CHAPTER 1

Introduction

The purpose of this manual is to provide healthcare professionals with current consensus recommendations for treating patients with pesticide-related illnesses or injuries. The Office of Pesticide Programs of the U.S. Environmental Protection Agency has sponsored the series since 1973. The 5th edition of this manual was published in 1999; since then, much has changed with regard to the pesticide products on the market. Most indoor uses of organophosphates have been eliminated, and a combination of EPA risk mitigation actions has limited their use on food crops. Pyrethroids have largely replaced organophosphates for residential pest control. While this conversion is beneficial in that the risk to human health is lower with this relatively less acutely toxic class of pesticide, it introduces a new set of health issues for consideration. Many new pesticide products have been registered and are not necessarily widely known among health professionals. This 6th edition includes a chapter that explores potential association between low-level exposure to pesticides over time and chronic diseases.

Treatments for pesticide exposure carry health risks of their own.

There is general agreement that *prevention* of pesticide poisoning remains a much surer path to safety and health than reliance on treatment. In addition to the inherent toxicity of pesticides, none of the medical procedures or drugs used in treating poisonings is risk free. In fact, many antidotes are toxic in their own right, and such apparently simple procedures as gastric intubation involve substantial risk. The clinician must weigh the hazards of various courses of action (including no treatment at all) against the risks of various interventions, such as gastric emptying, catharsis, administration of intravenous fluids or administration of an antidote, if available. Clinical management decisions have to be made promptly and, as often as not, on the basis of limited scientific and medical information. The complex circumstances of human poisonings rarely allow for precise comparisons of alternative management strategies. Therefore, it is important for the reader to keep in mind that the treatment recommendations in this book do not guarantee successful outcomes. They are merely consensus judgments of the best available clinical management options. Clinical toxicology is a dynamic field of medicine; new treatment methods are developed regularly, and the effectiveness of old as well as new modalities is subject to constant critical review.

Key Principles

General methods of managing pesticide poisonings are presented in **Chapter 3** and reflect a broad base of clinical experience. Several key points deserve emphasis. The need to protect the airway from aspiration of vomitus cannot be overstated. Death has resulted from aspiration, even following ingestion of substances having relatively low toxic potential. In poisonings by agents that depress central nervous system functions or cause convulsions, airway protection by early placement of a cuffed endotracheal tube (even when this requires light general anesthesia) may be life saving. Maintenance of adequate pulmonary gas exchange is another essential element of poisoning management that deserves constant reemphasis.

The amount of pesticide absorbed is a critical factor in making treatment decisions, and estimation of dosage in many circumstances of pesticide exposure remains difficult. The terms "small amount" and "large amount" used in this book are obviously ambiguous, but the quality of exposure information obtained rarely justifies more specific terminology. Sometimes the circumstances of exposure are a rough guide to the amount absorbed. Spray drift from a pesticide properly diluted for field application is not likely to convey a large dose unless exposure has been prolonged. However, drift is the leading cause of incidents among agricultural workers reported to the Sentinel Event Notification System for Occupational Risk (SENSOR)-Pesticides.[1] Farmworkers and pesticide applicators working with pesticides on a regular basis are at risk for acute pesticide poisonings. Spills of a concentrated chemical onto the skin or clothing may well represent a large dose of pesticide unless the contamination is promptly removed. Brief dermal exposure to foliage residues of cholinesterase-inhibiting pesticides is not likely to lead to poisoning, but prolonged exposures may.

Risk =

Toxicity
×
Exposure

Suicidal ingestions almost always involve "large amounts," requiring the most aggressive management. Except in children, accidental pesticide ingestions are likely to be spat out or vomited. Ingestions of pesticides by children are the most difficult to evaluate. The clinician usually must base clinical management decisions on "worst case" assumptions of dosage. Childhood poisonings are further complicated by the greater vulnerability of the very young, not only to the pesticides, but also to the drugs and treatment procedures. Children ingest a greater amount per body weight than adults. The nature of neurological development in children entails an additional level of risk that is not present in adults.

Underreporting

Pesticide incidents are underreported for several reasons. According to the OPP Report on Incident Information (EPA, 2007), these include:

Lack of a universal, mandatory legal duty to report incidents

Lack of a central reporting point for all incidents

Similarity of symptoms associated with pesticide poisonings to other causes

Misdiagnosis by physicians because of a lack of familiarity with pesticide effects

Inadequate investigation of incidents to identify the pesticide that caused the effects

Difficulty in identifying and tracking chronic effects

Reluctance or inability of physicians to report incidents

Limited geographic coverage of individual poisoning databases

Barriers to Proper Recognition and Management of Pesticide Poisonings

Pesticide-related illnesses are one example of a myriad of existing Environmental and Occupational Health (EOH) exposures of concern. For many reasons, accurate diagnosis and treatment of pesticide poisonings present a challenge to the clinician. Like many illnesses linked to environmental exposures, pesticide poisonings remain commonly under-diagnosed due in large part to barriers in seeking care and diagnosis of pesticide poisonings.

Seeking Care

One important factor contributing to under-diagnosis occurs if the exposed person does not, or is unable to, seek medical attention. A pesticide applicator, for example, may not perceive the incident as significant enough to seek care, particularly if he or she has been accustomed to low-level exposure scenarios on the job. Some agricultural workers are unable to readily address a pesticide poisoning because of a complex set of socioeconomic factors including inability to take off from work, transportation problems, language and cultural barriers, lack of health insurance, scarcity of available community health services and fear of losing employment. Another scenario is the exposed person may simply not recognize his or her symptoms as pesticide related.

Diagnosis

When an individual exposed to pesticides does seek care, diagnosis has its own set of challenges. Differential diagnosis is difficult because signs and symptoms of pesticide-related illnesses are often nonspecific and may be confused with common illnesses unrelated to pesticide exposure. The clinician may neglect to take an environmental and occupational exposure history,[2] a key to proper diagnosis, and thereby miss the opportunity to uncover a pesticide poisoning. Even when pesticide poisoning is suspected, few diagnostic tools are available. **Chapter 2** of this manual, entitled ***Making the Diagnosis***, is intended to guide clinicians in determining whether the patient may be experiencing symptoms of a pesticide poisoning, with an emphasis on taking an environmental and occupational exposure history.

Institutional

The 1999 edition of this manual stated, "Despite recommendations by the Institute of Medicine and others urging the integration of environmental medicine into medical education, healthcare providers generally receive a very limited amount of training in occupational and environmental health, and in pesticide-related illnesses, in particular."[3] Migrant Clinicians Network surveyed clinicians in 2000 and found that more than 80% reported little or no EOH training.[4] This reality remains largely unchanged.

"…environmental medicine education is largely omitted in the continuum of U.S. medical education, leaving future physicians and current practitioners without expertise in environmental medicine to provide or facilitate environmental preventative or curative patient care." (Gehel, et al., 2011)

Few healthcare providers are adequately trained in environmental medicine despite widespread recognition of a need to better prepare the nation's frontline in public health to respond to EOH issues.[5] There is growing interest in environmental medicine among practicing clinicians[6] and medical and nursing students, but the existing education system does little to address this demand.[5] Institutional change to expand an already stressed medical curriculum has proven to be a major obstacle to inserting EOH training.

Assessing the Relationship of Work or Environment to Disease

Pesticides and other chemical and physical hazards are often associated with nonspecific medical complaints so it is very important to link the symptoms with the timing of suspected exposure to the hazardous agent. The ***Index of Signs and Symptoms,*** beginning on page 244, provides a quick reference to symptoms and medical conditions associated with specific pesticides. Further details on the toxicology, confirmatory tests and treatment of illnesses related to pesticides are provided in each chapter of this manual. A general understanding of pesticide classes and some of the more common pesticide agents is helpful in making a pesticide-related disease diagnosis. A concurrent non-pesticide exposure can have no health effect, exacerbate an existing pesticide health effect or solely cause the health effect in a patient. In the more complicated exposure scenarios, assistance should be sought from environmental and occupational medicine (EOM) specialists.

Common Pesticide Poisonings

Following are three pesticide incident data tables created for this manual to illustrate which pesticides are most frequently implicated in incident reports to SENSOR-Pesticides, National Poison Data System (NPDS) and California's Pesticide Illness Surveillance Program (PISP). These tables cannot be considered representative of all incidents because they only show those that were reported to these three databases. The relative frequency of cases generally reflects how widely a product is used in the environment. Organophosphate (OP) insecticides have historically topped the list of most commonly reported exposures. EPA risk mitigation measures have greatly diminished the use of organophosphates for residential, particularly indoor, use. In the United States, pyrethroids have largely replaced the OPs in terms of widespread usage. As such, they now account for the most human case reports in the United States. Although they are relatively less acutely toxic than their predecessors, some severe poisonings have similar presenting signs and symptoms as that of OP poisoning, thus complicating the process of making the correct diagnosis.

Data Sources for Poisoning Incidents

Table 1. SENSOR-Pesticides Program

Table 2. National Poison Data System

Table 3. California Pesticide Illness and Surveillance Program

TABLE 1							
PESTICIDES MOST OFTEN IMPLICATED IN ACUTE OCCUPATIONAL PESTICIDE-RELATED ILLNESS AND INJURY CASES AND NUMBER OF CASES, SENSOR-PESTICIDES PROGRAM, 2005-2009 (N=9,906)							
Rank	**Pesticide Category**	**Number of Exposed Cases**				**Sum of Single + Multiple Exposure Cases* (n=9,906 individuals)**	
		Exposed to Single Substance (n=6,187 individuals)		**Exposed to Multiple Substances* (n=3,719 individuals)**			
		n	**%**	**n**	**%**	**n**	**%**
1	Pyrethroids	1,368	22.10	1,479	39.80	2,847	28.70
2	Chlorinated compounds	1,174	19.00	387	10.40	1,561	15.80
3	Organophosphorous compounds	600	9.70	429	11.50	1,029	10.40
4	Pyrethrins	358	5.80	620	16.70	978	9.90
5	Glyphosate	274	4.40	203	5.50	477	4.80
6	Ammonium/ammonia	32	0.50	361	9.70	393	4.00
7	N-methyl carbamates	249	4.00	112	3.00	361	3.60
8	DEET	292	4.70	59	1.60	351	3.50
9	Sulfur compounds	145	2.30	143	3.80	288	2.90
10	Triazines	168	2.70	60	1.60	228	2.30
11	Fipronil	26	0.40	135	3.60	161	1.60
12	Naphthalene	113	1.80	22	0.60	135	1.40
13	Imidacloprid	1	0.00	118	3.20	119	1.20
14	Thiocarbamates/ Dithiocarbamates	67	1.10	31	0.80	98	1.00
15	Glutaraldehyde	51	0.80	15	0.40	66	0.70
	All other	1,269	20.50	1,287	34.60	2,556	25.80
TOTAL INDIVIDUALS		**6,187**	**100.00**	**3,719**	**100.00**	**9,906**	**100.00**

**Because some of the individuals exposed to multiple substances appear in the totals of more than one pesticide category, the sum of the pesticide categories exceeds the number of individuals.*

Source: Edward J. Kasner, MPH and Geoffrey M. Calvert, MD, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.

TABLE 2								
PESTICIDE EXPOSURES MOST COMMONLY REPORTED TO NATIONAL POISON DATA SYSTEM ACCORDING TO THE 2010 ANNUAL REPORT[7]								
Rank	**Pesticide or Pesticide Class**		**Child <5 years**	**6-12 years**	**13-19 years**	**≥ 20 years**	**Unknown age**	**Total**
1	Pyrethrins and pyrethroids		7,717	1,672	1,222	14,800	2,706	28,117
2	Disinfectants	Hypochlorite disinfectants	5,024	563	837	5,471	1,355	13,250
		Other disinfectants (*e.g.*, pine oil and phenols)	6,994	619	433	2,435	537	11,018
3	Rodenticides	Anticoagulant rodenticides	9,176	204	95	796	225	10,496
		Other rodenticides	1,785	89	67	250	183	2,374
4	Insect repellents	DEET	3,194	685	251	934	189	5,253
		Others (*e.g.*, naphthalene moth repellent)	3,178	328	130	1,338	491	5,465
5	Herbicides (*e.g.*, glyphosate, chlorophenoxy herbicides)		2,019	362	246	4,593	817	8,037
6	Borates and boric acid pesticides		4,270	92	62	466	110	5,000
7	Organophosphates	OPs alone	722	171	107	1,331	321	2,652
		OP + carbamate and OP + non-carbamate insecticides	158	47	49	495	83	832
8	Carbamate insecticides		804	119	83	1,027	221	2,254
9	Fungicides		171	25	21	414	73	704
10	Organochlorine insecticides		182	30	15	245	58	530
11	Fumigants		48	19	14	213	56	350
	All other insecticides (including unknown)		5,526	615	387	5,264	1,371	13,163
TOTAL PESTICIDES/DISINFECTANTS			**50,968**	**5,640**	**4,019**	**40,072**	**8,796**	**109,495**

The pesticides most commonly reported to Poison Control Centers, according to the 2010 Annual Report data from the American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS) are listed in Table 2, above. Cases listed as organophosphates (and the other categories as well) may also include other insecticides such as carbamates and organochlorines in a single product. Asymptomatic cases are included in Table 2 only.

TABLE 3

SUMMARY OF PESTICIDE EXPOSURES AMONG CASES IDENTIFIED BY THE CALIFORNIA PESTICIDE ILLNESS SURVEILLANCE PROGRAM FROM 2005–2009 AND EVALUATED, AFTER INVESTIGATION, AS DEFINITELY, PROBABLY OR POSSIBLY RELATED TO PESTICIDE EXPOSURE, BY PESTICIDE CATEGORY

Pesticide category	Occupational		Non-Occupational	
	Only pesticide implicated	Two or more pesticides involved	Only pesticide implicated	Two or more pesticides involved
Antimicrobials				
Hypochlorite	422	69	98	81
Quaternary Ammonium	227	106	15	14
Glutaraldehyde	69	3	0	0
Other/Unknown	197	297	92	88
Insecticides/ Miticides/Insect Growth Regulators				
Organophosphates	162	227	52	91
Carbamates	13	16	12	4
Pyrethrins/ Pyrethroids	56	425	134	294
Organochlorines	0	1	0	2
Other/Unknown	61	612	124	136
Herbicides/Defoliants	80	184	28	44
Fungicides	81	548	29	62
Fumigants	228	106	366	134
Other/unknown*	41	568	83	97
TOTAL EXPOSURES	**1,637**	**3,162**	**1,033**	**1,047**

**The majority of other/unknown pesticides are adjuvants, which are registered in California but not necessarily identified by active ingredients. Additionally, this category includes a molluscicide, a nematicide and several pheromones, plant growth regulators, preservatives, repellents, rodenticides, synergists, pesticides with multiple functions and products that never were identified.*

Table 3 shows the numbers of occupational and non-occupational exposures from 2005–2009 that the California Pesticide Illness Surveillance Program associated with various categories of pesticides. All exposures that occurred while the affected person was at work are considered occupational. Occupational exposures probably continue to be more fully reported than non-occupational exposures. A case represents one individual's exposure to pesticide(s). Cases in which only one exposure was credibly implicated are distinguished from those to which any or all of two or more pesticides may have contributed. This table illustrates exposures; when more than one pesticide active ingredient is implicated, an exposure is counted for each person/pesticide combination. Multiple pesticide active ingredients were implicated in the cases of 2,657 people exposed occupationally and 432 exposed non-occupationally. These cases are counted in each pesticide category for which they qualify, for totals of 3,162 occupational exposures and 1,047 non-occupational exposures.

Special Populations and Environmental Justice

Environmental justice strives to ensure that no population is forced to shoulder a disproportionate burden of the negative human health and environmental impacts of pollution or other environmental hazards.[8] EPA seeks to ensure the fair treatment and meaningful involvement of all people regardless of race, color, national origin, educational level or income with respect to the development, implementation and enforcement of environmental laws, regulations and policies.[9]

With regard to pesticide exposure and environmental justice, the farmworker population is of particular concern. The majority of farmworkers and their family members in the United States are Latinos living in poverty. Farmworkers are the population most often affected by pesticide overexposure. Children represent another population of concern as they may be at greater risk from pesticide exposures because they are growing and developing. Women of reproductive age and pregnant and nursing women may also be more vulnerable because of the effects of pesticide exposures on fetuses and infants. These three populations face higher risk of harmful pesticide exposure because of occupation or developmental susceptibility, or combination thereof. Each is discussed in more detail below.

Agricultural Workers

In the United States, between 1 million and 2.5 million hired farmworkers earn their living from agriculture.[10,11] Farmworkers are the working population most often affected by pesticide overexposure, especially Latino farmworkers.[12] Farmworker patients should be considered to be at high risk for pesticide exposure; their screening or exposure history should include specific questions about any agricultural work being done. For example:

- Are pesticides being used at home or at work?
- Do you mix or apply pesticides?
- Are the fields or orchards wet when you pick, prune or harvest?
- Was spraying taking place in or near the fields or orchards while you were working?
- Do you get sick during or after working in the fields or orchards?
- Do you use agricultural pesticides in your home?
- Did you learn about adverse health effects of pesticides and how to protect yourself from exposure while using pesticides?

Farmworkers often reside in agricultural communities where they and their family members may be further exposed in their homes because of pesticide drift from spraying of nearby fields or orchards and drinking contaminated water. Para-occupational exposure factors such as pesticide residue on workers and their clothing, shoes and vehicles and lack of adequate facilities to clean pesticide-contaminated work clothes may increase the risk of pesticide exposure for other household members as well.

Children

Children face particular risks from pesticides, as their physical makeup, behavior and physiology may make them more susceptible than adults.[13,14,15] As such, it is important to assess pesticide exposures by asking about where pediatric patients live, the occupation of their parents and whether pesticides are used in the home, childcare facility, school and play areas. It is also important to remind parents to store pesticides out of the reach of children.

Children from agricultural families and those living in close proximity to agricultural areas are exposed to higher levels of pesticides than those whose parents do not work in agriculture and who do not live close to farms.[16,17,18] The higher pesticide levels may result from parents' tracking pesticides from the workplace into the home or by pesticide drift.[19,20]

Adolescents working in agriculture are also at risk of exposure to pesticides.[21,22] The incidence rate of acute occupational pesticide-related illness in adolescents is significantly higher compared to adolescents not working in agriculture.[23] This is a particular concern for young farmworkers since adolescents are permitted to work in agriculture at younger ages than in other industries. While the research examining the impact of neurotoxicants on the central nervous system of adolescents is limited,[24,25,26] there is strong evidence of neural remodeling and brain development during adolescence.[25,26,27,28] Dose responses, metabolic rates and routes of exposure may vary by age, gender and maturation.[21,22,28] Extra caution is merited as consideration is given to acute and chronic pesticide exposures of adolescents.[21,22]

Women of Reproductive Age and Pregnant Women

Pesticides may cause the most damage in humans during periods of rapid development, especially *in utero* through transplacental absorption.[29,30] Even prior to fetal periods of increased sensitivity, studies have found that *preconception* exposure of either the mother or father may have an effect on reproductive outcome and offspring.[31,32,33,34] Maternal exposure to pesticides should be minimized during pregnancy and during the preconception period. The period of maximal sensitivity to a teratogen varies depending on the birth defect, but is almost always within the first 10 weeks of the pregnancy. However, the central nervous system, eyes, teeth and external genitalia may be susceptible to teratogenic exposures throughout the pregnancy.[35] Although no pesticides have been proven to be human teratogens, several studies have shown associations between pesticide exposures and reproductive toxicity in humans. For example, *in utero* exposure to organophosphates has been associated with low birth weight, mental and motor delay, attention deficit hyperactivity disorder (ADHD), and reduced IQ.[36,37] Women who are pregnant or planning a pregnancy, especially those currently engaging in agricultural activities, should be informed of the implications of exposure before conception and during the pre- and peri-natal periods, and assisted in making decisions that are appropriate for their individual work and home situations.[38] See **Chapter 21, *Chronic Effects*,** for further information and examples.

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