Chapter 4
Children and Pesticides

Introduction

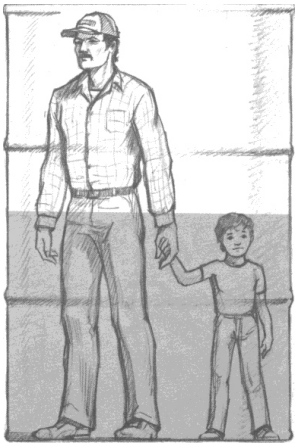
Children are not mini-adults. Under similar conditions of exposure, they respond differently to toxic chemicals. Children have more skin surface for their size; because of this larger surface-to-volume ratio, their metabolic rate is higher, and their oxygen consumption greater – 7 ml/kg body weight/min compared to 3.5 ml/kg for adults. Their respiratory rate is higher, which allows more particles to deposit into their upper and lower air passages Their immune systems are less mature, and they differ from adults in pathways of absorption, tissue distribution, and the ability to biotransform and eliminate chemicals [1,2,3 4].

During the fetal stage, a major pathway of absorption is the placenta. Most pesticides readily cross the placenta and can affect the developing child[5]. Fetal skin lacks keratin, the protective layer which is a major barrier to xenobiotic penetration. Newborn skin is highly absorptive since keratinization occurs over the three to five days following birth. Serious poisonings and deaths have occurred in newborn infants from percutaneous absorption of xenobiotics, including hexachlorophene[6], and diapers washed in a sodium pentachlorophenate solution[7]. Kidney function at birth is a fraction of normal, and glomerular filtration gradually increases to adult levels by about one year of age. Newborns do not concentrate urine at levels similar to adults until about 16 months of age[8].

Exposure

Children's exposure to pesticides includes not only residues in foods they regularly eat and drink, but often more importantly, to pesticide used in the home, lawn, or garden, or products applied directly to them such as lice treatments, and insect repellents. There are additional exposures at day care, schools, playgrounds, parks, swimming pools, and other locations.

Pesticides applied inside the home contaminate carpets, sofas, mattresses, and other household furnishings. Pesticide applied outside can be tracked in and incorporated into house dust. Both are a major source of exposure to infants and toddlers, who ingest particles adhering to food, surfaces in the home, and the skin, as well as absorption through the skin.



Vincent Perez/Artist

Under similar conditions of exposure children will absorb more than adults.

Farm worker children have additional exposures from the pesticide residues their parents carry home on their clothing, skin, hair, tools, and in their vehicles. Many live in close proximity to heavily sprayed agricultural crop areas.

Infants and toddlers are frequently placed on the floor or carpet, or on grass. Therefore, they have much more exposure to pesticide residues from flea bombs, and other applications. The breathing zone for an adult is typically four to six feet above the floor. A child's breathing zone is closer to the floor. Heavier chemicals and large respirable particulates settle out within these lower zones. Air concentrations of pesticides have been found to be higher closer to the floor[9]. Using home foggers according to label directions can result in levels of pesticide exposure to children that exceed EPA standards for children, and workplace standards for adults.

Very young children indulge in extreme oral exploratory behavior where they place everything they grasp into their mouths. A study of mouthing behavior found that children two years old and younger put things into their mouths twice as much as children older than two–81 mouthing events per day versus 42 (exclusive of eating). There were no differences between boys and girls[10]. Children are also much more likely to come in contact with contaminated

surfaces because of their "job" of exploring; nor can infants remove themselves from a toxic environment.

Risk to small children (age 1-6; mean body weight 16 kg) is usually estimated using the chronic oral reference dose (RfD) and assuming a daily intake of 100 mg of house dust [11,12]. Comparison with the maximum concentrations reviewed for chlorpyrifos, DDT, and diazinon indicates that the tolerable exposure concentration in house dust might be exceeded and that chlorpyrifos especially can be considered as a potential hazard to householders.

Tables 1 and 2 summarize findings of exposure studies in farm worker children and from home and other environmental exposures respectively. Table 3 shows the results in children of the testing of the general population for background levels of pesticide residues in blood and urine. Figure 1 shows that levels are higher in children for metabolites of commonly used pesticides.

Table 1
Pesticide Exposure in Farm Children

California children 1-3 years old[13]		Maximum farm worker children	0.44 ug/m
Of 33 pesticides % detected house dust	30.3%	Maximum controls	0.10 ug/m
Diazinon farm worker homes (4)	0.7-169 ppm	Higher in younger children - trend	p = 0.060
Non-farm worker homes (3)	0.2-2.5 ppm	Higher in younger vs older siblings	p = 0.040
Overall median	1 ppm	Live less than 200 ft from orchard	Incr. p=0.036
Chlorpyrifos farm worker homes (3)	0.2-33 ppm	US farmworker children play areas[©] [16]	
Non-farm worker homes (2)	< 1 ppm	House dust OPs[(d)]	< lod[(e)]-17,000ppm
Overall median	< 0.5 ppm	Play area soil	< lod[(e)]- 930 ppm
All other pesticides	< 2 ppm	Household dust detection	62% samples
Diazinon, chlorpyrifos per hands	20-220 ng	Homes containing at least one OP	> 1,000 ppm
Washington children agric. sprayers[14]	Absorbed /day	Control homes, all levels	< 1000 ppm
6- to 8-week spraying season	0-36 ug/kg	All 4 OPs lower non-farm homes	p < 0.05
> USEPA chronic dietary RfD	56%	Azinphosmethyl dust found in homes	100%
> WHO ADI azinphosmethyl	19%	US Children 9 months to 6 years old[17]	Median ug/g
> Phosmet reference values	< 10%	Dust - farm children	1. 92
Phosmet single dose estimates	0 -72 ug/kg	Dust - controls	0.27 p<0.001
> EPA acute RfD azinphosmethy	26%	Urine metabolites - farm children	0.05 ug/g creat
Urine adjusted volume vs creatinine	Greater	Urine metabolites controls	.01 ug/g p=.09
> Empirically derived NOELs	No estimates	Higher in children 200 ft of orchard	p=0.01
Washington orchard applicators' chn ≤6 yrs[15]	Median ug/m	Farm children OPs on hands (10 of 61)	16.4%
DMTP[(b)] detectable in 47%	0.021	Control children on hands	0%
Controls detectable in 27%	0.005p = .015		

(a) Dialkylphosphates, metabolites of organophosphates (OPs). **(b)** DMTP = dimetylthiophosphate, OP metabolite. **[c]** 26 farm, 22 farm worker, 11 non-farm families within 200 feet apple/pear orchard; non-farm ¼ mile or more.away.**(d)** Limit of detection,the smallest amount that can be found by the method used. **(e)** Organophosphates: azinphosmethyl, chlorpyrifos, parathion, phosmet.

Table 2
Pesticide Exposure in Children - Home, Other Non-Occupational

Canada boric acid (H_3BO_3) on toys[18]		
Pediatric LOAEL[(a)]		300 mg/kg bwt
MTD[(b)]		3 mg/kg bwt
MAC[©]		9.1 mg/kg toy
Italy children 6-7 yrs DAPs[(d)] urine[19]		geo. mean nmol/g cr
DMP detected in 96%		117 (7.4-1,472)
DMTP detected in 94%		104 (4-1,526)
DMDTP detected in 34%		14 (3.3-755)
DEP detected in 75%		33 (5.1-360)
DETP detected in 48%		16 (3.1-285)
DEDTP detected in 12%		7.7 (2.3-140)
Compared to adult levels		Signif. higher
UK chlorpyrifos home rx % NOEL[(e)20]		0.26-2.1%
US Arkansas children's urine[21]		Median
2,5-dichlorophenol[(f)] in 96%		9 ppb
Pentachlorophenol in 100%		14 ppb
2,4,5-trichlorophenol		1 ppb
Chlor. phenols, phenoxy herb.		LOD[(g)] 1 ppb
6 pesticides samples detected		> 10%
3 dichlorophenols detected		27%
2,4-D samples detected		20%
US Calif. Chlorpyrifos[(m)] in urine[22]	>	in parents
Chlorpyrifos infants/small chn[23]		0.0005 mg/kg/d
Cumulative OPs children		0.003 mg/kg/d
US MN[(h)] urine metabolites[24,25,26]		Pop. mean ug/l
Carbamates (1-Napthol)		3.9 (2.5-5.3)
Compared to adult levels		Lower
Malathion (MDA)		1.7 (1.1- 2.3)
Chlorpyrifos (3,5,6-TCPy)		9.6 (7.8-11)
Compared to adult levels		Much higher
Urban areas		7.2
Nonurban areas		4.7 p = 0.036
US MN[(h)] Dursban 3-7 hrs post appl.[27]		
Infant breathing zone/no ventilat.		94 ug/m^3
Infant zone ventilated room		61 ug/m^3
Infant dose[(l)] day of appl.		0.08-0.16 mg/kg
Day following application		0.04-0.06 mg/kg
US National homeowner use[28]		
Diazinon indoor inhalation		0.5 ug/kg/day
Chlorpyrifos outside perimeter		0.05 ug/kg/day
Ingestion carpet dust		0.01 ug/kg/day
Infant mouthing contribution		1-1.5 ug/kg/day
Estimates for chlorpyrifos		> EPA RfD[(j)]
Estimates for diazinon		< EPA RfD[(j)]
US National lawn-applied herbicides[29]		
Track-in by children, shoes		37x >
US Nat. PCP[(g)] log home chn v adts[30]		1.8 x > sig.
US Nat. chlorpyrifos infants,children[31]		0.0005 mg/kg-d
Cumulative organophosphates		0.003 mg/kg-d
US NC day care centers[32]		
Inhalation rates		8.3 m^3/day
Soil ingestion children 3-5 years		Lowest %
Oral dose - playing with toy		61%
Potential acute dose		356 ug/kg/day
US NJ Dursban toy dose 3-6 yrs-old[33]		208 ug/kg/day
Inhalation exposure		Negligible
Dermal dose		39%
US Texas 1% lindane treatment[34,35]		
Detected in blood after application		2-48 hours
Weight, surface area		Inversely related
Quantity of lindane applied.		Indep. related
US Texas home use chn 6 —5 yrs[36]		
Indoor air 9 homes detections		100%
Carpet dust amount / level		Highest found
23 of the 30 target pesticides[(l)]		Detected
US Seattle children 2-5 yr[37]		mean ug/mol/L
No garden use		0.09 p=.0.05
DETP[(d)] garden use		0.04
DETP[(d)] no garden use		0.03 p=0.02
At least one DAP[(d)] found		99%
DMTP and DETP[(d)]		70-75%
Pet, indoor residential use		No sig diff
Season, sex, age, income		No sig diff
DMTP[(d)] entire cohort		0.11 ug/mol/L
DETP[(d)] entire cohort		0.04 ug/mol/L
DMTP[(d)] garden use		0.19 ug/mol/L

(a) No Observable Effect Level for decreased plasma cholinest-erase (marker of organophosphate exposure). **(b)** Maximum tolerated dose. **[c]** Maximum allowable concentration. **(d)** Dialkylphosphates (see Appendix C). **(e)** No observable effect level. **(f)** Metabolite of para-dichlorobenzene, the active ingredient in moth balls, many consumer products. **(g)** Limit of detection, the smallest amount that can be found by the method used **(h)** MCPES: Miinnesota Children's Pesticide Exposure Study: probability-based sample 102 children 3-13 summer of 1997, 1-3 per urine samples per child. **(l)** 1.2 to -5.2 times the human NOEL. **(j)** Reference dose. **(k)** Pentachlorophenol, a wood preservative. **(l)** Most frequently detected Chlordane, chlorpyrifos, dieldrin, hepatachlor, pentachlorophenol. **(m)** Application by fogger, broadcast spray, crack-and-crevice treatment.

Table 3
Pesticide Residues in Blood and Urine - Children
Geometric Mean by Age
Source: National Health and Nutrition Examination Survey (NHANES) 1999-2000[38]

Chemical	Units	All ages	Age 6-11	Age 12-19
DMTP Metabolite of organophosphate pesticides	ug/g creat.	1.64	2.95	1.71
DEPMetabolite of organophosphate pesticides	ug/g creat.	0.924	1.43	0.818
3,5,6-TCPy trichloropyridinol chlorpyrifos (Dursban) metabolite	ug/g creat.	1.58	3.11	1.6
beta-HCH beta-Hexachlorcyclohexane isomer in lindane	ng/g lipid	15.0	NC*	NC*
p.p'-DDE metabolite of DDT	ng/g lipid	260	NC*	118
T**NA** trans-Nonachlor a metabolite of chlordane	ng/g lipid	18.3	NC*	NC*
2,4-6 TCP trichlorophenol [(a)]	ug/g creat.	2.54	4.82	2.4
1-Naphthol metabolite of carbaryl (Sevin)	ug/g creat.	1.52	NC*	1.04
2-Naphthol metabolite of naphthalene [(b)]	ug/g creat.	0.421	NC*	0.285
2,5-DCP 2,5-dichlorophenol , metabolite of PDB [c]	ug/g creat.	5.38	8.17	3.95
OPP ortho-phenylphenol fungicide and disinfectant	ug/g creat.	0.441	0.547	0.342

* NC = Not calculated. Proportion of results <limit of detection was too high to provide a valid result.
(a) A metabolite of several pesticides including lindane and hexachlorobenzene. **(b)** Other sources of this metabolite include tobacco smoke, and certain pollyaromatic hydrocarbons. **[c]** Paradichlorobenzene (mothballs). PDB is also used in many other consumer products.

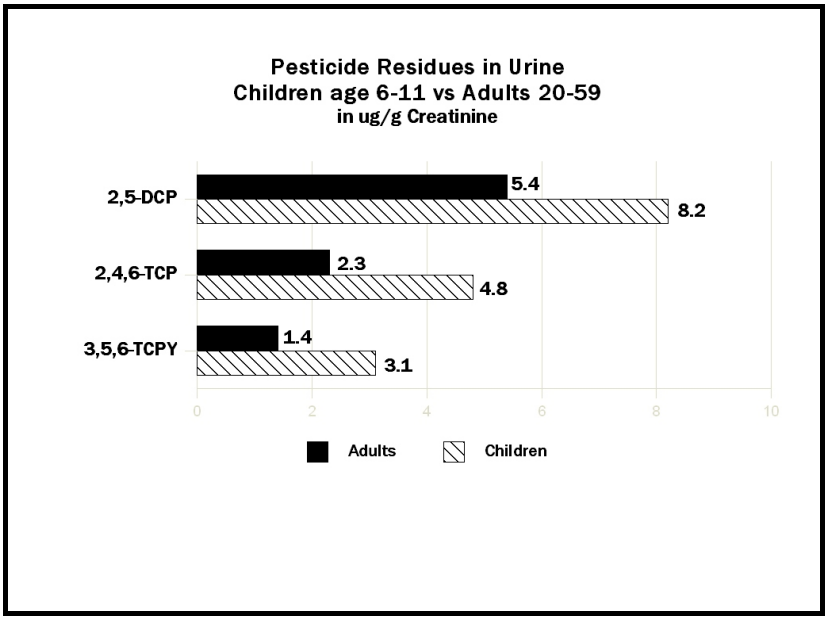


Figure 2. 2,5-DCP (2,5-dichlorophenol, metabolite of paradichlorobenzene active ingredient in mothballs). **2,4,-TCP** (2,4-trichlorophenol, a metabolite of several pesticides including hexachloro-benzene and lindane). **3,5,6-TCPy** (3,5,6-trichloropyridinol, a metabolite of chlorpyrifos.

Acute Poisoning

Deaths from pesticide poisoning in children have declined significantly in the U.S. since the 1950s. In California from 1951-1965, 128 deaths were attributed to poisoning from pesticides and other agricultural chemicals, of which 76 (59.4%) were children[39]. In North Carolina rom 1990 to 1993, 29% of the hospitalizations for pesticide poisoning were children; in South Carolina from 1971 to 1996, 28% to 37% were children. Most poisonings occur in toddlers about one year of age. Pesticide-related fatalities in children have steadily decreased for the last 20 years[40].

Organophosphate and N-methyl carbamate poisoning

Several infant poisonings from the organophosphate diazinon have been reported. A 12-week-old infant girl developed persistent hypertonicity of the extremities. Not until she was eight months old was it discovered that five weeks prior to the onset of symptoms, her home had been treated with an excessive application of diazinon. Six months after application diazinon residue remaining on the floor was 230 ng/cm^2, compared to 38 ng/cm^2 expected immediately after a normal application. Vacuum cleaner dust contained 1,700 parts per million of diazinon, and the air contained 2.8 ng/m^3. The infant's urine contained 60 parts per billion of the diazinon metabolite diethylphosphate, and 20 parts per billion of diethylthiophosphate for a dose of approximately 0.02 mg/kg/d of diazinon. When the infant was removed from the home, muscle tone returned to normal shortly thereafter[41].

Three week old twins were hospitalized with progressive respiratory distress which started about eight hours before. One twin was cyanotic, both were afebrile but had rapid, shallow breathing, profuse nasal and bronchial secretions and pinpoint pupils. They were treated with atropine and discharged after five days. The home had been sprayed by a licensed exterminator with a 1% diazinon solution for cockroach control on the morning of the day before the twins were hospitalized. The mother and three other children were out of the premises most of the day and remained well. The twins' immobility and age made them more vulnerable[42].

Transient bilateral vocal cord paralysis was reported in a three year old child who accidentally swallowed chlorpyrifos[43]. A poisoning with the organophosphate demeton-S-methyl was reported recently in a two year old[44]. Several cases of amitraz poisoning were reported in children from 2-1/2 to 6 years old , 30 to ninety minutes after accidental ingestion of an improperly stored liquid pesticide. Signs and symptoms were unconsciousness and drowsiness in all cases, myosis in 84% bradycardia in 45%, respiratory insufficiency 27%, and hypotension in 18%. All responded to treatment with atropine within eight to 14 hours and were discharged within 48 hours[45,46]. There are also other reports of amitraz poisoning in children[47],[48]

Caksen H, Odabas, D, Arslan S, et al. 2003. Report of eight children with amitraz intoxication. Hum Exp Toxicol 22(2):95-97.

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ABSTRACT: Many pesticides are formulated in organic solvents. An example is amitraz, one of the formamidine groups of pesticidal chemicals. It is commonly used for the treatment of generalized demodicosis in dogs and for the control of ticks and mites in cattle and sheep. In this article, the clinical and laboratory findings of eight children with amitraz intoxication are reviewed. The purpose was to enlighten the findings of amitraz intoxication in children. Of the eight patients, five (62.5%) were boys, three (37.5%) were girls, and the ages ranged from 1 to 4 years. All children accidentally ingested amitraz orally, with no dermal exposure. The most common observed signs were decreased consciousness and bradycardia. Leukocytosis, hyperglycemia, hypernatremia, increased serum aspartate transaminase level, and prolonged partial prothrombin time were diagnosed in children. None of the children had hypothermia, hypotension, or convulsion and none of the patients died. The findings show that the initial signs and symptoms of acute amitraz intoxication appeared severe but they disappeared, with only supportive care needed in most cases within a few days.

A report of pesticide poisoning in 37 infants and children, found that 76% were poisoned by ingesting an improperly stored liquid pesticide, and 14% after playing on carpets and floors of homes that had been sprayed or fogged by unlicensed exterminators. The most common signs and symptoms were miosis (73%), excessive salivation (70%), muscle weakness (68%), lethargy (54%) and tachycardia (49%), Seizures developed in 22%, and 38% required endotracheal intubation and mechanical ventilation. They responded to treatment with atropine and/or pralidoxime, and there were no deaths. Pneumonitis and/or atelectasis developed in ten patients, including six who had ingested a

petroleum distillate-containing insecticide[49].

Of 36 children and 24 adults who ingested rat poison containing methomyl or aldicarb, the children's signs and symptoms differed significantly from adults, although serum cholinesterase depression was similar. The predominant symptoms in young children were central nervous system depression and hypotonia. The most common muscarinic effect was diarrhea. In adults, the main signs were miosis and fasciculations, which were less frequent in children. Central nervous system depression, hypotonia, and diarrhea were uncommon in adults[50]. The clinical presentation of carbamate and organophosphate poisoning in early childhood and response to therapy differs from those of adults and older children[51].

A review of 5,541 children admitted to pediatric intensive care of a university hospital from 1990 to 2000, found 54 (1%) with cholinesterase inhibitor insecticide poisoning. Complications included coma (31%), seizures (30%), shock (9%), arrhythmias (9%), and respiratory failure requiring ventilation (35%). No significant differences were found in the incidence of seizures, cardiac arrhythmias, respiratory failure, mortality, duration of ventilation, or PICU stay, according to route of exposure, or state of decontamination. Four children died (7%). Mortality was associated with the presence of a cardiac arrhythmia (likelihood ratio 8.3) and respiratory failure (likelihood ratio 3.3)[52].

Acute pancreatitis was found in five children in a prospective study of 17 consecutive children with typical organophosphate and carbamate poisoning. They had significantly elevated serum levels of both immunoreactive trypsin, amylase, and glucose compared to other patients and controls. None had hypocalcemia, renal dysfunction, or acidosis, and all recovered completely[53].

Sood A, Midha V, Sood N. 2003. Gastric outlet obstruction as a late complication of ingestion of diazinon. Indian J Gastroenterol 22(3):106-107.
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ABSTRACT: Acute gastrointestinal symptoms are known to occur with organophosphorus compounds poisoning. Delayed complication in the form of gastric outlet obstruction has not been reported to date. We report gastric outlet obstruction developing after diazinon ingestion in a young girl. She responded to endoscopic balloon dilatation.

Permethrin poisoning
Permethrin is considered to have a low potential for poisoning. Severe permethrin toxicity was reported in three siblings aged 9, 7 and 19 months treated for head lice with a 1.0% permethrin cream rinse. The children's bedding was then saturated with 3 canisters of 0.5% permethrin spray, and two pounds of 0.25% permethrin powder was sprinkled throughout the home. Over the next 3 days all five family members developed mild diarrhea and emesis. The 19-month female developed progressive gastrointestinal symptoms and cough attributed to an infection. On day four she presented with agitation, ataxia, seizures, fasiculations, cardiac conduction blockade, and respiratory failure due to severe pulmonary edema. An infectious disease work-up was negative, and the permethrin exposure was elucidated the day of ICU admission. Surface swab testing of the family's home for permethrin revealed 2.4 ppm in the parent's bedroom, 277 ppm in the child's upholstered chair, 15.3 ppm in the family room carpet, 70.9 ppm in the child's bedroom carpet, 9.7 ppm in the child's toys, and 2 ppm in the kitchen. Only mild effects were noted in two adults and two older siblings[54].

Lindane poisoning
There is a recent report of poisoning in toddlers from accidental ingestion of lindane, in which a 17- month-old girl suffered a single seizure. A 3-year-old boy was listless, nauseated, pale, and had decreased responsiveness to verbal and tactile stimulation. A 4-year-old girl became nauseated and required bag-valve-mask ventilation for hypoventilation. All three recovered without apparent sequelae[55]. A follow-up study of 41 children less than five years old, acutely poisoned by lindane ingestion, found one child with a persistent seizure disorder[56].

Boric acid poisoning
Boric acid solution was inadvertently used to dilute concentrated formula and fed to 24 day old and 14 month old siblings, who developed irritability, diarrhea, and perineal erythema in the 24 day old. The 24 day old was treated with peritoneal dialysis, both recovered completely without sequelae. The total amount ingested was 2.6 g in the 24

day old (peak level 146 ug/ml), and 1.95 g in the 14 month old (peak levels 56 ug/ml)[57].

Other pesticide poisonings

Poisoning with the phenoxy herbicide MCPA in a three month old child successfully treated with plasmapharesis was reported[58]. Most cases of paraquat poisoning and deaths in children are from accidental ingestion[59,60,61,62,63]. Homicide by paraquat was reported in two children who presented with gastrointestinal ulceration and acute respiratory distress, and pneumomediastinitis. Bullous emphysema was a common autopsy finding [64]. Attempted homicide with the herbicide imazapyr (Arsenal) involving a child was also reported[65]. Illegal pesticides continue to be a source of poisoning of children[66,67].

Report from Iran show that most non-occupational pesticides poisonings are in children less than six, and more boys are poisoned than girls[68]. In Costa Rica children less than five accounted for 39.2% pesticide poisoning cases in 1997, and the prevalence was the same in boys and girls[69].

Barrueto F Jr, Furdyna PM, Hoffman RS, et al. 2003. Status epilepticus from an illegally imported Chinese rodenticide: "tetramine". J Toxicol Clin Toxicol 41(7):991-994.

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ABSTRACT: INTRODUCTION: The following case report demonstrates the severe consequences of refractory convulsive status epilepticus from an unfamiliar imported toxin, tetramethylenedisulfotetramine (TETS), and the difficulties of identifying the offending agent.

CASE REPORT: A previously healthy 15-month-old girl was found by her parents playing with a white rodenticide powder brought from China. Fifteen minutes later, the child developed generalized seizures and was brought to an Emergency Department (ED). Her initial fingerstick blood glucose was 108 mg/dL. In the ED, the child was intubated for status epilepticus. Despite aggressive therapy with lorazepam, phenobarbital, and pyridoxine, she had 4 h of intermittent generalized seizure activity. She was extubated on the third hospital day, but appeared to have absence seizures and cortical blindness. Continuous electroencephalogram monitoring, performed weeks later, revealed severe diffuse cerebral dysfunction with multiple epileptogenic foci. The child remains developmentally delayed and is on valproic acid therapy for seizure control. Translation of the Chinese package labeling did not clarify its contents. Tetramethylenedisulfotetramine was finally confirmed by gas chromatography-mass spectrometry (GC-MS) in this rodenticide product and then quantified against a TETS standard that was synthesized in our laboratory.

CONCLUSION: Tetramethylenedisulfotetramine is grouped with other "cage convulsants," such as picrotoxin, since they have a similar intercalating cyclical molecular structure and cause seizures through non-competitive gamma-aminobutyric acid (GABA) antagonism. The oral lethal dose 50% (LD50) in humans is estimated to be as low as 100 microg/kg. Our patient has severe diffuse cerebral dysfunction likely secondary to prolonged seizure activity after exposure to TETS.

Poisoning in working children

There are almost no data on pesticide poisoning in working children. A survey of eight states and poison control centers found 531 youths with acute occupational pesticide-related illnesses. Most were related to insecticides (68%), and most were of minor severity (79%). The average annual incidence rate among youths aged 15 to 17 years was 20.4 per billion hours worked, and the incidence rate ratio among youths compared to adults was 1.71 (1.53, 1.91)[70]. A study of pesticide signs and symptoms among farmers' families in five agricultural communities in rural El Salvador, found detectable levels of organophosphate metabolites in nearly half of 358 samples, 30% in those who did not work in agriculture. The levels were similar for children and adults[71].

Deet poisoning (N-N-diethyltoluamide, OFF!, Skintastic)

It is estimated that deet is used on 23-29% of children annually in the U.S[72]. A poison control study of deet related calls found that the greatest number of reported exposures involved infants and children, but this group experienced lower rates of adverse effects than teens or adults[73]

Deet is very toxic to the brain and nervous system. Signs and symptoms of mild poisoning include headache,

restlessness, irritability, crying spells and other changes in behavior. In more severe poisoning there can be slurring of speech, tremor (shakiness), convulsions, and coma. Deet has caused death in children from absorption through the skin when it was applied repeatedly and/or in a high concentration. There is a report of a five year old child at a day camp who had a major seizure (convulsion) without any other symptoms shortly after deet was applied to his skin.

A review of 17 cases of toxic encephalopathy in children (56% girls) found it occurred not only after ingestion or repeated and extensive application, but also from brief exposure to a product containing 45% deet. Of the skin application cases, 33% were in a product containing less than 20%t. The review described a case in an 18-month-old boy following brief exposure to 17.6% deet[74].

Four healthy boys three to seven years old, who had never had a seizure or neurologic problem, developed seizures eight to 48 hours after three or less applications of deet at a summer camp. One boy who had a rash before his seizure developed a rash to the dilantin medication used to control the seizures[75]. A five year old girl, sprayed with deet nightly for three months, developed headaches and slurred speech, progressing to staggering gait, shaking, screaming, and seizures, and episodes of stiffening into sitting position, extending extremities, flexing fingers and dorsiflexing toes. She died 24 days later. At autopsy the brain showed generalized edema with intense congestion of meninges. The same author reported another case in an 18 month old who ingested an unknown amount of liquid deet. She displayed extreme irritability and bizarre movements, but her condition improved steadily [76].

A 5-year-old boy with mild developmental delay , experienced a major motor seizure at day camp after topical application that morning and later in the day of deet. His seizures continued in the emergency room and were eventually brought under control with diazepam[77]. A case report of seizures and coma which developed in a child two hours after accidental ingestion of a low dose of deet. (80 mg/kg). He recovered without sequelae[78] Seizures and acute behavior change developed in an 8-year-old girl following exposure to deet, with recover in three days after anticonvulsant medication[79]. A one year old child died after development of seizures and coma one hour after accidental ingestion of a large amount of concentrated deet[80].A case was reported of a four year old boy with mental retardation, impaired sensorimotor coordination, and craniofacial dysmorphology, whose mother applied deet daily throughout her pregnancy, in addition to taking the anti-malaria drug chloroquine prophylactically[81].

A Reye-like syndrome was reported in a 6 year old girl with extensive exposure to deet who was deficient in ornithine carbamoyl transferase (OCT). This deficiency delayed metabolism of deet in the liver and removal from the body, increasing its toxic effect. The author suggest that other cases of deet related toxic encephalopathy might also have suffered from OCT deficiency[82].

Generalized urticaria has also been reported[83].

Asthma: Pesticide exposure, even at low levels, can trigger severe reactions among persons with asthma, especially children. However there is almost no epidemiological data on pesticide exposure as an independent risk factor for asthma in children. A fatality associated with sudden irreversible bronchospasm from a pyrethrin shampoo was reported[84].

Wheezing among Iowa farm children has been associated with herbicide exposure[85], but other studies show farmer's children to be at lower risk of allergic disease, including hay fever[86, 87].

A study in New Zealand found no adverse effects on asthmatic children from community spraying of Bacillus thuringiensis (BT)[88]. In a pesticide fire, respiratory symptoms in the affected surrounding community were highest in preschool children and asthmatics[89]

Cancer in Children: Childhood cancer, notably leukemia, brain cancer, non-Hodgkin's lymphoma, soft tissue sarcoma, and Hodgkin's disease, has been associated with pesticide exposure, often with greater relative risks than among exposed adults, suggesting greater susceptibility in children. These differences in risk may be due to developmental factors or differences in pesticide exposure.

In 1983, there were reports of "too many children with cancer" in the small agricultural town of McFarland in Kern County, California. From 1982 to 1985, when one case of cancer was expected, there were eight children with cancer: two cases of acute lymphocytic leukemia, two of soft tissue sarcoma, and one case each of Wilms' tumor, brain cancer, non-Hodgkin lymphoma, and osteosarcoma. Most were children of farm workers.

Six years later, there was a report of another cancer cluster in farm worker children in Earlimart, a town in Tulare county 14 miles north of McFarland. From 1986 to 1989, when less than 2 cases were expected, there were six children with cancer: three cases of acute lymphocytic leukemia, and one case each of Wilm's tumor, lymphoma, and soft tissue sarcoma. All were children of farm workers. Both McFarland and Earlimart were confirmed as cancer clusters by the State of California Department of Health Services.[1]

Cancer in Children	
Leukemia	30%
Brain and spinal cord	21%
Neuroblastoma	7.3%
Wilm's tumor	5.9%
Hodgkin disease	4.4%
Non-Hodgkin lymphoma	4.0%
Soft tissue sarcoma	3.4%
Retinoblastoma	2.8%
Osteosarcoma	2.7%
Ewing sarcoma	1.8%

More pesticides are used in the San Joaquin Valley where the children live, than any other area in California. pesticide use area in California. A large percentage of the pesticides used are known or suspect carcinogens (see Appendix B). Infants and young children are the most vulnerable to adverse health effects of pesticides. They can be affected by levels that are not toxicologically significant in adults. Children are less likely to have exposure to other to toxic substances such as alcohol, tobacco, and drug then adults. The amount of time between exposure and adverse chronic effects is much shorter in children. It is therefore not surprising that some of the highest pesticide related cancer risks are seen in children.

At the time of the discovery of a cancer cluster in McFarland in 1983, there were no studies of pesticide exposure as a risk factor for cancer in children. There are now many studies reporting that parent's work, home, and other exposure to pesticides, can increase the risk of cancer in their children. The types of cancer are the same as those first reported in the farm worker children.

The following discussion summarizes the findings in studies of cancer in children potentially related to pesticides. As discussed earlier, it includes only study results that were statistically significant, and some of borderline significance. Because the source and type of exposure affects risk, the summary discusses cancer in children in two categories: occupational exposure of their parents (see Tables 1,3), and home and other non-occupational exposures (see Table 2,3). The citations are in the tables.

Bone Cancer

Reported risks are higher for Ewing's sarcoma than for osteosarcoma. An 880% increase in Ewing's sarcoma was found in children if the father was a farm worker, and a 780% increase if the mother was a farm worker exposed to pesticides. A borderline significant increase was found if the father was a farmer. A 390% increase in risk of osteosarcoma was found if the parents were farmers. There are no reports of risk for home or other non-occupational exposures.

Brain Cancer

A 1,080% increase found if there was prenatal home use of pet flea/tick sprays and foggers is the highest reported. A 620% increase was found if there was home use of aerosol bombs and foggers, and increases for use of pet flea collars, termite treatment, and pest strips. A 480% increase found for Kwell (lindane) treatment of head lice was borderline significant. nother study found a smaller increase for home use of pest strips.

Leukemia

The highest reported risk is a 1,240% increase in acute non-lymphocytic leukemia (ANLL) in children whose parents

[1] (1) California DHS. 1988. Epidemiologic Study of Adverse Health Effects in Children in McFarland, California, Phase II Report. Epidemiological Studies and Surveillance Section. Berkeley, California, January 19, 1988. (2) Coye MJ, Neutra R. Investigation of the Earlimart childhood cancer cluster. California DHS Environmental Health Investigations Branch. Berkeley, California.

had prolonged exposure to pesticides at work. There are several reports of an increase in acute lymphocytic leukemia (ALL) if the mother was exposed at work. A 650% Increase in ALL was found for parents' use of home garden pesticides at least once a month, with an additional 250% increase if the mother was the user. Indoor use of pesticides more than once a week almost quadrupled the risk. A 280% increase was found for commercial home extermination during pregnancy in the first three years of life, and a 360% increased risk if the home was treated in the second year after birth.

Non-Hodgkin Lymphoma
The highest reported risk is a 1,380% increase if the mother was exposed to pesticides at work during pregnancy. Frequent home use increased risk 730%[32]. Non-Hodgkin Lymphoma is the type of cancer most frequently found in adults with pesticide exposure.

Neuroblastoma
Over 200% increased risk was found if the parents were farmers, if the parents were exposed to insecticides at work,, and for home garden use if the child was younger than one year of age[33].

Soft Tissue Sarcoma
An increase in this rare type of cancer was found if the mother was a farmer, and for home yard pesticide use[24].

Wilm's Tumor
A study in Brazil, which has one of the highest rates of Wilm's tumor in the world, found a very high risk if the parents were farmers or farm workers. A lower increase was found for commercial home extermination.

Other Cancers
A 1,000% increase in the risk of retinoblastoma was found if the maternal grandparents were farmers. Having farmer parents increased the risk of eye cancer, Hodgkin's disease, and non-seminoma testicular cancer.

Other Conditions
Sudden Infant Death Syndrome (SIDS)
A study of 34 unexplained infant deaths and 72 controls done in homes illegally sprayed with methyl parathion, found that SIDS infants were 4.6 times more likely to have lived in an illegally treated home, but the confidence interval was very wide. Methyl parathion was detected in wipe samples (>0.02 mg/100 cm^2) in five homes, three previously occupied by case infants. The authors conclude the association was not statistically significant and should be interpreted cautiously[90].

Chlorinated hydrocarbon pesticide residues (hexachlorbenzene, alpha, beta and gamma hexachlorcyclohexane, heptachlor epoxide, dieldrin, total DDT) were measured in subcutaneous fat of SIDS cases from rural and urban areas and controls. No significant differences were found[91].

An autopsy study of 54 SIDs cases and 108 controls in which tissue levels of arsenic, lead, cadmium, mercury, and pentachlorphenol were measured in several organs, found no differences between SIDS cases and controls. Nor was there a correlation between infections of the respiratory system and higher concentrations of these agents in the organs of SIDS cases[92].

Table 3
Parents' Agricultural and Other Occupational Pesticide Exposures and Increased Cancer Risk in Children
(See Appendix F for explanation of the table)

Bone Cancer	
Australia father a farmer[(a)93]	OR 3.5 bs*
Child lived on a farm	OR 1.6 bs*
Canada maternal farm pesticide exposure[(a)94]	OR 7.8
Norway farmer parents[(b)95]	RR 2.9
US California father an agricultural worker[(a)96]	OR 8.8
Father exposed pesticides, fertilizers	OR 6.1
Brain Cancer	
Europe father works in agriculture[97]	OR 2.2 bs*
France child lived on a farm[98]	OR 6.7
Germany wood preservative[99]	OR 3.28
Norway pesticide purchases[3]	RR 1.6
Parents pig farmers (all)	RR 1.59
Parents pig farmers[©)]	RR 3.11
Grain farming[©)]	OR 1.72
Grain farmers (all)	RR 1.29 bs*
Sweden parental exposure[(d)100]	OR 2.36
US maternal prenatal exposure to pigs[(e)101]	OR 11.9
Child prenatal exposure to pigs	OR 3.0
Child farm residence	OR 3.8
Maternal exposure to pigs	OR 4.0
Maternal prenatal exposure to poultry	OR 3.0
Child prenatal exposure to poultry	OR 2.2
Maternal exposure horses in pregnancy	OR 2.2 bs*
US/Canada[(f)] farm residence[(g)] > 1 year[(e)102]	OR 5.0
Eye Cancer	
Norway farmer parents[3]	OR 3.17
US/Canada[(h)] maternal grandparents farmers[103]	OR 10.0
Hodgkin Disease	
Norway farmer parents[2]	RR 2.68
Kidney Cancer	
England/Wales parental pesticide exposure[104]	PMR 1.59
Leukemia	
China pesticide exposure during pregnancy[105]	OR 3.5
Germany pest. exposure during pregnancy[106]	OR 3.6
Maternal exposure ever	OR 2.5
Paternal exposure ever	OR 1.6
Pesticide use on farms	OR 1.5 bs*
Germany maternal occupational exposure[107]	Increase
Italy farmer parents[108]	Increase
Japan prenatal parental exposure[109]	Increase
Norway parents pig farmers[3]	RR 2.10
US California propargite use area[110]	OR 1.48
US/Canada[(h)] preconceptual exposure[111]	OR 2.09
US/Canada[(h)] child less than 5 years old[(l)112]	OR 11.4
Children all ages[(l)]	OR 3.8
Father exposed more than 1,000 days	OR 2.7 bs*
Non-Hodgkin Lymphoma	
Germany exposure during pregnancy[14]	OR 11.8
Maternal pesticide exposure ever	OR 4.1
Paternal pesticide exposure ever	OR 1.9 bs*
Neuroblastoma	
Norway farmer parents[3]	RR 2.51
US New York maternal exposure insecticides[113]	OR 2.3
Paternal exposure to creosote	OR 2.1
US/Canada father a landscaper[114]	OR 2.3 bs*
Soft Tissue Sarcoma	
Italy maternal occupation as a farmer[16]	Increase
Testicular Cancer	
Norway farmer parents[3]	SIR 1.25
Fertilizer use	RR 2.44
Non-seminoma type	RR 4.21
Wilm's Tumor	
Brazil father a farm worker[115]	OR 3.24
Mother a farm worker[(j)]	OR 128
Father exposed, diagnosed age less than 2	OR 4.0
Mother exposed, diagnosed age less than 4	OR 14.8
Father exposed, boys	OR 8.56
Norway farmer parents[3]	RR 8.87

* bs = borderline significance

(a) Ewing sarcoma. **(b)** Osteosarcoma **[c]** Nervous system tumors **(d)** Non-astrocytic neuroepithelial type only **(e)** Primitive neuroectodermal **(f)** Retinoblastoma **(g)** The Children's Cancer Study Group, a collaboration between the U.S.: CO, DC, IL, IN, IA, MI, MN, NJ, NY, NC, OH, OR, PA, TN, TX, UT, WI, and Canada: BC, NS, ONT. **(h)** One year before to 3 years after birth. **(I)** Parent exposed more than 1,000 days **(j)** Based on a very small number of cases.

Table 4
Home, Garden, Pet, and other Pesticide Exposures
Increased Cancer Risk in Children
(See Appendix F for explanation of table)

Brain Cancer	
France home treatment in childhood[7]	OR 2.0 bs*
US Denver pest strip use[116]	OR 1.8[(a)]
US Los Angeles flea/tick foggers, sprays only[117]	OR 10.8
Prenatal exposure child < age 5 at diagnosis	OR 5.4
Not following label instructions	OR 3.7
Treating more than 1 pet (trend significant)	OR 3.5
Child less than age 5 at diagnosis	OR 2.5
Mother applied product, cleaned up	OR 2.2
Use of any type of pet flea/tick products	OR 1.7
US Missouri use bombs and foggers[118]	OR 6.2
Any termite treatment	OR 5.2
Pet flea collar use	OR 5.5
Pest strip use	OR 4.4
Kwell /lindane head lice treatment	OR 4.8 bs*
Garden/orchard insecticide use	OR 4.6 bs*
Garden use diazinon	OR 4.6
Garden use carbaryl	OR 3.0
Yard herbicide use	OR 2.6
US Ohio home use during pregnancy[119]	Increase
Leukemia	
England/Wales propoxur use mosquito control[120]	OR 9.7
Germany (West) home and garden use[14]	OR 2.5 bs*
US California professional extermination[(b)121]	OR 2.8[e]
Second year after birth	OR 3.6
Insecticide use during pregnancy	OR 2.1
Insecticide use 3 months prior to pregnancy	OR 1.8
US Los Angeles garden use by mother[122]	OR 9.0
Garden use once per month either parent	OR 6.5
Father's use indoors	OR 4.0
Indoor use more than once a week	OR 3.8
Mother's use indoors	OR 3.2
US Denver pest strip use[24]	OR 3.0[©)]
Pest strip use	OR 1.7[(d)]
Pest strip use	OR 2.6[(a)]
US/Canada postnatal rodenticide use[19]	OR 1.8
US St. Jude Hospital garden use[123]	OR 2.1
Non-Hodgkin Lymphoma	
Germany professional home treatment[14]	OR 2.6
US St. Jude Hospital garden use	X^2 17.2
US Denver home extermination[24]	OR 1.8[(d)]
US/Canada frequent home use[124]	OR 7.3[(e)]
Home extermination	OR 3.0
Post natal exposure	OR 2.4
Neuroblastoma	
US/Canada home garden use[125]	OR 2.2[f]
Mother applied pesticide	OR 2.2
Garden herbicide use	OR 1.9
Ant, roach product use	OR 1.8 bs*
Pesticide use in garden	OR 1.7 bs*
Pesticide use in home	OR 1.6 bs*
Soft Tissue Sarcoma	
US Denver yard pesticide use[24]	OR 3.9[(a)]
Wilm's Tumor	
US/Canada home extermination ever[126]	OR 2.16
Home extermination once a year	OR 2.41
Home extermination more than twice a year	OR 2.19

* bs = borderline significance

(a) Two years prior to diagnosis through diagnosis. **(b)** One year before to 3 years after birth. **[c]** In the last three months of pregnancy. **(d)** Birth through 2 years prior to diagnosis. **(e)** Trend significant for use on most days. **(f)** Child less than age 1 at diagnosis.

Table 5
Pesticide Exposure a nd Cancer in Children
Decreased Risk or No Associations Found
(See Appendix F for information of table)

Parental Occupational Exposure		Home, Garden, Other Exposure	
All Types of Cancer		**Brain Cancer**	
US California agricultural pesticide use[18]	OR 0.95	Australia home pesticide use[35]	No association
Brain		Germany pesticide exposure[7]	No association
Australia living on a farm[127]	Decrease	US Los Angeles head lice treatment[25]	No association
Germany parents exposed to pesticides[7]	No association	Yard and garden use	No association
Leukemia		**Leukemia**	
Canada father chlorophenate (sawmills)[128]	No association	US Denver yard treatment[24]	OR 0.9[(a)]
Sweden parental pesticide exposure[8]	No association	**Non-Hodgkin Lymphoma**	
Non-Hodgkin Lymphoma		Germany garden pesticide use[14]	OR 0.8
Germany farm pesticide use[14]	OR 0.5	**Soft Tissue Sarcoma**	
Testicular		US Denver yard treatment[24]	OR 0.8 [(b)]
Denmark parents in agriculture[129]	No association		
Child lived on a farm	No association		
Wilm's Tumor			
Germany parental pesticide exposure[7]	No association		

(a) Birth through 2 years prior to diagnosis.
(b) In the last three months of pregnancy

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