aldicarb sulfoxide was not found in the fetuses at autopsy. Ten other jurisdictions reported 483 probable or possible cases: Alberta , Canada (20), Alaska (47), Arizona (one), British Columbia (206), Colorado (one), Hawaii (two), Idaho (80), Nevada (four), Oregon (104), and Washington State (18).

The most common signs and symptoms were nausea, vomiting, diarrhea, profuse sweating, excessive tearing, muscle fasciculations, and bradycardia, which occurred within a half an hour or less after eating the watermelon. More severe signs and symptoms included seizures, loss of consciousness, cardiac arrhythmia, hypotension, dehydration, and anaphylaxis. Estimated dose levels of adicarb sulfoxide were 0.0023- 0.06 mg/kg body weight, and most were well below the 0.025 mg/kg LOEL (Lowest Observed Effect Level) for subclinical RBC cholinesterase depression previously reported for humans [206,207,208,209].

Illegal Use of Aldicarb as a Rodenticide. Poisoning and fatalities have resulted from illegal use of aldicarb as a rodenticide, a use for which it is not registered. The cases in the U.S. were from a product called “Tres Pasitos” illegally imported from the Carribean[210,211,212,213].

Fate in the Body. Organophosphates and N-methyl carbamates are rapidly excreted from the body, primarily in the urine. They do not accumulate and are not stored in fatty tissue or breast milk.

Pyrethrum, Pyrethrins, Synthetic Pyrethroids

Pyrethrum and pyrethrins are natural compounds derived from a tropical chrysanthemum flower. Pyrethrum is made from the petals, and pyrethrins are chemicals extracted from the flower with solvents. Pyrethroids are man-made synthetic chemical analogues of pyrethrins.

Most are not highly acutely toxic and are unlikely to cause serious work related poisoning, since they are readily metabolized and excreted from the body.

It is not correct that only the natural plant based products are allergenic and not the synthetic pyrethroids. While it is true that the flower based natural products contain allergens that cross-react with ragweed and other pollens – both the natural and synthetic forms can cause allergies The group most at risk from exposure to this class of compounds are asthmatics.(see Table 5).

Pyrethrum, Pyrethrins and Synthetic Pyrethroids

Natural Compounds

Pyrethrum
Pyrethrins

Type I Synthetic Pyrethroids

Allethrin	Cyfluthrin
Bioallethrin	Permethrin
Bioresmethrin	Resmethrin
Biopermethrin	Tetramethrin
Cismethrin	

Type 2 Synthetic Pyrethroids

Cypermethrin	Fenothrin
Cyphenothrin	Flucythrinate
Deltamethrin,	Fluvalinate
Fenvalerate	Tralomethrin

Allergic rhinitis reactions to pyrethrum are frequent [214,215,216,217,218] .
Hypersensitivity pneumonitis was reported in a woman who used two and a half cans of pyrethrum-based insecticide in her home every week. She was hospitalized with fatigue, chest pain, coughing, and shortness of breath; a lung biopsy showed interstitial fibrosis. She recovered fully after supportive treatment, and remained asymptomatic after

discontinuing use of the insect spray. A pulmonary challenge test with the insecticide gave positive results, and a skin test with pyrethrum alone was positive[219].

A study of workers formulating pyrethrum powder found 30% had erythema, skin roughening, and pruritus, which subsided on cessation of exposure. One worker developed facial reddening, burning and itching, with rapid development of periorbital edema, and severe pruritus , which disappeared two days after removal from exposure[220].

Pyrethrins

Pyrethrins are in many over-the-counter products, especially aerosol sprays. A 24 year old man sprayed his dog and the floor of his bedroom with pyrethrin flea spray with no ventilation, rubbing the spray into the dog's fur with ungloved hands. Within an hour he developed shortness of breath, abdominal cramping, and vomiting. In the emergency room, his symptoms abated within two hours except for fatigue[221]. No information was reported about the dog. See section on asthma below for effects of pyrethrin shampoos.

Synthetic Pyrethroids

The synthetic pyrethroids are sodium channel toxins. They are divided into two groups depending on whether they have a cyano group (CN). The cyano group (CN) Type I pyrethroids are more toxic than the Type II without this group (see box). Animal studies show that Type I pyrethroids produce reflex hyperexcitability and fine tremor. Type II pyrethroids produce salivation, hyperexcitability, horeoathetosis, and seizures. Both types are potent activators of the sympathetic nervous system.

For commercial pesticides, the type II pyrethroids are more potent and more toxic than Type I. If type II poisoning advances to central hyper excitation, seizures can be difficult to control. Pyrethroids are also toxic to the nervous system, but are not cholinesterase inhibitors. The cyano groups pyrethroids are also more likely to cause the characteristic paraesthesia and dysesthesias (skin sensations of stinging, tingling itching, and numbness), lasting.18 to 24 hours and thought to be due to effects on from contact with sensory nerve endings[157]. Pyrethroids are readily metabolized and excreted, primarily in the urine. There are no biomarkers of exposure as there are for the organophosphates and N-methyl carbamates.

Table 5
Acute Pyrethroid Poisoning Signs and Symptoms

Dizziness	60.6%;
Headache	44.5 %
Nausea	59.7 %
Anorexia	45 %
Fatigue	26%
Vomiting	16%
Chest tightness	13.1 %
Parasthesia	11.89 %
Palpitation	13.1 %
Blurred vision	7 %
Increased sweating	6.% .

Source: Reference 193

A study of volunteers found significant differences in cyfluthrin metabolism in pesticide applicators. Those with a slower rate of metabolism had more symptoms from exposure than those with a faster rate of metabolism and excretion[222].

Hypersensitivity and allergic reactions are less common with the synthetic pyrethroids than with pyrethrum and the pyrethrins, but they do occur. A farmer using flumethrine as a sheep deep without using protective clothing developed abdominal pain, vomiting, fatigue, muscle aches, and polyarthralgia. Immunological testing revealed increased levels of IgE[223].

Nursery workers had imitative symptoms of the skin and upper respiratory tract in 73% of those exposed to fenvalerate, in 63% to permethrin (trans/cis 75/25) and in 33% for permethrin (trans/cis 60/40)[224].

Pyrethroid insecticides were found to be only very light cutaneous irritants or sensitizers in 82 workers patch tested with 1, 2, or 5% allethrin, cypermethrin, deltamethrin, fenothrin, fenvalerate, permethrin, and resmethrin. Two non-atopic workers had an irritant reaction to resmethrin. Of the two with allergic reactions to fenvalerate, one was a farmer with chronic hand dermatitis, and the other a hobby gardener[104].

A 59-year-old man who drank 600 ml of 20% permethrin developed vomiting and diarrhea soon after ingestion. in a suicide attempt. No clinical neurotoxicity such as tremor, hyper excitation, ataxia, convulsions, or paralysis occurred,

and he recovered with supportive treatment[225].

Pyrethroid fatality: Cypermethrin was the first pyrethroid reported to cause a human fatality. In Greece a man died three hours after eating a meal cooked in a 10% cypermethrin concentrate mistakenly used instead of oil. Nausea, prolonged vomiting with colicky pain, tenesmus, and diarrhea began within a few minutes, progressing to convulsions, unconsciousness, and coma. Death due to respiratory failure occurred despite intensive emergency treatment. Other family members developed less severe symptoms and survived[226].

Most of what we know about acute occupation poisoning from pyrethroids comes from a study of 292 Chinese farmers spraying deltamethrin, cypermethrin, and fenvalerate. Handling and hygienic practices were very poor, including use of higher concentrations than allowed, spraying for longer periods of time than recommended, clearing stoppages of equipment with mouth and hands, and not wearing personal protective equipment. Coarse muscular fasciculations developed in large muscles of extremities in the more serious cases. In those suffering from convulsions, seizures could occur up to 30 times a day in the first week. Most fully recovered in about six weeks[227].

Chlordimeform hemorrhagic cystitis
Severe illness occurred over a three day period in 1975 among nine workers packaging the cotton insecticide chlordimeform (Galecron) in a shed separate from other workers. They developed abdominal pain, dysuria, urgency to void, and hematuria (blood in the urine). Bladder biopsy specimens showed severe hemorrhagic cystitis. Three days after exposure, chlordimeform and 2-methyl-4-chloroaniline, a metabolite of chlordimeform, were present in the urine. The illness lasted from one week to two months[228].

Chlordimeform is readily absorbed through the skin of pesticide applicators. A study of urinary metabolites of 132 cotton applicators and handlers in California , found that despite the use of protective clothing and closed system transfer devices, chlordimeform metabolites were excreted in the urine. Mixer/loaders and equipment cleaning and maintenance workers had the greatest exposure [229]. Because of the adverse health effects seen in heavily exposed worker, cancerous tumors seen in mice, and the inability to protect workers from the risk of bladder cancer, chlordimeform was banned and the registrant voluntarily withdrew the registration in 1989[230,231.]

Deet Insect Repellent (N,N-diethyl-m-toluamide, OFF!)
Deet use in the U.S. is estimated to be about 200,000 applications per year[232]. Deet is more rapidly absorbed if the skin is sunburned, damaged, or irritated skin. It is excreted mostly in the urine, and does not accumulate in the body. Deet does cross the placenta; a study of 50 pregnant women who applied deet found the chemical in the cord blood of 8% of newborns[233]. There no specific antidote to poisoning. Treatment includes decontamination (removing contaminated clothing, washing the pesticide from the skin and hair, pumping it out of the stomach, if swallowed), seizure control, treatment of signs and symptoms, and support of respiration, blood pressure, and other body systems. There are no readily available blood or urine tests. See Chapter 7 for effects in children

Deet is a neurotoxin and toxic encephalopathy with seizures have been reported. Signs and symptoms of mild poisoning include headache, restlessness, irritability, and other changes in behavior. In more severe poisoning there can be slurring of speech, tremor (shakiness), convulsions, and coma. A 29-yr-old male suffered seizures eight to forty-eight hours following daily application to the skin daily from June through August[234], and a healthy adult male after topical application[235]. Neurologic signs and symptoms, including muscle cramping, insomnia, irritability, depression, and episodes of confusion were reported by National Park Service workers after exposure to 4 grams or more of deet per week [236]. Poisoning due to accidental or deliberate ingestion in 5 patients, aged one to 33, with two deaths[237]. Three cases following ingestion with complete recovery in all cases[238]

Cardiotoxicity has been reported in cases of severe poisoning in an adult male[239] , and in a 19 year old girl who attempted suicide by drinking 15-25 mls of a 95% formulation[240]. A study of 20,764 calls to poison control centers from 1993 to 1997 for exposures involving deet, in nearly 70% there were no exposure related symptoms. The highest rates of symptoms related to the eyes. There were two deaths, one in a 26-year-old male, and one in a 34-year-old female, both following skin application. Twenty-six reports involved major effects (0.13%). Although there were more reports involving infants and children, they had lower rates of adverse effects than teens or adults[241]

Fumigants

Fumigants are powerful poisons in the form of a gas that can severely injure any tissue they come into contact with. A review of 1,192 definite, probable, or possible cases of pesticide-related illnesses by the Washington State Department of Health from 1992-1996, found 39 cases related to fumigants (3.3%). The exposures were to aluminum phosphide (15), methyl bromide (12), metam-sodium (9), and zinc phosphide (3). Symptoms included respiratory problems and eye and/or skin irritation for the majority of exposures. No deaths were reported. The exposures were to applicators (17), reentry into a fumigated structure (9), improper storage or disposal (6), reentry into treated agricultural fields (4), drift from treated fields (2), and other (1).

Fumigants

Available Over-the-Counter

Dichlorvos (Pest Strips)
Metam-sodium (Vapam)
Paradichlorobenzene (mothballs)
Naphthalene (mothflakes)

Commercial Use Only

Aluminum phosphide (Phosphine)
Chloropicrin
1,3-Dichloropropene (Telone)
Methyl bromide
Sulfuryl fluoride (Vikane)

Methyl bromide. Methyl bromide can cause severe chemical burns which cannot be prevented by standard protective clothing[242]. A crew of six workers fumigating a 13th century castle developed erythematous skin with multiple vesicles and large bullae within 8 hours of exposure, primarily in the axillae, groin, vulva, scrotum, perineum, and umbilicus. The skin returned to normal in four weeks, except for some residual hyperpigmentation[243]. Severe poisoning has been reported in applicators not wearing adequate footwear[121].

Farm workers developed fatigue and light-headedness, respiratory, and gastrointestinal symptoms after removing polyethylene sheets from soil fumigated with methyl bromide four days earlier. Their symptoms resolved over several days, but neuropsychiatric symptoms persisted for several weeks.[244]. Workers fumigating crops for export experienced insomnia, headache, paresthesias, mood changes and loss of memory and concentration[245]. Toxic encephalopathy, toxic myoclonus[246,247,248, 249,250,251], and permanent neurological sequelae[252, 253,254] have been reported in survivors of acute methyl bromide poisoning[255].

Methyl bromide fatalities: There are many methyl bromide fatalities reported in the literature: a grain fumigation worker[256], a 19 year old pancake house manager who re-entered the restaurant too soon after it was fumigated[257], a 12 year old and a 23 year old who entered fumigated railroad cars[258], and four burglars who entered tented fumigated houses[259].

An unusual incident was the death of a young woman from methyl bromide seeping through underground conduits from a fumigated building to an adjacent guest house on the same property. She developed refractory seizures, intermittent fever, and multi-organ system failure before dying 19 days later[260]. A similar sad case was the death of a newborn baby 12 hours after a neighbor's house was fumigated. The sewage pipes serving the two houses had been sucked empty only one to two hours prior to the start of fumigation, resulting in an open sewage connection between the houses and permitting methyl bromide to leak from the treated house into the house of the affected family[261].

Victims of methyl bromide poisoning have a higher amount of inorganic bromide in their blood than the usual background level[262]. There are no specific biomarkers, and blood and urine tests are not readily available.

Sulfuryl fluoride (Vikane). Sulfuryl fluoride's primary use is in termite control, and agricultural is not a significant user. There are very few reports of non-fatal poisoning in humans even though it is a highly toxic gas.

A 30 year old man developed nausea, vomiting, abdominal cramping, pruritis, reddening of the conjunctivae, pharynx and nasal mucosa, and pin-prick anesthesia of the lateral border of one leg. after four hours exposure to sulfuryl fluoride in an unventilated room. He recovered in four days with supportive treatment[263].

An elderly couple was allowed to re-enter their home that had been fumigated with sulfuryl fluoride the day before, five hours after ventilation procedures were completed. Within 24 hours of their return, the wife developed weakness, nausea, and repeated vomiting. Her husband complained of restlessness, and dyspnea (difficulty breathing) which became progressively worse. The next morning he had a generalized seizure followed by

cardiopulmonary arrest, and died in the emergency room where he could not be resuscitated. Three days later his widow went to see her family doctor, complaining of severe weakness, dyspnea, intermittent chills, and anorexia; she was unable to walk into office. She was admitted to the hospital where a chest x-ray showed diffuse pulmonary infiltrates. She developed ventricular fibrillation and died the next day.

It was later determined that the pest control operator failed to measure the air concentration of gas inside the home before allowing the couple to return. Neither of the two workers who removed the tarpaulin and ventilated the house was licensed; they were working under the supervision of a certified supervisor who was not on the premises as the law required. Because the product used in the home was manufactured before the requirement for a certified applicator to be on the premises was made law, the statement for this requirement was not on the label (most regulations changes have a clause that allows the use of "existing stock"). Since "the label is the law' technically there was no violation of the law[264]

Herbicides

Herbicides kill plants by affecting chemical reactions and metabolic pathways that don't exist in human beings. Plant growth regulators (PGR) act like plant hormones and slow down or speed up growth. Many herbicides and PGRs can cause irritant effects in the eyes, skin, nose and throat. Some can also cause allergic reactions in sensitive individuals. In general, they are not highly toxic and are unlikely to cause serious poisoning under usual conditions of exposure with the great exception of paraquat.

Herbicides

Available Over-the-Counter

Aciflurofen (Goal)	Glyphosate (Roundup)
Atrazine	MCPA
Benefin	MCPP
2,4-D (Weed-b-Gon)	MSMA
2,4-DP	Napropamide (Devrinol)
DCPA (Dacthal)	Oryzalin (Surflan)
Dalapon	Sodium chlorate
Dicamba	Prometon
Diquat,	Trichlopyr
EPTC	Trifluralin (Treflan)
Fluazifop-butyl (Fusilade)	

Commercial Use

Bromacil (Hyvar)	Metolachlor
Bromethalin	Oxadiazon (Ronstar)
Cacodylic acid (organic arsenic)	Paraquat (Gramoxone)
Chlormequat	Pronamide (Kerb)
Chlorsulfuron (Telar, Glean)	Simazine
Dichlobenil (Casaron)	Sulfometuron-methyl (Oust)
Duron	Ttrifluralin (Treflan)

Paraquat (Gramoxone) is the most common cause of fatal herbicide poisoning, mostly through oral ingestion. It can be lethal in very small amounts when swallowed and is the pesticide most often used for suicide throughout the world[265,266,267,268,269,270,271,272,273,274]. Occupational fatalities have occurred in farmers and in a landscape maintenance worker from absorption through the skin[275,276,277,278,279]. Systemic poisoning could occur if a concentrated form gets in the eyes or on the skin, or if it is swallowed[280].

Any exposure to paraquat must be evaluated, even if several days have passed since the herbicide was ingested. Signs of lung deterioration is often a sign of impending fatality.

Despite animal toxicity similar to paraquat, diquat does not cause similar lung effects in human poisonings, and reported deaths have been from other causes. Poisoned patients who receive appropriate and timely treatment are virtually assured of complete recovery from most insecticide and herbicide poisonings.

Plant Growth Regulators

Daminozide (B-nine, Alar
Dikegulac sodium (Atrinal)
Ethephon (Ethrel)
Gibberellic acid
Maleic hydrazide
Mefluidide (Embark)
Naphthyleneacetic acid (NAA).

Deaths and long-term sequelae most often result from respiratory complications, which may occur as complications of the intoxication or from other constituents in the insecticide or herbicide formulation. Good supportive care with meticulous attention to, and anticipation of, respiratory complications is absolutely essential to prevent long-term squelae or death from hypoxia.

There is no specific antidote to poisoning. Treatment includes decontamination (removing contaminated clothing, washing the pesticide from the skin and hair, pumping it out of the stomach, if swallowed), treatment of signs and symptoms, and support of respiration, blood pressure, and other body systems.

Most herbicides are excreted into the urine within one to four days after exposure. They do not accumulate in the

body. There are no readily available blood or urine tests.

A problem with herbicide products is a false sense of security. Because in general they are not acutely toxic and do not cause immediate apparent illness, they are considered "safe". A concern with this group of chemicals is their chronic toxicity discussed in Chapters 5 and 7.

Fungicides

Fungi do not share any attributes with human beings; therefore, fungicides tend to have low acute toxicity for humans. Many are eye and skin irritants, and can cause skin rashes. As a group they are the most likely to cause allergic skin reactions, and can sensitize the skin at low levels (see Tables 1,2 and 5.

Fungicides

Aliette (Fosetyl-al)	Mancozeb
Anilazine (Dyrene)	Maneb
Benomyl (Benlate)	Metalaxyl (Ridomil
Captan	Oxycarboxin (Plantvax)
Chlorothalonil (Daconil,	PCNB
Bravo)	Piperalin (Pipron)
Copper compounds	Sulfur/lime sulfur
Dazomet (Basamid)	Thiabendazole
Dicloran (DCNA)	Thiophanate-methy
Fenarimol (Rubigan)	Thiram
Fenbutatin oxide	Triadimefon (Bayleton)
(Hexakis,Vendex)	Triforine (Funginex).
Iprodione	Vinclozolin (Ronilan).
Lime sulfur	

Because of their low acute toxicity, fungicides are unlikely to cause serious poisoning. Of the examples listed, thiram can cause an unusual reaction. It is chemically similar to antabuse, a pill taken by alcoholics who are trying to quit. If they drink while taking the pill they get nausea, vomiting, pounding headache, dizziness, difficulty breathing, abdominal pain, and profuse sweating, among other symptoms. The same problem is possible with thiram if used while drinking alcohol, but has only been reported in workers[281].

Most fungicides are poorly absorbed and excreted primarily in the urine; they do not accumulate in the body. There are no readily available blood and urine tests.

As with most herbicides, a problem with many fungicides is a false sense of security. Because they are not acutely toxic and do not cause immediate apparent illness they are considered to be "safe." The greater concern with this group of chemicals is their chronic toxicity which is discussed in Chapter 5.

Rodenticides

The anticoagulant rodenticides are blood thinners and cause internal bleeding. The aluminum, magnesium, and zinc phosphide fumigants form phosphine gas on contact with moisture in the air, which is a potent tissue toxin. Strychnine (a natural toxin also known as nux vomica) violently attacks the nervous system.

Rodenticides

Anticoagulants

Brodifacoum
Bomadiolone
Clorophacinone
Diphacinone
Pindone (Pival, Pivalyn).
Warfarin

Fumigants

Aluminum phosphide (Phostoxin)
Magnesium phosphide
Zinc phosphide

Botanical

Strychnine

The anticoagulants and strychnine are in the form of baits, in which the greatest risk of poisoning is from ingestion (swallowing). The anticoagulants can cause nosebleeds, bruises, and blood in the urine and stool depending on the amount ingested. If large amounts are swallowed it can be fatal.

Strychnine causes violent seizures (convulsions) which can cause asphyxiation and death. Phosphine gas released from zinc and magnesium phosphide causes severe irritation of the lungs. If the dose is high enough it can cause pulmonary edema (fluid in the lungs) which can be fatal.

Vitamin K_1 is the antidote to poisoning from anticoagulants rodenticides. There is no antidote to strychnine. Treatment includes seizure control, support of respiration, and kidney dialysis if needed. There is no antidote to phosphine. Management includes treatment of signs and symptoms, and support of respiration, blood pressure, and other body systems.

Except for the fumigants, most are poorly absorbed into the body and excreted primarily in the urine. They do not accumulate. The anticoagulants affect a clotting factor in the blood called prothrombin. The prothrombin time test determines when the clotting ability of the blood is back to normal. There are no readily available blood or urine

tests for strychnine or phosphine.

Chlorinated Hydrocarbons
DDT and related chemicals are no longer widely used in pest control, and many have been banned. Of those still on the market, endosulfan is the most toxic. Lindane is still available by prescription for headlice. The hallmark of poisoning with the chlorinated hydrocarbon pesticides is seizures (convulsions), which can occur without other symptoms. Milder poisoning is characterized by headache, dizziness, nausea, vomiting, incoordination, tremor, mental confusion, and jerky muscle movements (myoclonus).There is no specific antidote and treatment include removing contaminated clothing, washing the pesticide from the skin and hair, pumping it out of the stomach, if swallowed, seizure control, and support of respiration, and other body systems.

Most are readily absorbed through the skin and excreted in the urine and feces. Those in current use (see list above) are not stored in the body for any length of time, except for lindane metabolites α-HCH, and β-HCH. Dicofol is contaminated with DDT which does accumulate and stays in the body for many years. primarily in fat.

Detectable in the blood, but is not a routine test. Analysis is not necessary for treatment of poisoning and tests are done in most toxicology laboratories. Except for lindane, it is unlikely that residues will be found if the exposure occurred a week or more prior to the test, unless there were unusual exposure conditions.

Chlorinated Hydrocabon Insecticides

Still in Use in the U. S.

Dicofol (Kelthane)	Lindane
Dienochlor	Methoxychlor
Endosulfan	

No Longer Registered in the U.S.

BHC	Emdrin
Chlordane	Hexachlorobenzene
Chlorobenzilate	Kepone
DDT	Mirex
Dieldrin	Toxaphene

DDE, a metabolite of DDT is the most commonly found, but dieldrin, chlordane (transnonachlor), and hexachlorobenze are found in blood, fat, breast milk, and other body tissues. Chlorinated hydrocarbons pass from mother to fetus across the placenta, and are also found in semen and ovarian follicular fluid (see Chapter 6).

Inert Ingredients
Petroleum distillates, toluene, xylene, alcohols, glycols, ethers, and other solvents are added to pesticides to dissolve, emulsify, or stabilize them, or to facilitate spreading, sticking, and penetration of the pesticide. Many cause irritation of the eyes, mucus membranes and skin.

The greatest hazard is chemical pneumonia (also called hydrocarbon pneumonitis) from aspiration of even tiny amounts into the lungs. This can occur if the victim vomits, vomiting is induced or the stomach is pumped. Signs and symptoms of chemical pneumonia are fever, rapid heart beat, rapid breathing, and cyanosis (turns blue). This type of pneumonia can be fatal, and recovery can take several weeks.

Many inerts are chlorinated hydrocarbons that can cause damage to the liver, heart, and kidneys if swallowed. There is no specific antidote to poisoning. The standard tests should be done to determine if there is damage to the liver, heart, or kidneys.

Natural Substances
Abamectin is an antibiotic with a narrow spectrum of activity. Bacillus thuringiensis (BT) is a bacterium with exotoxins toxic to insects. These agents have a narrow spectrum of activity. That is, their toxicity is specific to the particular target pest they are being used against. They are the least likely to pose a human health hazard. However any product can potentially be an irritant or cause local skin reactions, or other acute reactions.

Diatomaceous earth is made from diatoms (fossils), and like **silica gel** kills insects by drying out the waxy coating on the insects' protective outer cover, called the cuticle. The diatomaceous earth registered for use as a pesticide is *not*

Natural Substances Used as Pesticides

Available Over-the-Counter
Arsenic
Avermectin / abamectin / ivermectin
Bacillus thuringiensis (Bt)
Boric acid
Diatomaceous earth
Neem (azadirachtin)
Silica gel (silicon dioxide

Commercial Use Only
Liquid nitrogen.
Nicotine (Black Leaf 40)

the same product as that used as a filtering agent in swimming pools. The swimming pool product is higher in free silica, the crystalline form that can cause scarring of the lungs (silicosis).

Neem is a tree oil from India that kills insects by unknown mechanisms.

Boric acid is a tissue and stomach poison if swallowed. Boric acid powders are not absorbed through the skin but can be mildly irritating (including borax). Any pesticide product can potentially cause skin irritation or rash in some individuals. Acute poisoning results from swallowing) the pesticide. If only a small amount is swallowed there may be no symptoms. Vomiting, abdominal pain, and diarrhea are common symptoms when they do occur. Boric acid is poorly absorbed through the skin and is excreted in the urine in about 24 hours. Borates (from boric acid) can be measured in the blood, serum, and urine.

Arsenic acts as a tissue poison by combining with sulfur and phosphate in proteins and enzymes, interfering with their normal function. Arsenic causes skin problems, but it is unlikely from home use. Acute poisoning results from swallowing the pesticide. The breath and feces can smell like garlic. There is abdominal pain, and watery diarrhea that might have blood in it. The nervous system, heart, liver, kidneys, and bone marrow can also be affected. BAL (dimercaprol) is an antidote to arsenic poisoning; D-penicillamine is another antidote that can be used if the victim is not allergic to penicillin. Arsenic is also excreted in the urine.

Nitrogen is a gas (78% of the air we breathe) which freezes when compressed into a liquid. It kills termites and other wood destroying insects by freezing them to death. An exterminator applying liquid nitrogen died from suffocation while working in an enclosed wall space without any ventilation. There is no danger to the home owner when the gas dissipates since it is a normal part of the air we breathe.

Nicotine is the most acutely toxic of the natural group of pesticides. It attacks the brain, nervous system, and nerve-muscle connections, but does not affect cholinesterase activity. The signs and symptoms of mild to moderate nicotine poisoning are very similar to those from nerve-gas type pesticides – excess salivation (drooling), nausea, vomiting, and miosis (small pupils). Severe poisoning results in muscle paralysis, shock (collapse of the heart and vascular system with drastic lowering of blood pressure), and respiratory paralysis. There is no specific antidote to nicotine poisoning, but atropine can control the excess secretions. Treatment in all cases includes decontamination (removing contaminated clothing, washing the pesticide from skin and hair, inducing vomiting or pumping the stomach if swallowed, treatment of signs and symptoms, and support of respiration, blood pressure, and other body systems. Nicotine is readily absorbed and is transformed by the liver into several simpler chemicals (metabolites) which are excreted into the urine within a few hours. Cotinine is the major metabolite in urine.

Pesticides and Asthma

Asthma is the most frequently diagnosed occupational lung disease, and typically signs and symptoms worsen on work days and improve on days off and holidays. Occupational asthma is also less frequently related to seasonal variations, exacerbation by allergies, pets and stress, or a family history of the disease[282]. Exposure to pesticides can trigger or exacerbate asthma, induce bronchospasm, or increase bronchial hyperreactivity. See Chapter 7 for a discussion of asthma in children related to pesticide exposure.

Table 5
Pesticides Linked to Asthma, Wheezing, and Hyperreactive Airway Disease

Antimicrobials
Bromine, hydrobromic acid
Chloramine-T
Chloramines
Chlorine
Quarternary ammonium
Fumigants
Ethylene oxide
Metam-sodium
Fungicides
Captafol
Chlorothalonil
Dithiocarbamates
Fluazinam
Tributyltin oxide
Inerts
Denatonium benzoate
Herbicides
Alachlor
Atrazine
EPTC
Paraquat
Insecticides
Carbofuran
Chlorpyrifos
Dichlorvo
Ethoprop
Insecticide aerosols
Insecticide coils
Malathion
Paraquat
Pyrethrins
Pyrethrum
Tetramethrin

Asthma and Occupational Exposure

Agricultural Exposures: Use of paraquat, parathion, chlorpyrifos, atrazine and alachlor were found to be related to wheezing in 3,889 farmer applicators. A significant dose response trend was found. Malathion and EPTC were also associated with wheeze, but did not show a dose response trend. There was no association with 2,4-D use[283].

A male Japanese farmer with recurrent episodes of dyspnea and wheezing for 10 years was found to have chlorothalonil induced asthma. Patch testing showed a positive but a specific IgE antibody twas not found. Entering a treated greenhouse produced dyspnea, wheezing, and a sharp drop in pulmonary function (FEV1). Bronchial challenge with 0.1% TCPN induced an early and late asthmatic response that lasted 48 hours[284].

Insecticide and fertilizer use in several villages in rural China was found to increase the risk of asthma-like symptoms[285].

Paraquat applicators on 15 Nicaraguan banana plantations with more than two years cumulative exposure had a three fold increase in episodic wheezing compared to workers who had never applied paraquat. Shortness of breath also occurred among the more intensely exposed workers. There was no relationship between exposure and pulmonary function findings[148]. A case report of asthma related to paraquat was reported from Italy[76].

A review of cases reported to the California Pesticide Illness Surveillance Program raised concerns of asthma potentially associated with exposure to contaminants in organophosphate insecticides[286].

A worker with contact sensitivity to captafol (Difolatan) was skin test positive, but his asthma was not exacerbated by exposure to the pesticide[57].

Aerial pesticide applicators had no difference in asthma prevalence compared to controls[287].

Pesticide Factory workers: No differences were found in bronchial hyperreactivity between factory workers exposed to pesticide dusts and controls[288]. After several years of exposure to captafol, a pesticide manufacturing worker had new onset of work-related asthma. He had a marked and persistent decrease in pulmonary function (FEV1) upon bronchial challenge with captafol. Removal from exposure resulted in improved symptoms and pulmonary function[289]. A report of two cases of occupational asthma in workers from the same pesticide plant, caused by sensitization to powdered fungicides fluazinam and chlorothaloni. The diagnosis in each case was confirmed by pulmonary function testing and bronchial challenge tests.[290].

Pest Control Operators: Six years after beginning work as a pest control operator, a 47 year old man developed asthma. He was forced to quit his job one year later. Challenge testing showed positive reaction to tetramethrin, which also caused a 30% drop in FEV1[291] . In one of the few studies to report mortality from asthma, outdoor workers exposed to pesticides in Australia were found to be at increased risk, SMR 3.45 (1.39-7.1)[292]

Other workers: Female nurses manifested asthma symptoms upon handling disinfectant solutions containing benzalkonium chloride. They had work related decreased pulmonary function, and positive response to bronchial challenge[293].

A cook who worked an eight hour shift in a closed room that had been treated the day before with dichlorvos, presented with progressive respiratory symptoms and wheezing eight days after the exposure. A decrease in serum cholinesterase activity was noted. Decreased pulmonary function was still present 20 days later. He developed severe cortisol dependent asthma cortisol treatment and one year was still unable to participate in sports[294].

Two women packaging Chloramine T dust developed bronchial asthma after several years exposure, and a male welder/equipment repair worker developed progressively severe dyspnea and wheezing with repeated exposure to Chloramine T dust equipment and containers. All three had s chloramine-T specific IgE antibodies in their serum and skin prick test reactions of greater than 2+[295]. A woman developed sneezing, coughing and dyspnea shortly after being use of a new disinfectant, chloramine-T, at work cleaning showers and saunas at a municipal indoor swimming

pool. She developed rhinorrhea, coughing, dyspnea and bronchial wheezing after provocation with 2 ug of the chemical[296]. Seven brewery workers developed asthmatic symptoms from exposure to chloramine disinfectant which resolved with removal from exposure. Skin tests produced a weak positive flare reaction[297].

A case report of a railway station repair worker who was exposed to high levels of ethylene-oxide (over 700 ppm) from a leak, developed coughing, shortness of breath, and wheezing after four days exposure. Three years later he had not change in his clinical respiratory state and pulmonary function[298]. Other reports in health care worker were in a nurse[299], and a surgeon induced by ethylene-oxide used to sterilize gloves[300].

A report of three cases of asthma caused by inert ingredient ethanolamine, confirmed by challenge testing Two were metal workers exposed to a cutting fluid containing triethanolamine, and the other a cleaner exposed to a detergent containing monoethanolamine. Persistence of the symptoms after exposure ended was a common feature of the three cases[301].

A previously healthy female venipuncture technician developed acute retrosternal chest pain, nausea, and lethargy within a few hours of arriving at work. The symptoms cleared when she took two days off, but recurred along with chest tightness, cough, and wheeze when she returned to work. Thirty six hours before her first episode, the carpet in her workplace, which had been flooded, was treated with a deodorizer /fungicide preparation that contained tributyltin oxide TBTO). Bronchial challenge testing with TBTO caused a 19% decrease in FEV1 within 1 hour. The asthma continued to recur at work and she quit her job[302].

Decreased risk: European animal farmers 20 to 44 years old in Denmark, Germany, Switzerland, and Spain were found to have a lower prevalence of wheezing, shortness of breath, and asthma than the general population[303].

Asthma - Nonoccupational and Household Exposure

Pyrethrins: A 43-yr-old woman with a history of asthma and ragweed allergy, experienced an anaphylactic reaction after using a pyrethrin lice shampoo. Periorbital edema appeared within an hour; the next morning, she developed shortness of breath, chest tightness, numbness and became unresponsive. She responded to treatment with naloxone, epinephrine, aminophylline, albuterol, methyl-prednisolone and prednisone[304].

Pyrethrin fatalities: A 36 yr old woman with a history of asthma developed severe shortness of breath five minutes after she began washing her dog with a 0.05% pyrethrin shampoo. Within five minutes she was in cardiopulmonary arrest and could not be resuscitated[305]. Another fatality from exposure to a pyrethrin insecticide was attributed to sudden irreversible bronchospasm[306]

A study of seven patients with asthma from exposure to a household aerosol insecticide spray found bronchial challenge with the insecticide produced chest tightness and a decrease in pulmonary function, but no changes in bronchial reactivity to inhaled histamine.[307]. A study of standard and low irritant insecticide formulations found that some aerosols trigger symptoms and impair lung function in asthmatics[308].

Household use: The use of mosquito coils inside the home was associated with an higher prevalence of asthma in a study in Durban, South Africa[309]. A survey in Hawaii found that those using household insecticides daily were 40% more likely to have asthma than nonusers[310]

Hot Tub: Two cases of acute pneumonitis followed by reactive airways dysfunction syndrome developed after bathing in a hot tub. A bromine disinfectant which releases hydrobromic acid was implicated as the underlying cause[311].

Dentamonium: A 30 yr old male developed asthma and pruritus after using an insecticidal spray (Pyrex). The same symptoms appeared with an alcoholic skin disinfectant (M-sprit) and other spirituous preparations denatured with denatonium benzoate (Bitrex). An open epicutaneous test (20 min) showed wheal and erythema to Pyrex, spirit and Bitrex diluted to 26 mg/l. The contact urticaria elicited by denatonium benzoate apparently was caused by an immunologic mechanism of the immediate hypersensitivity type[312].

Asthma and Environmental Exposure

Community residents near a potato field treated with Ethoprop which releases n-propyl mercaptan, a highly odorous and volatile gas as a degradation product, were surveyed for odor-related illness. An increase in asthma attacks (six week prevalence OR 6.0) was found[14].

A follow up study after a tank car spill of metam-sodium released methyisothiocyanate gas to surrounding communities. Follow-up studies found 20 cases of persistent irritant-induced asthma and 10 cases of persistent exacerbation of asthma[313].

Asthma and Swimming Pools

A study in New Zealand of communities near aerial spraying with Foray 48B(Bt), and follow up three months later in the same participants, found no increase in symptoms in previously diagnosed asthmatics.[314].

Chlorine reacts with bodily proteins to form chloramines, of which the most volatile and prevalent in the air above swimming pools is nitrogen trichloride. A study in lifeguards and a swimming instructor with asthma, showed a positive specific challenge to nitrogen trichloride at 0.5 mg/m^3, with negative challenges to chlorine released from sodium hypochlorite. Swimming-pool asthma due to airborne nitrogen trichloride can occur in workers who do not enter the water because of this chloramine in the air[315,316] A study of swimming pool lifeguards nitrogen trichloride could not rule out risk of exposure related transient bronchial hyperresponsiveness[317].

Significant ly higher bronchial response to histamine challenge was found in members of the Finnish swim team (48%) than controls (16%). Sputum eosinophilia was found in 21% of the swimmers and none of the controls. The authors conclude that long-term and repeated exposure to chlorine compounds in swimming pools during training and competition may contribute to bronchial hyperresponsiveness and airway inflammation in swimmers[318].

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