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Health Effects of Common Home, Lawn, and Garden Pesticides

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Pesticides are a source of concern and confusion for both parents and health care providers. This confusion reflects the diversity of products available and their widespread use where children live, go to school, play, and in the food supply coupled with evolving evidence of potential harm from cumulative exposure. The National Home and Garden Pesticide Use Survey conducted by the US Environmental Protection Agency (EPA) found that 82% of households in the United States use pesticides, with an average of three to four different pesticide products used per home [1]. A landmark review in 1993 by the National Academy of Sciences concluded that children may be especially vulnerable to adverse health effects from pesticides [2]. In the last decade studies have demonstrated that the biologic mechanisms underlying this increased susceptibility include both behavioral and developmental factors that can increase the dose and toxicity children experience as compared with adults [3]. Recent studies in pediatric populations have begun to address multiple routes of exposure, exposure to multiple pesticides, and the influence of gene–environment interactions [4–6]. Population-based surveys by the Centers for Disease Control and Prevention have reported

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the pervasive presence of a variety of pesticides in the blood and urine of children in the U.S. The third National Report on Human Exposure to Environmental Chemicals, released in July 2005, included testing of 44 pesticide metabolites in a sample representative of the civilian, noninstitutionalized U.S. population over age six years. Of these chemicals, 29 were detectable in most people sampled, with organophosphate and organochlorine insecticides reported to be most prevalent in the population [7].

The pediatric health burden of pesticide exposure includes both acute and chronic health impacts. Acute symptoms range from mild and subtle to severe (eg, nausea, headaches, skin rashes, eye irritation, seizures, coma, and death). Chronic conditions associated with pesticides in epidemiologic studies of children include birth defects, cancer, asthma, and neurodevelopmental/neurobehavioral effects.

Case study

On the day her house was sprayed, a full-term, previously healthy 4-month-old girl became irritable and congested in her upper airway with a thick, whitish nasal discharge. Over the next several days these symptoms persisted; she began to refuse food, she developed a fever and more frequent bowel movements, and her sleep decreased. On day 6 she was brought to the emergency department, received intravenous fluids for hypernatremia and dehydration, and was discharged with a diagnosis of upper respiratory infection. The infant's condition worsened, and she was admitted to the pediatric ICU later that night. A thorough infectious work-up was negative. She received supportive therapy and antibiotics for a week and was discharged without medications, but she continued to have a head lag. Fourteen months later, her home was evaluated when an epidemic of illegal applications of the agricultural pesticide methyl parathion in residences was recognized. Her urinary level for p-nitrophenol, a metabolite of methyl parathion, was elevated at 89 ppb (the reference range based on the National Health and Nutrition Examination Survey is 0–63 ppb) [8].

Recognizing pesticide poisonings in children

Acute intoxications in children frequently are misdiagnosed, despite being linked closely in time with generally high exposures [9,10]. Associating low-level exposures with health consequences that manifest days, weeks, months, or years later is particularly challenging. The pediatrician plays a critical role in recognizing and preventing both poisonings and chronic health effects. Without recognition, opportunities to remove the child and other affected individuals from exposure are missed, appropriate diagnosis and treatment is compromised, and chronic sequelae may develop. In the case described, analysis of blood samples for plasma pseudocholinesterase

and red blood cell acetylcholinesterase inhibition would have ensured timely diagnosis of organophosphate toxicity and allowed prompt administration of atropine sulfate and pralidoxime as an antidote (Table 1). Many other affected individuals also could have been diagnosed and treated appropriately. In many states, physicians are mandated to report suspected pesticide-related incidents in an effort to recognize epidemics and identify hazards for targeted prevention strategies (Box 1).

An environmental exposure history is required to raise the index of suspicion and to clarify the relevance of pesticides to patient health. Evaluating exposures through questions about pesticide use helps establish the role of pesticides during "sick visits" and also provides anticipatory guidance. During well-child examinations, questions about pesticide use in and around the home, at the child's school, and at the parent's workplace provide an opportunity for and indicate the appropriateness of anticipatory guidance on safe practices and prevention. When pesticide exposure is suspected in an illness or symptomatic complaint, the environmental history elicits which pesticides might be involved and the type and extent of exposure. This information provides a context for assessing whether the toxicity of the product, the exposure scenario, and the likely dose support the need for consideration of specific evaluation and treatment versus reassurance. In some cases, specialty consultation with a clinical toxicologist or occupational/environmental medicine specialist is required (see Box 1).

In addition to developing an index of suspicion, it is helpful to recognize the main pesticide groups or chemical classes and to understand their common toxicity characteristics and management (see Table 1). Pesticides can be classified in several ways. Categorization may reflect their intended use (eg, as insecticides, fungicides, herbicides, and rodenticides, among others). These classifications have little toxicologic significance but are important to understand because consumers and manufacturers classify products in this way. Pesticides also can be classified according to their chemical class (eg, as organophosphates, *N*-methyl carbamates, pyrethroids, triazines, and superwarfarins). These categories are meaningful toxicologically but may not be readily apparent from product name, label, or usage category. The product label itself includes the brand name and the active ingredient (the ingredient that kills the pest). There are readily available resources that can help with identification of chemical class or toxicity based on active ingredients (see Box 1).

The common presenting symptoms and some key features of clinical evaluation and management of poisoning for pesticides commonly used in the home and garden, on pets, or applied directly to children are provided in Table 1. For symptomatic pesticide illness among young children reported to the Poison Control network, the insecticides, particularly organophosphates, pyrethrin/pyrethroids, and the repellent n,n-diethyl-m-toluamide (DEET), followed by rodenticides (long-acting superwarfarin), are most frequently represented. Borates/boric acid and carbamate insecticides also

Table 1
Acute signs and symptoms and clinical evaluation considerations for common household and garden pesticides by chemical class

Agent	Acute signs and symptoms	Clinical evaluation considerations
Insecticides		
Organophosphates (examples of active ingredients: malathion, tetrachlorvinphos, tribufos [DEF], dichlorvos [DDVP], acephate, dimethoate, ethoprop, fenitrothion, fenthion, naled, terbufos, chlorpyrifos [Dursban][a], diazinon[b])	Headache Excess salivation Lacrimation Muscle twitching Nausea Diarrhea Respiratory depression Seizures Hypotonia CNS depression Miosis	Diagnostic testing: Plasma pseudocholinesterase Red blood cell cholinesterase Certain organophosphates selectively inhibit one or the other of these enzymes. The plasma enzyme effects generally persist days to weeks; the red blood cell enzyme effects last 1 to 3 months. Consider repeat testing 3 months after exposure to determine individual nonexposed baseline. Urinary alkyl phosphates are useful up to 48 hours after exposure to document exposure. Clinical interpretation of concentrations is unknown. Neuropsychologic testing has identified persistent sequelae in some adults after acute poisoning. Treatment: Atropine sulfate Pralidoxime
N-methyl carbamates (examples of active ingredients: carbaryl [Sevin], propoxur [Baygon])	Similar to organophosphates	Diagnostic testing: Plasma pseudocholinesterase Red blood cell cholinesterase The inhibition of these enzymes by carbamates is rapidly reversible, making these less reliable for diagnostic purposes (false negative) Treatment: Atropine sulfate
Pyrethrins/pyrethroids (examples of active ingredients: permethrin, bifenthrin, cyfluthrin, cypermethrin, deltamethrin, esfenvalerate)	Allergic reactions (dermatitis, asthma, rhinitis)	Diagnostic testing: None available Treatment:

	Paresthesias (stinging, burning, itching, tingling, numbness) Facial sensations Headache Fatigue Salivation Nausea and vomiting Tremor Diarrhea Irritability Seizures	Symptomatic treatment (eg, antihistamines, topical corticosteroids). Vitamin E oils are effective in preventing and stopping the paresthetic reaction
Diethyltoluamide (DEET)	Headache Restlessness Irritability Ataxia Loss of consciousness Hypotension Seizures	Diagnosis: Methods for measuring blood concentrations and urinary metabolites are not widely available
Boric acid	Mucous membrane irritation and dryness Cough Shortness of breath Beefy red skin rash on palms soles, buttocks, scrotum Nausea Diarrhea Hypothermia	Diagnosis: Urine or serum levels can be measured for confirmation

(*continued on next page*)

Table 1 (*continued*)

Agent	Acute signs and symptoms	Clinical evaluation considerations
Herbicides		
Chlorphenoxy compounds (examples of active ingredients: 2,4-dichorophenoxyacetic acid (2,4-D), mecoprop, dicamba)	Mucous membrane irritant Skin irritant Vomiting Diarrhea Headache Confusion Bizarre or aggressive behavior Myotonia, muscle weakness Peculiar odor on breath Metabolic acidosis, renal failure	Diagnosis: Urine concentrations can confirm overexposure (must be collected immediately; complete excretion occurs within 24–72 hours) Electromyographic and nerve conduction velocities in recovering adult patients have demonstrated mild proximal neuropathy and myopathy that persists months after acute poisoning Treatment: Alkaline diuresis in severe poisonings
Phosphonates (active ingredient: glyphosate [Roundup, Glyfonox])	Mucous membrane irritation Skin irritant	—
Rodenticides		
Coumarins and indadiones (examples of active ingredients: brodifacoum, warfarin, bromadiolone, coumachlor, coumatetralyl, difenacoum, chlorophacinone, diphacinone, pivalyn)	Bleeding/bruising (gum, nose) Fatigue Dyspnea on exertion	Diagnosis: Prothrombin time at 24 and 48 hours (Occurs within 24–48 hours of ingestion and persists 1–3 weeks) Treatment: None if certain no more than mouthful of treated bait was ingested Vitamin K1 (phytonadione) if prothrombin time is elevated or there are clinical signs of bleeding

Abbreviation: CNS, central nervous symptoms.

[a] Sale of products for indoor use banned in 2001.

[b] Sale of products for indoor use banned in 2002.

Box 1. Additional resources for pediatricians addressing pesticide toxicity concerns

Determining the types of pesticide ingredients/chemicals in specific products

The National Library of Medicine's Household Products Database provides a readily available interface to identify product ingredients based on product brand names at http://hpd.nlm.nih.gov/.

A treating physician can obtain the full list of product ingredients (including inert ingredients) directly from the company by calling the telephone number listed on the product label. To obtain this information, the physician may be required to sign a confidentiality agreement.

Once the list of ingredients is available, the chemical class can be obtained from various sources. The Pesticide Action Network database on pesticide exposures, symptoms, and toxicity (http://www.pesticideinfo.org) provides information on chemical class, covers both acute and chronic health effects, and is especially useful for agricultural exposures.

Clinical information on acute exposure signs and symptoms and recommended diagnostic and treatment strategies for specific pesticides

The EPA's *Handbook Recognition and Management of Pesticide Poisonings* covers toxicology, signs and symptoms of poisoning, and treatment of the major types of pesticides. The most recent fifth edition (1999) is available in Spanish, English, and on the Web (http://www.epa.gov/pesticides/safety/healthcare/handbook/handbook.htm).

Regional Poison Control Centers and their affiliated clinical toxicologists can be reached at 1-800-222-1222.

Information about chronic exposure to specific pesticides and other professional consultation on pesticide toxicity

The National Pesticide Medical Monitoring Program (NPMMP) is a cooperative agreement between Oregon State University and the United States Environmental Protection Agency. The NPMMP provides informational assistance in the assessment of human exposure to pesticides by e-mail (npmmp@oregonstate.edu) or by fax at (541) 737-9047.

The Pediatric Environmental Health Specialty Units are coordinated by the Association of Occupational and Environmental Clinics to provide regional academically based free consultation for health care providers. Funding is provided by the EPA and the Agency

for Toxic Substances and Disease Registry (ATSDR). The Web site is http://www.aoec.org/PEHSU.htm. The toll-free telephone number is (888) 347-AOEC (2632).

Pesticide incident reporting requirements for health care providers

Contact the State Health Department

Analytical laboratories for pesticides in blood and urine

The NPMMP is affiliated with the Centers for Disease Control and provides quantitative laboratory measurements of pesticides in environmental or biologic samples in select cases involving human exposure to pesticides

For identification of commercial laboratories capable of nonroutine analyses for pesticides and metabolites, contact the regional Poison Control Center or regional Pediatric Environmental Health Specialty Unit.

Patient information on pest-control alternatives, safe use of pesticides

The EPA publication, *Citizens Guide to Pest Control and Pesticide Safety*, teaches consumers how to control pests in and around the home, alternatives to chemical pesticides, how to choose pesticides, and how to use, store, and dispose of them safely. It also discusses how to reduce exposure when others use pesticides, how to prevent pesticide poisoning and how to handle an emergency, how to choose a pest-control company, and what to do if someone is poisoned by a pesticide. (2.4 MB, available at http://www.epa.gov/OPPTpubs/Cit_Guide/citguide.pdf.)

The University of California maintains a Web site on integrated pest-management approaches for common home and garden pests. (Available at http://www.ipm.ucdavis.edu/.)

Workplace health and safety information

Information on the EPA worker protection standards is available at http://www.epa.gov/pesticides/health/worker.htm.

Employee fact sheets developed by the State of California Worker Health and Safety Branch are available at http://www.cdpr.ca.gov/docs/whs/psisenglish.htm.

Other resources

The National Library of Medicine has a comprehensive and well-organized list of Web link resources on pesticides. It can be accessed at http://sis.nlm.nih.gov/enviro/pesticides.html.

constitute a large proportion of reports to poison centers. The following sections discuss some of the common exposure issues encountered in general pediatric practice.

Organophosphates

In the case of organophosphate poisoning presented previously, the classic symptoms of cholinergic excess from the inhibition of acetylcholinesterase were not apparent. Medical students, clinical toxicologists, and emergency room physicians often are taught acronyms for the constellation of symptoms reflecting this toxicologic mechanism. One example is M-U-D-D-L-E-S: miosis, urination, diarrhea, diaphoresis, lacrimation, excitation of the central nervous system, and salivation. This acronym works reasonably well in adults. Reviews of case series, however, indicate that pediatric organophosphate poisonings often manifest with hypotonia or changes in mental status such as lethargy and coma, as well as seizures, the last being relatively rare in adult organophosphate poisoning [11]. The nonspecific symptoms of acute pesticide toxicity are easily attributed to common pediatric diagnoses such as respiratory infections, viral syndromes, gastroenteritis, atopic dermatitis, or drug-related encephalopathy. This differential underscores the importance of questions about pesticide in a thorough pediatric exposure history.

n,n-Diethyl-m-toluamide

Although technically DEET is a repellent, not a pesticide, it is discussed here because it is used against pests and is recommended by the Centers for Disease Control and Prevention and the American Academy of Pediatrics (AAP) as a strategy for prevention of mosquito-borne disease such as West Nile encephalitis [12,13]. Although rare, there have been reports of severe neurotoxicity associated with exposure to DEET; therefore the AAP recommends precautions when this product is used on children [14–16]. For example, using lower concentrations of DEET products (preferably 10% and no more than 30%), avoiding formulations containing ethanol or permethrin, and using the product only on intact, uncovered skin will reduce the dermally absorbed dose. Infants less than 2 months of age have increased dermal absorption, so use in this population is not recommended. In addition, products containing mixtures of DEET and sunscreen should be avoided, because sunscreen may require reapplication for effectiveness, and no more than a single daily application of DEET is recommended.

Scabicides and pediculocides

Permethrin and malathion, and in some cases lindane, may be used as topically applied insecticides to treat lice and scabies. The potential toxicity of malathion and its flammable alcohol base make it undesirable. Lindane has been associated with significant neurotoxicity, and the AAP recommends

its cautious use as a second-line agent in select populations of older children [17]. Its use has been banned entirely in some states and in numerous other countries because of the potential for serious water contamination, environmental toxicity, and long-term environmental persistence [18]. The pyrethrin/pyrethroid-containing products have been used extensively with limited adverse events reports. There is an adult case report of an anaphylactoid reaction after use of a pyrethrin-containing shampoo and a case of a fatal asthma death occurred in a child after she applied a pyrethrin-based animal shampoo on a pet [19,20]. Although the process is labor intensive, head lice in children can be managed effectively and safely with repeated combing of hair and washing of clothing and bedding in hot water.

Residential products

Following recent bans on chlorpyrifos and diazinon (both organophosphates) for residential use, the household insecticides now in common use contain other organophosphates (malathion, tetrachlorvinphos, dichlorvos), *N*-methyl carbamates (carbaryl, propoxur), and, increasingly, pyrethroids/pyrethrins, or combinations. Broadcast applications, including sprays, "flea bombs," and foggers are more problematic than spot or crack and crevice applications; the latter methods, in turn, can be replaced safely in many situations by enclosed insect baits or traps. After spraying, insecticide residues can linger on the floor, in the air, in carpets, on toys, and in the dust [21,22]. Children crawling on these surfaces and putting their hands or objects in their mouths can ingest significant quantities of pesticides [23]. The vapor of some pesticide sprays lingers near ground level, in the breathing zone of a toddler [24]. Even lawn and garden herbicides can be tracked in to homes, especially homes where a dog uses the back yard, and can linger in carpets, resulting in potentially significant child exposures [25].

The symptomatic complaints related to pyrethrin/pyrethroids are often skin related (stinging, burning, itching, tingling, numbness, paresthesias), and these agents have been associated with contact dermatitis and allergic respiratory reaction (rhinitis, asthma) [11]. Their other signs and symptoms overlap with the nonspecific nature of organophosphate overexposure (see Table 1).

For most household pest problems (as well as lawn and garden uses), less toxic alternatives and integrated pest-management approaches can be employed and should be encouraged (see Box 1). In particular, insecticides can be replaced by an approach that includes cleaning up food and water, sealing cracks and crevices, and using pesticides that are contained in baits or traps, which are far less likely to pose a health concern compared with any type of spray application. Lawns and gardens can be maintained by avoiding combination products with pesticides and fertilizers (ie, "weed and feed" preparations) that tend to result in overapplication of pesticides. Hand weeding is always a reasonable alternative to herbicides. If herbicides

are used, some (such as glyphosate) have far better toxicity profiles than others (such as 2,4-dichlorophenoxyacetic acid). Parents also should be advised regarding proper storage of pesticides (in a locked cabinet or building) and against reuse of pesticide containers.

As sold to consumers, pesticide products contain a mixture of active ingredients (usually one or two) and a variety of other ingredients (sometimes called "inert" ingredients). The concentration of the active ingredient varies widely from one product to another; for example, DEET formulations range from 10% to 100%, and the concentration of permethrin products can range from 0.02% to 99.5%. Inert ingredients include solvents, emulsifiers, diluents, stabilizers, adjuvants, and even fragrances. Any ingredient that does not kill the pest is considered an inert ingredient. Inert ingredients are listed on the label as "other ingredients" and are not named specifically. Generally the other ingredients are trade secrets, and it is difficult to get any information about them. These chemicals may have their own toxicities, however, particularly as irritants to skin and mucous membranes, including the lower respiratory tract. A health care provider who is treating a patient exposed to a particular pesticide product can call the manufacturer and obtain the full list of ingredients. To do so often involves signing an agreement not to disclose the information to anyone.

Other important sources of household pesticide exposure

Occupational exposures to parent and child

Other important exposure scenarios for children include their own or parent's occupation. Adolescents may find summer employment in landscaping, pool care, or agricultural work. Although this work may be temporary or part-time in nature, adolescents may be less likely to appreciate or be informed about the risk of using chemicals in their work. In most states, a person under age 18 years cannot become a licensed pesticide applicator, although unlicensed pesticide application is common, and pesticide exposures can occur even if the child is not applying the chemical. Working parents and children may carry home exposure as residues on clothing or shoes. People who may be occupationally exposed to pesticides should understand the importance of personal protective equipment such as appropriate respirators, gloves, and coveralls, hand washing after contact with chemicals, removal of work clothes, and separate laundering of work clothes. Parents who handle pesticides at work should be careful not to come home with residues on their skin, clothes, or shoes.

Pesticides in the food supply

Dietary exposures to pesticide residues also may be important, especially because children eat a relatively restricted diet, choose certain dietary items (eg, bananas or apples) relatively frequently, and consume far larger

portions on a bodyweight-adjusted basis than do adults [26]. The dietary pathway has become a significant concern relative to the organophosphate insecticides. These chemicals are used heavily on some of the fruits that are common dietary staples among children. A study in which children were placed on an organic diet for a period of 5 consecutive days revealed a rapid and dramatic drop in their urinary excretion of organophosphate metabolites [27].

High-risk populations

Pesticide exposures are not distributed evenly across the population. Children of farm workers and urban poor children may be at particular risk. In addition, individual child behaviors can have an important impact. Studies of toddlers at day care centers have demonstrate that children who are more active and interact more intimately with their environment (eg, by frequently putting objects in their mouths) receive a dermal dose of pesticide that is 600-fold greater than that of other toddlers in the same environment [28]. Children living in agricultural communities and those whose parents work in agriculture have been shown to be exposed to higher concentrations of insecticides and to excrete metabolites of pesticides that are not registered for household use in their urine [29]. Low-income households of color are more likely to use broadcast, dispersive methods of insecticidal application [30], probably reflecting the quality of the housing stock and the lack of control in making decisions about pesticide use. Housing with many cracks, moisture problems, and holes is more likely to harbor pest infestations. Similarly, living in rental housing or public housing, where landlords may engage in routine spraying, does not offer parents much opportunity to make their own decisions about pesticide use around their children.

Chronic health concerns with pesticide exposures

Fortunately, acute poisoning events in children are relatively rare. The health implications of exposures encountered routinely at low levels have become an increasing focus of concern for scientists, regulators, and communities [31,32]. Although a pediatrician may never diagnose an acute poisoning, most will be relied upon as a trusted source for questions about potential long-term or subtle health effects from pesticide residues on food, in water, or used in homes or schools.

Responding to such questions requires an exposure history to clarify the extent and types of exposures, some knowledge about the toxicity of various chemicals and outcomes, and a common-sense approach toward recommending the safest practical alternative. Helpful data may come from experimental animal models, veterinary science, and epidemiologic studies. The breadth of possibilities and evidence are beyond the scope of this article and the expected knowledge base of the primary care pediatrician. Awareness of the primary

outcomes for which there is a body of suggestive epidemiological evidence—neurodevelopmental effects, childhood cancer, birth defects, and asthma—provides a useful foundation for responding to parental concerns. A brief description of the state of the evidence is provided here.

Review articles describe a number of ecologic and case-control studies that have associated parental exposures or pesticide use in the home with childhood brain tumors, leukemias and lymphomas, and a number of other tumor types [33,34]. The reader is referred to the article by Buka, Koranteng, and Vargas in this issue for more detail on the strengths and limitations of these and more recent data.

Birth defects studies have linked parental occupational pesticide exposure with cryptorchidism, orofacial clefts, limb reduction defects, and heart defects in their children [35–37]. Associations have been observed with both maternal and paternal exposures. For most of these and the pediatric cancer studies, however, the assessment of exposure is for pesticides in general rather than for specific agents or classes of agents. Thus the understanding of the associations is limited and the ability to specify prevention strategies is hampered.

In contrast, much of the evidence for neurodevelopmental effects is focused specifically on studies of organophosphate insecticide exposure. There has been a rapid emergence of evidence demonstrating the neurodevelopmental toxicity of these agents at relatively low exposure levels [38–40]. This evidence includes animal studies describing the mechanistic basis as well as emerging data from studies in the United States population. Animal studies demonstrate that the timing of exposure as well as the dose influences the toxicity manifestations, and adverse effects occur even at low exposure levels that do not affect acetylcholinesterase [41].

Epidemiologic evidence of harm to young children has been described in three large ongoing cohort studies in the United States [6,39,40]. These studies recruited pregnant women and characterized their exposure to certain organophosphates (and in some cases to other pesticides and other environmental contaminants) in pregnancy and in the newborn period using environmental measures, questionnaires, and biologic markers. The newborns were followed through infancy and early childhood to assess their neurodevelopmental health and determine if pesticide exposure in utero and early childhood has adverse effects on neurodevelopmental and behavioral function. Adverse birth outcomes also were evaluated, and respiratory health evaluations are planned as the children age.

Two of these studies are based in urban New York City. The Mt. Sinai–based Children's Environmental cohort study reported that among mothers who had detectable levels of chlorpyrifos metabolites (an organophosphate) in their urine, those with low activity of the enzyme paraoxonase (PON1), which is involved in the detoxification of chlorpyrifos, gave birth to infants with significantly reduced head circumferences compared with mothers with higher activity of PON1 [6]. The authors note that because small head size

has been shown to predict subsequent cognitive ability, these data suggest that exposure to chlorpyrifos may have an adverse effect on the fetal neurodevelopment in offspring of mothers who have genetic risk factors (low PON1 activity).

Preliminary findings from a cohort of mothers and infants being studied by the Columbia Center for Children's Environmental Health also suggest that children who have high chlorpyrifos exposure prenatally have an increased risk of motor and cognitive development delay. In addition, among the most highly exposed, a significantly higher number of children manifested symptoms of inattention at age 3 years [39].

A study of farm workers' children in California, conducted by The Center for the Heath Assessment of Mothers and Children of Salinas, assessed infants in the first months of life using the Brazelton Neonatal Behavioral Assessment Scale (BNBAS) [40]. As maternal prenatal metabolite levels of organophosphate insecticides increased, a dose-related increase in abnormal reflexes was observed. A 10-fold increase of maternal metabolites was associated with a fivefold increase of more than three abnormal reflexes (odds ratio [OR], 4.9; 95% confidence interval [CI], 1.5–16.1). No association was observed between maternal postnatal urinary metabolite concentrations and BNBAS findings.

As these cohort studies evaluate respiratory health and asthma development in children from infancy to school age, they will augment a limited body of epidemiologic data regarding the role of pesticides in pediatric asthma and respiratory health. Existing published reports are few and mixed. An assessment of children in agricultural Iowa did not find an association between pesticide use indoors and out and increased asthma symptoms [42]. A large survey of Lebanese children, however, found that pesticide exposure in the home, pesticide exposure related to parent's occupation, and pesticide exposure outside the home were associated with an increased risk of respiratory diseases overall [43]. The highest risk was observed for children whose parents had occupational exposure to pesticides (OR, 4.61; 95% CI, 2.06–10.29). Evidence of an adverse association also is seen in a nested case-control study of children involved in the Children's Health Study of Southern California. Among environmental exposures examined in the first year of life, herbicides and pesticides had the strongest association with asthma diagnosis before age 5 years (OR, 4.58; 95% CI, 1.36–15.43 and OR, 2.39; 95% CI, 1.17–4.89, respectively) [44]. Data are accumulating from large studies that p,p′-dichlorodiphenyldichloroethylene (DDE), a metabolite of the now-banned but persistent environmental contaminant, the insecticide dichlorodiphenyltrichloroethane (DDT), may be a risk factor for asthma and elevated IgE levels [45,46].

Clearly, the state of the evidence concerning the effect of pesticide exposure on pediatric health has a number of inadequacies. Most epidemiologic studies have limited exposure assessment, so risk cannot be assessed in relation to specific pesticide types or doses. Studies are not uniform in

identifying health risks. Many pesticide compounds have not been investigated for chronic health effects, in either animal models or epidemiologic designs. Nonetheless, there is a growing and improving body of suggestive evidence of harm at exposure levels that occur in United States populations. Of note, investigators have begun to explore the potential modification of risk based on genetic influences [5,6]. These approaches can reveal associations that are not apparent when the gene–environment effect is not considered.

Addressing common questions in primary care pediatrics

The pediatrician may encounter a wide range of questions from patients regarding exposures to pesticides and health risks. Examples of the nature of questions might include.

Will my daughter's attention deficit hyperactivity disorder be worsened if we use pesticides on our lawn?

Is it because my husband is a pesticide applicator that my daughter has a heart defect?

Should I buy organic food for my children?

Is my exterminator right that my 2-year-old is at no risk from flea bombing our house if I air the house out sufficiently before returning?

I have ants in the house and want to get rid of them. What's the safest way?

Although there are a variety of ways of dealing with such questions, it is helpful to have a preventive, compassionate approach as well as ideas for resources where patients may seek additional information. Questions about whether historical pesticide exposure may have caused a disease or birth defect in a child are very difficult to answer. Sometimes these questions arise in a legal context, but often they show a concern that a patient expresses simply out of an effort to make sense of an adverse event. Although it certainly is possible to establish causation of acute pesticide poisoning, it is extremely difficult to associate an historic pesticide exposure—to parents or children—with a specific adverse outcome in a child. Such questions are best addressed by a specialist in pediatric environmental health (see Box 1).

Questions regarding the safety of pesticide use in the garden and home and regarding ways to solve specific pest problems safely are extremely common. Although pesticides can be useful in certain circumstances and can be used safely, it is best to use least-toxic approaches first. In communicating this philosophy to a patient, it is helpful to clarify that although the use of pesticides will be unlikely to result in a specific health effect (such as worsening of a child's attention deficit hyperactivity disorder, as in the example given previously), pesticides are designed to be potent toxic chemicals, and a precautionary approach would advise their avoidance when possible. This method of pest control is called "integrated pest management." Some

resources for integrated pest-management approaches to home and garden pest control are listed in Box 1.

Often parents want to know whether they should feed their children an organic-only diet. Organic food is a rapidly growing segment of the United States food market. It is possible to obtain organic foods in most parts of the country at most times of year, but organic foods usually are higher priced. Conventionally grown foods frequently contain pesticide residues at low concentrations, and such residues are rarely found on organic food. Children placed experimentally on an organic diet experienced a dramatic decline in organophosphate pesticide metabolites in their urine over 5 days [27]. Reviews of government residue-testing data suggest that certain foods, such as apples, bell peppers, celery, imported grapes, cherries, peaches, potatoes, pears, raspberries, spinach, and strawberries, tend to be high in pesticide residues and should be priorities for purchasing organically, whereas others, such as asparagus, avocado, bananas, broccoli, sweet corn, onions, and peas, rarely contain residues even if grown conventionally [47]. These guidelines may be useful for consumers who are concerned about pesticide residues on food but cannot afford to purchase only organically grown food for their children.

Summary

Pediatricians are a trusted source of information, can positively influence parental behavior, and can provide important anticipatory guidance regarding pesticide exposure. Both the potential for acute poisoning and concern about effects on chronic health make it essential that the pediatric care provider maintain a high index of suspicion and offer informed guidance on reduction of pesticide exposure. Anticipatory guidance to prevent direct access by children to pesticides and also to reduce the use of broadcast pesticide applications in children's environments can prevent potentially significant exposures. To address patient concerns, it is important for pediatricians to know the basic facts and have appropriate resources to turn to for answers.

References

[1] Whitmore RW, Kelly JE, Reading PL. The national home and garden pesticide survey. vol. 1. Executive summary, results, and recommendations. Prepared by Research Triangle Institute. Rpt no RTI/5100/17–01F. Washington, DC: U.S. Environmental Protection Agency; 1992.

[2] Committee on Pesticides in the Diets of Infants and Children. Pesticides in the diets of infants and children. Washington, DC: National Academies Press; 1993. Available at: http://www.nap.edu/catalog/2126.html. Accessed January 15, 2007.

[3] Faustman EM, Silbernagel SM, Fenske RA, et al. Mechanisms underlying children's susceptibility to environmental toxicants. Environ Health Perspect 2000;108(Suppl 1):13–21.

[4] Bradman A, Whyatt RM. Characterizing exposures to non persistent pesticides during pregnancy and early childhood in the national children's study: a review of monitoring and measurement methodologies. Environ Health Perspect 2005;113:1092–9.

[5] Nielsen SS, Mueller BA, DeRoos AJ, et al. Risk of brain tumors in children and susceptibility to organophosphorus insecticides: the potential role of paraoxonase (PON1). Environ Health Perspect 2005;113:909–13.
[6] Berkowitz GS, Wetmur JG, Birman-Deych E, et al. In utero pesticide exposure, maternal paraoxonase activity, and head circumference. Environ Health Perspect 2004;112: 388–9.
[7] National Center for Environmental Health Division of Laboratory Sciences. National Report on Human Exposure to Environmental Chemicals. Atlanta, GA: Centers for Disease Control and Prevention; 2005. NCEH Pub. No. 05-0570. http://www.cdc.gov/exposurereport/.
[8] Rubin C, Esteban E, Kieszak S, et al. Assessment of human exposure and human health effects after indoor application of methyl parathion in Lorain County, Ohio, 1995-1996. Environ Health Perspect 2002;110(Suppl 6):1047–51.
[9] Zwiener RJ, Ginsburg CM. Organophosphate and carbamate poisoning in infants and children [published erratum appears in Pediatrics 1988 May;81(5):683]. Pediatrics 1988;81: 121–6.
[10] Sopher S, Tal A, Shahak E. Carbamate and organophosphate poisoning in early childhood. Pediatr Emerg Care 1989;5:222–5.
[11] Reigart JR, Roberts JR. Recognition and management of pesticide poisonings. Fifth edition. Washington, DC: U.S. EPA; 1999.
[12] Kiely T, Donaldson D, Grube A. Pesticide industry sales and usage: 2000–2001 market estimates. U.S. Environmental Protection Agency, Washington, DC. May 2004.
[13] American Academy of Pediatrics Committee on Infectious Diseases. Prevention of lyme disease. Pediatrics 2000;105(1):142–7.
[14] Osimitz TG, Murphy JV. Neurological effects associated with use of the insect repellent N,N-diethyl-m-toluamide (DEET). J Toxicol Clin Toxicol 1997;35(5):435–41.
[15] Sudakin DL, Trevathan WR. DEET: a review and update of safety and risk in the general population. J Toxicol Clin Toxicol 2003;41(6):831–9.
[16] American Academy of Pediatrics Committee on Environmental Health. Follow safety precautions when using DEET on children. AAP News 2003;22:99.
[17] Frankowski BL, Weiner LB. Committee on School Health the Committee on Infectious Diseases. American Academy of Pediatrics. Head lice. Pediatrics 2002;110:638–43.
[18] Frankowski BL. American Academy of Pediatrics guidelines for the prevention and treatment of head lice infestation. Am J Manag Care 2004;10(9 Suppl):S269–72.
[19] Culver CA, Malina JJ, Talbert RL. Probable anaphylactoid reaction to a pyrethrin pediculocide shampoo. Clin Pharm 1988;7:846–9.
[20] Wagner SL. Fatal asthma in a child after use of an animal shampoo containing pyrethrin. West J Med 2000;173(2):86–7.
[21] Lewis RG, Fortune CR, Blanchard FT, et al. Movement and deposition of two organophosphorus pesticides within a residence after interior and exterior applications. J Air Waste Manag Assoc 2001;51(3):339–51.
[22] Hore P, Robson M, Freeman N, et al. Chlorpyrifos accumulation patterns for child-accessible surfaces and objects and urinary metabolite excretion by children for 2 weeks after crack-and-crevice application. Environ Health Perspect 2005;113:211–9.
[23] Gurunathan S, Robson M, Freeman N, et al. Accumulation of chlorpyrifos on residential surfaces and toys accessible to children. Environ Health Perspect 1998;106(1):9–16.
[24] Fenske RA, Black KG, Elkner KP, et al. Potential exposure and health risks of infants following indoor residential pesticide applications. Am J Public Health 1990;80(6):689–93.
[25] Nishioka MG, Lewis RG, Brinkman MC, et al. Distribution of 2,4-D in air and on surfaces inside residences after lawn applications: comparing exposure estimates from various media for young children. Environ Health Perspect 2001;109(11):1185–91.
[26] Selevan SG, Kimmel CA, Mendola P. Identifying critical windows of exposure for children's health. Environ Health Perspect 2000;108(suppl 3):451–5.

[27] Lu C, Toepel K, Irish R, et al. Organic diets significantly lower children's dietary exposure to organophosphorus pesticides. Environ Health Perspect 2006;114(2):260–3.
[28] Cohen Hubal EA, Egeghy PP, Leovic KW, et al. Measuring potential dermal transfer of a pesticide to children in a child care center. Environ Health Perspect 2006;114(2): 264–9.
[29] Lu C, Fenske RA, Simcox NJ, et al. Pesticide exposure of children in an agricultural community: evidence of household proximity to farmland and take home exposure pathways. Environ Res 2000;84(3):290–302.
[30] McKelvey W, Kass D, Sorkin M, et al. Early reports from an urban pesticide tracking system: the use and misuse of pesticides in New York City. New York: Department of Health and Mental Hygiene; 2005.
[31] U.S. Environmental Protection Agency. Food Quality Protection Act of 1996. (P.L. 104-170).
[32] National Institute of Environmental Health Sciences. Children's Environmental Health Research Centers Press Release August 10, 1998 (#15–98). Available at: http://www.niehs.nih.gov/oc/news/niehsepa.htm. Accessed January 15, 2007.
[33] Daniels JL, Olshan AF, Savitz DA. Pesticides and childhood cancers. Environ Health Perspect 1997;105(10):1068–77.
[34] Zahm SH, Devesa SS. Childhood cancer: overview of incidence trends and environmental carcinogens. Environ Health Perspec 1995;103(Suppl 3):177–84.
[35] Hanke W, Jurewicz J. The risk of adverse reproductive and developmental disorders due to occupational pesticide exposure: an overview of current epidemiological evidence. Int J Occup Med Environ Health 2004;17:223–43.
[36] Garcia AM. Occupational exposure to pesticides and congenital malformations: a review of mechanisms, methods, and results. Am J Ind Med 1998;33:232–40.
[37] Shaw GM, Wasserman CR, O'Malley CD, et al. Maternal pesticide exposure from multiple sources and selected congenital anomalies. Epidemiology 1999;10:60–6.
[38] Slotkin TA. Cholinergic systems in brain development and disruption by neurotoxicants: nicotine, environmental tobacco smoke, organophosphates. Toxicol Appl Pharmacol 2004;198:132–51.
[39] Rauh VA, Garfinkel R, Perera FP, et al. Impact of prenatal chlorpyrifos exposure on neurodevelopment in the first 3 years of life among inner-city children. Pediatrics 2006;118: e1845–59.
[40] Young JG, Eskenazi B, Gladstone EA, et al. Association between in utero organophosphate pesticide exposure and abnormal reflexes in neonates. NeuroToxicology 2005;26:199–209.
[41] Slotkin TA. Guidelines for developmental neurotoxicity and their impact on organophosphate pesticides: a personal view from an academic perspective. Neurotoxicology 2004; 25(4):631–40.
[42] Merchant JA, Naleway AL, Svendsen ER, et al. Asthma and farm exposures in a cohort of rural Iowa children. Environ Health Perspect 2005;113:350–6.
[43] Salameh PR, Baldi I, Brochard P, et al. Respiratory symptoms in children and exposure to pesticides. Eur Respir J 2003;22:507–12.
[44] Salam MT, Yu-Fen L, Langholz B, et al. Early life environmental risk factors for asthma: findings from the children's health study. Environ Health Perspect 2004;112:760–5.
[45] Karmaus W, Kruse H. Infections and atopic disorders in childhood and organochlorine exposure. Arch Env Health 2001;56:485–92.
[46] Sunyer J, Torrent M, Muñoz-Ortiz L, et al. Prenatal dichlorodiphenyldichloroethylene (DDE) and asthma in children. Environ Health Perspect 2005;113:1787–90.
[47] Environmental Working Group. Shoppers guide to pesticides in produce. Washington, DC. Available at: http://www.foodnews.org/walletguide.php. Accessed June 10, 2006.