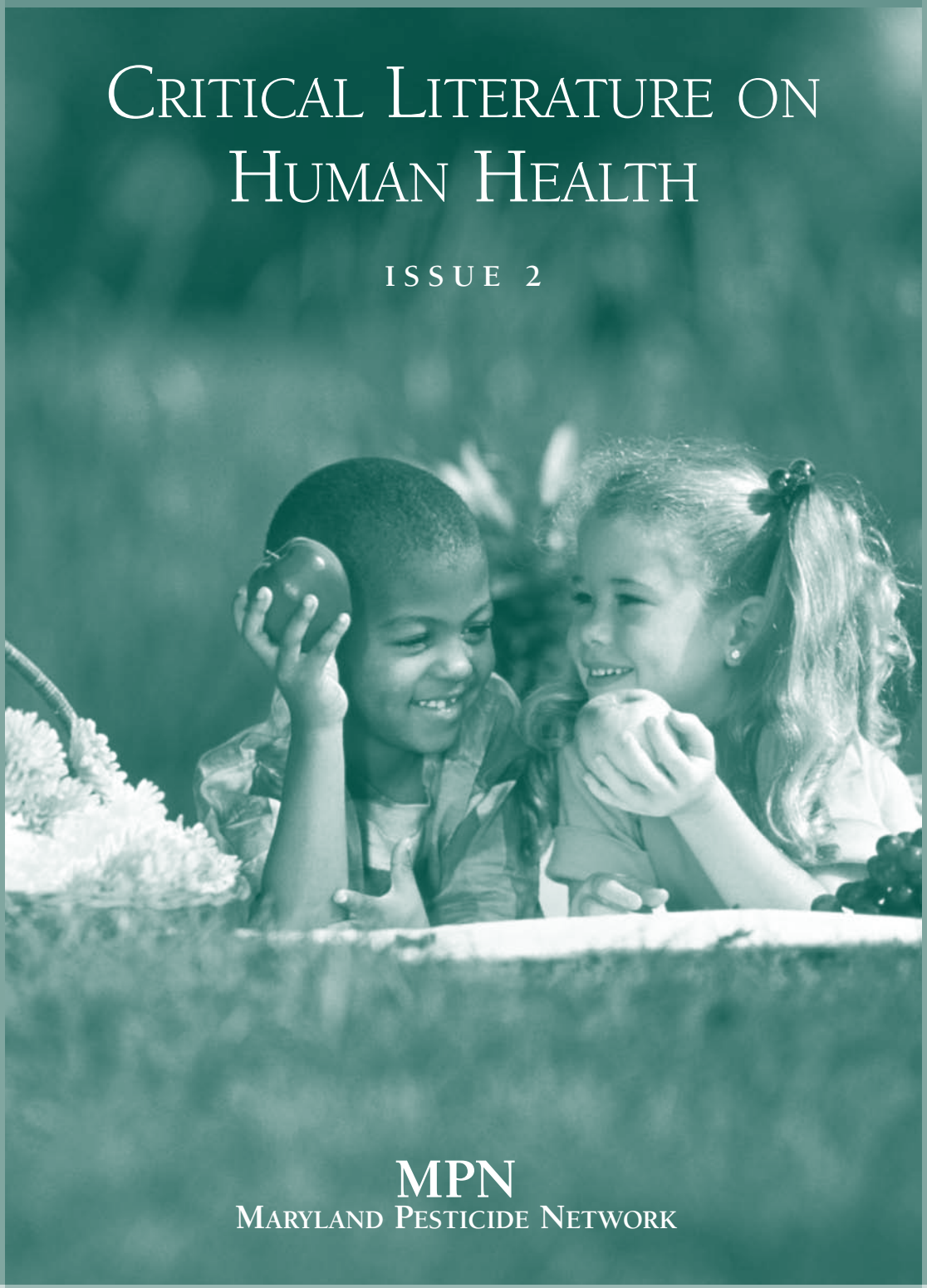
Pesticides and Public Health

Critical Literature on Human Health

ISSUE 2



MPN
Maryland Pesticide Network

FALL 2007

MARYLAND DEPARTMENT OF HEALTH AND MENTAL HYGIENE
John M. Colmers, Secretary

COMMUNITY HEALTH ADMINISTRATION
Peter A. Sybinsky, Ph.D., Director
Richard W. Stringer, Deputy Director

ENVIRONMENTAL HEALTH COORDINATION PROGRAM
Clifford S. Mitchell, MS, MD, MPH, Director

September 1, 2007

Dear Health Care Provider:

Under Maryland regulation, health care providers are required to report cases of known or suspected pesticide-related illnesses to the health department (Code of Maryland Regulations 10.06.01.03). Like contagious diseases, pesticide-related illnesses are potentially preventable, and the keys are early recognition and surveillance. Your assistance can help prevent pesticide-related illness, by helping us to develop more effective and targeted interventions and educational campaigns. In addition, by providing reports to the health department, you increase our ability to detect trends and focus our attention on at-risk populations.

I hope you will look at the information we have assembled on pesticide-related illnesses by visiting our web page, at http://www.cha.state.md.us/oeh/html/pesticide.html. The page also describes how to report pesticide-related illness, including our on-line report form. It takes only a short time to complete and submit a report, but the information you provide is vital in our efforts to eliminate pesticide-related illness. If you have any questions, please contact the Environmental Health Coordination Program at the Department of Health and Mental Hygiene.

Thank you for your assistance.

Clifford S. Mitchell, MS, MD, MPH
Director, Environmental Health Coordination Program

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[Editor's Note: Please see p. 27 for more information regarding mandatory injury reporting]

Fall 2007

Dear Health Care Provider:

Welcome to the second edition of *Pesticides and Public Health: Critical Literature on Human Health*. This Journal is designed to keep you current about the latest research on this critical issue as well as relevant news. In this edition we have expanded our coverage to include studies dealing with the relationship of pesticide exposures to psychiatric disorders.

Our patients and communities are exposed to pesticides through air, food and water, or through dermal absorption. Thousands of pesticide products exist for many uses. In addition to insect, rodent and landscape management, pesticides are also used in antimicrobial hand soaps, cosmetics and cleaning products. Yet the impact of cumulative pesticide exposure and the synergistic effects of exposure to multiple pesticides and other chemicals are rarely considered in the registration process, which typically only assesses the risks of exposure to an individual pesticide. Initial research indicates that neurological, endocrine, immune or developmental effects increase when combined exposures are studied. The full health impact of multiple exposures to any one pesticide, or to multiple pesticides over an extended time, remains unknown.

U.S. EPA has yet to fulfill its mandated evaluation of pesticides for their role as endocrine disruptors. "Inert" ingredients generally make up the largest percentage of a pesticide product or formulation. Some inert ingredients may be just as or even more toxic as the active ingredient, yet the law allows these materials to remain undisclosed to the public because they are considered "trade secrets." The data required by EPA for inerts is much less stringent than for active pesticide ingredients.

Given the multiple pathways of exposures, the inadequate federal oversight regarding registered pesticides and the growing body of research on the impacts of pesticides on public health, it is critical for our professional community to be educated on the potential adverse effects of pesticides, as well as safer alternatives, so that we can advise our patients and communities on limiting exposures and on using safer and least-toxic alternatives.

We look forward to your feedback. Please help us better serve your needs by completing the enclosed survey or sending feedback via email to info@mdpestnet.org. We also encourage you to contact us with any questions or suggestions.

Respectfully,

The Maryland Pesticide Network Health Care Provider Committee

Ruth Berlin, LCSW-C
Lorne K. Garrettson, M.D. (Chair)
Richard L. Humphrey, M.D.
Lawrence A. Plumlee, M.D.
Jo Ann Schropp, R.N., M.S.N.

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The following abstracts regarding pesticides and public health studies are peer-reviewed epidemiological studies chosen for their relevance to health care providers and public health professionals.

Comments following each abstract are provided by Pediatrician and Medical Toxicologist Lorne K. Garrettson (L.K.G.), M.D., Chair of Maryland Pesticide Network's Health Care Provider committee; and the committee members: Psychotherapist Ruth Berlin (R.B.), L.C.S.W.-C., Oncologist Richard L. Humphrey (R.L.H.), M.D., Physician Lawrence A. Plumlee (L.A.P.), M.D., and Psychiatric Nurse Jo Anne Schropp (J.A.S.), R.N., M.S.N. (For additional information, see page 29, MPN Health Care Provider Committee members.)

PEDIATRICS

MATERNAL RESIDENCE NEAR AGRICULTURAL PESTICIDE APPLICATIONS AND AUTISM SPECTRUM DISORDERS AMONG CHILDREN IN THE CALIFORNIA CENTRAL VALLEY

Eric M. Roberts[1], Paul B. English[2], Judith K. Grether[2], Gayle C. Windham[2], Lucia Somberg[3], and Craig Wolff[2]

[1] *Public Health Institute, Oakland, CA*
[2] *California Department of Health Services, Richmond, CA*
[3] *School of Public Health, University of California, Berkeley, CA*

Background: Ambient levels of pesticides ("pesticide drift") are detectable at residences near agricultural field sites.

Objective: To evaluate the hypothesis that maternal residence near agricultural pesticide applications during key periods of gestation could be associated with the development of Autism Spectrum Disorders (ASD) in children.

Methods: We identified 465 children with ASD born during 1996-1998 using the California Department of Developmental Services electronic files and matched them by maternal date of last menstrual period to 6,975 live born, normal birthweight, term infants as controls. Proximity to pesticide applications was determined using California Department of Pesticide Regulation records refined using Department of Water Resources land use polygons. A staged analytic design applying a priori criteria to the results of conditional logistic regressions was employed to exclude associations likely due to multiple testing error.

Results: Of 249 unique hypotheses, four that described organochlorine pesticide applications—specifically those of dicofol and endosulfan—occurring during the period immediately prior to and concurrent with CNS embryogenesis (clinical weeks 1 through 8) met a priori criteria and were unlikely to be a result of multiple testing. Multivariate a posteriori models comparing children of mothers living within 500 m of field sites with the highest non-zero quartile of organochlorine poundage to those with mothers not living near field sites suggested an odds ratio for ASD of 6.1 (95%-confidence interval 2.4-15.3). ASD risk increased with poundage of organochlorine applied and decreased with distance from field sites.

Conclusions: The association between residential proximity to organochlorine pesticide applications during gestation and ASD among children should be further studied.

Environmental Health Perspectives. doi:10.1289/ehp.10168. Online 30 July 2007.

Comment: *Using high-powered epidemiological analysis, the authors have been able to dissect the exposure-disease connection of ASD and pesticides in a most compelling manner. While this pesticide-disease link doesn't appear to hold the only answer for the rise in ASD in the population, it creates a focus for study that will surely be forthcoming. The association was only made with organochlorine (OC) pesticides. We will want to know why the association wasn't seen when OC's were the dominant insecticides in use and were used widely in domestic settings. We will look for studies of the mechanism of effect of the two OC's implicated in this study with neural development. Because of the complexity of the epidemiological analysis, we will look for the critiques that will follow to see if there are significant holes in the authors' logic. What we may not see is a replication of this study because the quality and size of the data set used will just not be available anywhere but in California. The cause of ASD has been sought for years. We have eliminated lead and mercury as significant contenders. While it seems unlikely that OC's can offer the whole answer, they may be a part of the answer and may lead to further insight on the timing and nature of environmental triggers that are linked to the disease. –L.K.G.*

EARLY-LIFE ENVIRONMENTAL RISK FACTORS FOR ASTHMA: FINDINGS FROM THE CHILDREN'S HEALTH STUDY

Salam MT, Li YF, Langholz B, Gilliland FD; Children's Health Study.

Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California 90033, USA.

Early-life experiences and environmental exposures have been associated with childhood asthma. To investigate further whether the timing of such experiences and exposures is associated with the occurrence of asthma by 5 years of age, we conducted a prevalence case-control study nested within

the Children's Health Study, a population-based study of > 4,000 school-aged children in 12 southern California communities. Cases were defined as physician-diagnosed asthma by age 5, and controls were asthma-free at study entry, frequency-matched on age, sex, and community of residence and countermatched on in-utero exposure to maternal smoking. Telephone interviews were conducted with mothers to collect additional exposure and asthma histories. Conditional logistic regression models were fitted to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Asthma diagnosis before 5 years of age was associated with exposures in the first year of life to wood or oil smoke, soot, or exhaust (OR = 1.74; 95% CI, 1.02-2.96), cockroaches (OR = 2.03; 95% CI, 1.03-4.02), herbicides (OR = 4.58; 95% CI, 1.36-15.43), pesticides (OR = 2.39; 95% CI, 1.17-4.89), and farm crops, farm dust, or farm animals (OR = 1.88; 95% CI, 1.07-3.28). The ORs for herbicide, pesticide, farm animal, and crops were largest among children with early-onset persistent asthma. The risk of asthma decreased with an increasing number of siblings (ptrend = 0.01). Day care attendance within the first 4 months of life was positively associated with early-onset transient wheezing (OR = 2.42; 95% CI, 1.28-4.59). In conclusion, environmental exposures during the first year of life are associated with childhood asthma risk.

Environmental Health Perspectives. 2004 May; 112(6): 760-5.PMID: 15121522

Comment: *The true causation of asthma, other than inheritance of atopic genes, is still poorly understood. Yet, there is a mounting body of evidence that environmental exposures can lead to the development of asthma. This study builds on that evidence. The question for care-givers will be: When do we act? It is not unreasonable in the mind of this reviewer to begin to caution pregnant women about the potential for pesticides and herbicides to have this action. There are alternative control measures for pests. The control measures for asthma need to be persistent over time and are costly and a nuisance at best. –L.K.G.*

PERSISTENT PESTICIDES IN HUMAN BREAST MILK AND CRYPTORCHIDISM

Damgaard IN, Skakkebaek NE, Toppari J, Virtanen HE, Shen H, Schramm KW, Petersen

JH, Jensen TK, Main KM; Nordic Cryptorchidism Study Group, University Department of Growth and Reproduction, Copenhagen, Denmark

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Introduction: Prenatal exposure to some pesticides can adversely affect male reproductive health in animals. We investigated a possible human association between maternal exposure to 27 organochlorine compounds used as pesticides and cryptorchidism among male children.

Design: Within a prospective birth cohort, we performed a case-control study; 62 milk samples from mothers of cryptorchid boys and 68 from mothers of healthy boys were selected. Milk was collected as individual pools between 1 and 3 months postpartum and analyzed for 27 organochlorine pesticides.

Results: Eight organochlorine pesticides were measurable in all samples (medians; nanograms per gram lipid) for cases/controls: 1,1-dichloro-2,2-bis(4-chlorophenyl) ethylene (p,p -DDE): 97.3/83.8; beta-hexachlorocyclohexane (beta-HCH): 13.6/12.3; hexachlorobenzene (HCB): 10.6/8.8; alpha-endosulfan: 7.0/6.7; oxychlordane: 4.5/4.1; 1,1,1-trichloro-2,2-bis(4-chlorophenyl) ethane (p,p -DDT): 4.6/4.0; dieldrin: 4.1/3.1; cis-heptachloroepoxide (cis-HE): 2.5/2.2. Five compounds [octachlorostyrene (OCS); pentachlorobenzene, 1,1-dichloro-2,2-bis(4-chlorophenyl) ethane(p,p -DDD); o,p -DDT; mirex] were measurable in most samples (detection rates 90.8-99.2%) but in lower concentrations. For methoxychlor, cis-chlordane, pentachloroanisole (PCA), gamma-HCH, 1,1-dichloro-2-(2-chlorophenyl) -2,2(4-chlorophenyl) ethane, trans-chlordane, alpha-HCH, and o,p -DDE, both concentrations and detection rates were low (26.5-71.5%). Heptachlor, HCH (lc delta, epsilon), aldrin, beta-endosulfan and trans-heptachloroepoxide were detected at negligible concentrations and low detection rates and were not analyzed further. Seventeen of 21 organochlorine pesticides [p,p -DDT, p,p-DDE, p,p-DDD, o,p-DDT, HCH (alpha, beta, gamma), HCB, PCA, alpha-endosulfan, cis-HE, chlordane (cis-, trans-) oxychlordane, methoxychlor, OCS, and dieldrin] were measured in higher median concentrations in case milk than in control milk. Apart from trans-chlordane ($p = 0.012$), there were no significant differences between cryptorchid and healthy boys for individual chemicals. However, combined statistical analysis of the eight most abundant persistent pesticides showed that pesticide levels in breast milk were significantly higher in boys with cryptorchidism ($p = 0.032$).

Conclusion: The association between congenital cryptorchidism and some persistent pesticides in breast milk as a proxy for maternal exposure suggests that testicular descent in the fetus may be adversely affected.

Environmental Health Perspectives. 2006, Jul; 114(7):1133-8. PMID: 16835070

Comment: *Many of the compounds analyzed in this study have not been used in years but are persistent organochlorine compounds. If they are causative of cryptorchidism, it appears to be an additive effect. It will not be enough to counsel avoidance for pregnant women. Humans are exposed to many environmental chemicals, some of which can persist in the body. -L.K.G.*

CONCENTRATIONS OF ENVIRONMENTAL CHEMICALS ASSOCIATED WITH NEURODEVELOPMENTAL EFFECTS IN U.S. POPULATION

Needham LL, Barr DB, Caudill SP, Pirkle JL, Turner WE, Osterloh J, Jones RL, Sampson EJ.

Organic Analytical Toxicology potentially affects neurodevelopment. Fetuses, infants, and young children are the most susceptible to the effects of these chemicals. As part of the National Health and Examination Survey, 1999-2000, the Centers for Disease Control and Prevention analyzed biological samples for many of these chemicals in a representative sampling of the U.S. population. Concentration data of selected metals, persistent organic pollutants, organophosphorus and carbamate insecticides, and cotinine are presented. For example, the 95th percentile estimates for serum total PCBs (whole weight) in the population aged 20 years and older is about 2.7 ng/g. The 95th percentile estimates for serum dioxin total toxic equivalence in the U.S. population aged 20 years and older is between 40 and 50 pg/g lipid basis. In general, human levels of these chemicals are decreasing over time in the U.S. population. This reflects the effects of legislation, industry efforts, and changes in lifestyle/activity patterns in the U.S. population. These data will continue to be collected in 2-year cycles and thus allow changes in human levels to be followed.

Neurotoxicology. 2005 Aug;26(4):531-45. Epub 2005 Jan 11. PMID: 16112319

Comment: *The biomonitoring program of the National Center for Environmental Health has now reported population analyses of environmental exposures for four cycles. They have planned to study trends but have had insufficient time to be sure of changes. This is the first analysis we have seen in which they have identified a trend. It is reassuring that the trends are generally downward on U.S. population exposures. However, pesticides are a significant part of this assessment and the report finds the following pesticides or their metabolites in greater than 50% of the subjects tested: permethrin, cypermethrin, deltamethrin, chlorpyrifos, methyl and ethyl parathion, 2,4-D, lindane, chlordane, 2,5-dichlorophenol (moth balls) and DDT. Sampling doesn't permit the identification of areas where there is no decline or even a rise in levels. But we should be thankful that the CDC has initiated this valuable program and that the first assessment of trends is favorable. –L.K.G.*

AN INTERVENTION TO REDUCE RESIDENTIAL INSECTICIDE EXPOSURE DURING PREGNANCY AMONG AN INNER-CITY COHORT

Williams MK, Barr DB, Camann DE, Cruz LA, Carlton EJ, Borjas M, Reyes A, Evans D, Kinney PL,Whitehead RD, Perera FP, Matsoanne S, Whyatt RM.

Columbia Center for Children's Environmental Health, Mailman School of Public Health, Columbia University, New York, New York 10032, USA.

Background: We previously reported widespread insecticide exposure during pregnancy among inner-city women from New York City. Here we report on a pilot intervention using integrated pest management (IPM) to reduce pest infestations and residential insecticide exposures among pregnant New York City African-American and Latina women (25 intervention and 27 control homes).

Methods: The IPM consisted of professional cleaning, sealing of pest entry points, application of low-toxicity pesticides, and education. Cockroach infestation levels and 2-week integrated indoor air samples were collected at baseline and one month post intervention. The insecticides detected in the indoor air samples were also measured in maternal and umbilical cord blood collected at delivery.

Results: Cockroach infestations decreased significantly (p= 0.016) after the intervention among intervention cases but not control households. Among the intervention group, levels of piperonyl butoxide (a pyrethroid synergist) were significantly lower in indoor air samples after the intervention (p = 0.016). Insecticides were detected in maternal blood samples collected at delivery from controls but not from the intervention group. The difference was significant for trans-permethrin (p= 0.008) and of borderline significance (p= 0.1) for cis-permethrin and 2-isopropoxyphenol (a propoxur metabolite).

Conclusion: To our knowledge, this is the first study to use biologic dosimeters of prenatal pesticide exposure for assessing effectiveness of IPM. These pilot data suggest that IPM is an effective strategy for reducing pest infestation levels and the internal dose of insecticides during pregnancy.

Environmental Health Perspectives. 2006 Nov; 114(11):1684-9. PMID: 17107853

Comments: *This is another study of integrated pest management (IPM) but this one uses biochemical monitoring to assess the level of exposure in the subjects, making it a stronger study. It is clear from this and other studies that IPM successfully controls pests. It lowers exposure which has been shown to have measurable detrimental effects on the fetus, in particular. IPM must become the standard approach to insect control with insecticides only used as a last resort and then with real controls to reduce exposure particularly of pregnant women.-L.K.G.*

PESTICIDE MEASUREMENTS FROM THE FIRST NATIONAL ENVIRONMENTAL HEALTH SURVEY OF CHILD CARE CENTERS USING A MULTI-RESIDUE GC/MS ANALYSIS METHOD

Tulve NS, Jones PA, Nishioka MG, Fortmann RC, Croghan CW, Zhou JY, Fraser A, Cave C, Friedman W.

National Exposure Research Laboratory, U.S. Environmental Protection Agency, MD-E20504, Research Triangle Park, North Carolina 27709, USA.

The U.S. Department of Housing and Urban Development, in collaboration with the U.S. Consumer Product Safety Commission and the U.S. Environmental Protection Agency, characterized the environments of young children (<6 years) by measuring lead, allergens, and pesticides in a randomly selected nationally representative sample of licensed institutional child care centers. Multi-stage sampling with clustering was used to select 168 child care centers in 30 primary sampling units in the United States. Centers were recruited into the study by telephone interviewers. Samples for pesticides, lead, and allergens were collected at multiple locations in each center by field technicians. Field sampling was conducted from July through October 2001. Wipe samples from indoor surfaces (floors, tabletops, desks) and soil samples were collected at the centers and analyzed using a multi-residue GC/MS analysis method. Based on the questionnaire responses, pyrethroids were the most commonly used pesticides among centers applying pesticides. Among the 63% of centers reporting pesticide applications, the number of pesticides used in each center ranged from 1 to 10 and the frequency of use ranged from 1 to 107 times annually. Numerous organophosphate and pyrethroid pesticides were detected in the indoor floor wipe samples. Chlorpyrifos (0.004-28 ng/cm2), diazinon (0.002-18 ng/cm2), cis-permethrin (0.004-3 ng/cm2), and trans-permethrin (0.004-7 ng/cm2) were detected in >67% of the centers. Associations exist between residues measured on the floor and other surfaces for several pesticides (p-values range from <0.0001 to 0.002), but to a lesser degree between floor and soil and other surfaces and soil. Regional analyses indicate no differences in mean level of pesticide loading between the four Census regions ($0.08 < p < 0.88$). Results show that there is the potential for exposure to pesticides in child care centers.

Environmental Science & Technology; 2006 Oct 15;40(20):6269-74. PMID 17120552

Comment: *This was an extensive analysis of exposure potential in day care facilities. The conclusion is clear: there is potential for exposure of young children. This exposure potential is increased because children of this age crawl in play and is exacerbated by their hand-to-mouth behavior. Spraying organophosphates in day care centers must be a target for education and process revision. Maryland law requires a program of integrated pest management in our schools where all non-toxic options must be exhausted or shown to be unreasonable prior to considering pesticides in order to limit the exposure of children to pesticides. However, the law does not include child care facilities. These facilities must begin to use the cheaper and equally (or more) effective pest control measures that integrated pest management provides. –L.K.G.*

A LONGITUDINAL APPROACH TO ASSESSING URBAN AND SUBURBAN CHILDREN'S EXPOSURE TO PYRETHROID PESTICIDES

Lu C, Barr DB, Pearson M, Bartell S, Bravo R.

Department of Environmental and Occupational Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, USA.

We conducted a longitudinal study to assess the exposure of 23 elementary school–age children to pyrethroid pesticides, using urinary pyrethroid metabolites as exposure biomarkers. We substituted most of the children's conventional diets with organic food items for 5 consecutive days and collected two daily spot urine samples, first morning and before bedtime voids, throughout the 15-day study period. We analyzed urine samples for five common pyrethroid metabolites. We found an association between the parents' self-reported pyrethroid use in the residential environment and elevated pyrethroid metabolite levels found in their children's urine. Children were also exposed to pyrethroids through their conventional diets, although the magnitude was smaller than for the residential exposure. Children's ages appear to be significantly associated with pyrethroids exposure, which is likely attributed to the use of pyrethroids around the premises or in the facilities where older children engaged in the outdoor activities. We conclude that residential pesticide use represents the most important risk factor for children's exposure to pyrethroid insecticides. Because of the wide use of pyrethroids in the United States, the findings of this study are important for both children's pesticide exposure assessment and environmental public health.

Environmental Health Perspectives. 2006 September; 114(9):1419–1423. PMID: 16966099

Comment: *While synthetic pyrethroids can exacerbate respiratory illnesses including asthma and may cause allergic reactions in sensitive populations, they have generally been considered to have low acute toxicity. However, because of their widespread use, it is of concern that they are suspect as carcinogens, endocrine disrupters, and may have some neurodevelopmental impact. To learn more about exposure this group has analyzed data from a large study. Their conclusions are that home exposure is the dominant source for children. This is important information in attempts to lower pesticide exposure for children. –L.K.G.*

CHRONIC FATIGUE SYNDROME AND MULTIPLE CHEMICAL HYPERSENSITIVITY AFTER INSECTICIDE EXPOSURE

Fernandez-Sola J, Padierna ML, Xarau SN, Mas PM.

Servicio de Medicina Interna. Unidad Multidisciplinar de Fatiga Cronica. Hospital Clinic de Barcelona. IDIBAPS. Universitat de Barcelona, España.

Background and objective: Chronic Fatigue Syndrome (CFS) and Multiple Chemical Sensitivity (MCS) are well-defined illnesses that may appear after some toxic exposures.

Patients and method: We report a consecutive series of 26 patients who developed CFS after exposure to insecticide products. It was associated with MCS in a third of cases.

Results: Toxic exposure was of labour origin after returning to usual work place after a process of fumigation. In 42% of cases there was no fulfillment of fumigation safety rules. The majority of patients were mean-aged women who developed an acute upper airway inflammatory syndrome, without muscarinic or nicotinic manifestations, followed by digestive syndrome, neurocognitive, fibromyalgic and chronic fatigue manifestations. The course of disease was shorter than 1 year in 5 cases (19%), longer than 1 year in 15 (58%), and disabling in 6 cases (23%).

Conclusions: Due to the possible prevention of this toxic exposure, it is very important to carefully follow measures of environment isolation and ventilation after insecticide use in order to avoid the development of these diseases.

Medicina Clinica (Barc). 2005 Apr 2;124(12):451-3. PMID: 15826581

Comment: *This study affirms several others which have found onset of multiple chemical sensitivity after insecticide exposure, including the following abstract, and one by Miller and Metzel in Arch Environ Health 1995 Mar-Apr, 50(2):119-29. Other authors have also shown some overlap between chronic fatigue syndrome and multiple chemical sensitivity: Psychosomatic Medicine 62:655-663 (2000), Arch Environ Health 1999; 54: 147–9. –L.A.P.*

A REVIEW OF A TWO-PHASE POPULATION STUDY OF MULTIPLE CHEMICAL SENSITIVITIES

Caress SM, Steinemann AC

State University of West Georgia, Pafford Building Room 121, 1601Maple Street, Carrollton, GA 30118, USA.

In this review we summarize the findings of a two-phase study of the prevalence, symptomatology, and etiology of multiple chemical sensitivities (MCS). We also explore possible triggers, the potential linkage between MCS and other disorders, and the lifestyle alterations produced by MCS. The first phase of the study consisted of a random sampling of 1,582 individuals from the Atlanta, Georgia, metropolitan area to determine the reported prevalence of a hypersensitivity to common chemicals. In this phase, 12.6% of the sample reported a hypersensitivity. Further questioning of individuals with a hypersensitivity indicated that 13.5% (1.8% of the entire sample) reported losing their jobs because of their hypersensitivity. The second phase was a follow-up questioning of the respondents who initially reported hypersensitivity. In this phase, we found that individuals with hypersensitivity experience a variety of symptoms and triggers. A significant percentage (27.5%) reported that their hypersensitivity was initiated by an exposure to pesticides, whereas an equal percentage (27.5%) attributed it to solvents. Only 1.4% had a history of prior emotional problems, but 37.7% developed these problems after the physical symptoms emerged. This suggests that MCS has a physiologic and not a psychologic etiology.

Environmental Health Perspectives. 2003 Sep;111(12):1490-7. PMID: 12948889.

Comment: *This study affirms in a much larger population the findings of C.S. Miller and H.C. Mitzel published in Arch Environ Health. 1995 Mar-Apr; 50(2):119-29. In this study, the pesticide-exposed group reported significantly greater symptom severity than did the remodeling-exposed group, especially for neuromuscular, affective, airway, gastrointestinal, and cardiac symptoms. In this Caress and Steinemann study, it is of interest that subjects reported an increase of emotional problems from 1.4% before chemical exposure to 37.7% after exposure. –L.A.P.*

GENE-ENVIRONMENT STUDY OF THE PARAOXONASE 1 GENE AND PESTICIDES IN AMYOTROPHIC LATERAL SCLEROSIS

Morahan JM, Yu B, Trent RJ, Pamphlett R.

The Stacey MND Laboratory, Department of Pathology, The University of Sydney, Sydney, NSW 2006, Australia; Department of Molecular and Clinical Genetics, Royal Prince Alfred Hospital, Australia.

Sporadic amyotrophic lateral sclerosis (SALS) causes progressive muscle weakness because of the loss of motor neurons. SALS has been associated with exposure to environmental toxins, including pesticides and chemical warfare agents, many of which are organophosphates. The enzyme paraoxonase 1 (PON1) detoxifies organophosphates and the efficacy of this enzyme varies with polymorphisms in the PON1 gene. To determine if an impaired ability to break down organophosphates underlies some cases of SALS, we compared the frequencies of PON1 polymorphisms in SALS patients and controls and investigated gene-environment interactions with self-reported pesticide/herbicide exposure. The PON1 coding polymorphisms L55M, Q192R and I102V, and the promoter polymorphisms -909c>g, -832g>a, -162g>a and -108c>t, were genotyped in 143 SALS patients and 143 matched controls. Statistical comparisons were carried out at allele, genotype and haplotype levels. The PON1 promoter allele-108t, which reduces PON1 expression, was strongly associated with SALS. Overall, promoter haplotypes that decrease PON1 expression were associated with SALS, whereas haplotypes that increase expression were associated with controls. Coding polymorphisms did not correlate with SALS. Gene-environment interactions were identified at the allele level for some promoter SNPs and pesticide/herbicide exposure, but not at the genotype or haplotype level. In conclusion, some PON1 promoter polymorphisms may predispose to SALS, possibly by making motor neurons more susceptible to organophosphate-containing toxins.

Neurotoxicology. 2007 May;28(3):532-40. Epub 2006 Nov 26. PMID: 8766847.

Comment: *Lockridge and Masson predicted the importance of detoxification enzyme variants in increasing the risk of toxic damage in illnesses of neurotoxic origin (Arch Environ Health. 2001 May-Jun:56(3):196-207). Further, correlations of multiple chemical sensitivity with detoxification variants were reported in the International Journal of Epidemiology 2004;33:1¬8. –L.A.P.*

NEUROLOGICAL AND PSYCHOLOGICAL DISORDERS

PESTICIDE EXPOSURE AND RISK FOR PARKINSON'S DISEASE

Ascherio A, Chen H, Weisskopf MG, O'Reilly E, McCullough ML, Calle EE, Schwarzschild MA, Thun MJ.

Department of Nutrition, Harvard School of Public Health, Boston, MA, USA.

Objective: Chronic, low-dose exposure to pesticides is suspected to increase the risk for Parkinson's disease (PD), but data are inconclusive.

Methods: We prospectively examined whether individuals exposed to pesticides have higher risk for PD than those not exposed. The study population comprised participants in the Cancer Prevention Study II Nutrition Cohort, a longitudinal investigation of US men and women initiated in 1992 by the American Cancer Society. Follow-up surveys were conducted in 1997, 1999, and 2001. The 143,325 individuals who returned the 2001 survey and did not have a diagnosis or symptoms of PD at baseline (1992) were included in the analyses.

Results: Exposure to pesticides was reported by 7,864 participants (5.7%), including 1,956 farmers, ranchers, or fishermen. Individuals exposed to pesticides had a 70% higher incidence of PD than those not exposed (adjusted relative risk, 1.7; 95% confidence interval, 1.2-2.3; p = 0.002). The relative risk for pesticide exposure was similar in farmers and nonfarmers. No relation was found between risk for PD and exposure to asbestos, chemical/acids/solvents, coal or stone dust, or eight other occupational exposures.

Interpretation: These data support the hypothesis that exposure to pesticides may increase risk for PD. Future studies should seek to identify the specific chemicals responsible for this association.

Annals of Neurology. 2006 Aug;60(2):197-203. PMID: 16802290

Comment: *See p. 7 (left column).*

DEVELOPMENTAL EXPOSURE TO THE PESTICIDE DIELDRIN ALTERS THE DOPAMINE SYSTEM AND INCREASES NEUROTOXICITY IN AN ANIMAL MODEL OF PARKINSON'S DISEASE

Richardson JR, Caudle WM, Wang M, Dean ED, Pennell KD, Miller GW.

Center for Neurodegenerative Disease, School of Medicine Emory University, Atlanta, Georgia 30322, USA.

Exposure to pesticides has been suggested to increase the risk of Parkinson's disease (PD), but the mechanisms responsible for this association are not clear. Here, we report that perinatal exposure of mice during gestation and lactation to low levels of dieldrin (0.3, 1, or 3 mg/kg every 3 days) alters dopaminergic neurochemistry in their offspring and exacerbates MPTP toxicity. At 12 weeks of age, protein and mRNA levels of the dopamine transporter (DAT) and vesicular monoamine transporter 2 (VMAT2) were increased by perinatal dieldrin exposure in a dose-related manner. We then administered MPTP (2x10 mg/kg s.c) at 12 wk of age and observed a greater reduction of striatal dopamine in dieldrin-exposed offspring, which was associated with a greater DAT:VMAT2 ratio. Additionally, dieldrin exposure during development potentiated the increase in GFAP and alpha-synuclein levels induced by MPTP, indicating increased neurotoxicity. In all cases there were greater effects observed in the male offspring than the female, similar to that observed in human cases of PD. These data suggest that developmental exposure to dieldrin leads to persistent alterations of the developing dopaminergic system and that these alterations induce a "silent" state of dopamine dysfunction, thereby rendering dopamine neurons more vulnerable later in life.

FASEB J. 2006 Aug;20(10):1695-7. Epub 2006 Jun 29. PMID: 16809432

Comment: *The large epidemiological study (Alberto Ascherio et.al) extends the data that explores the link between pesticide exposure and Parkinson's disease. Other studies have shown similar correlation between exposure and risk. While a low relative risk, the incidence of the disease makes the exploration of this relationship a compelling exercise. Lacking in previous discussions of the Parkinson's disease-pesticide relationship has been a possible mechanism. The second paper provides a new idea in this dilemma. If this hypothesis proves to be true, and the human behaves like the rat, this is a developmental toxicity that does not manifest until later in life. – L.K.G.*

NEUROLOGIC SYMPTOMS IN LICENSED PRIVATE PESTICIDE APPLICATORS IN THE AGRICULTURAL HEALTH STUDY

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Exposure to high levels of many pesticides has both acute and long-term neurologic consequences, but little is known about the neurotoxicity of chronic exposure to moderate levels of pesticides. We analyzed cross-sectional data from 18,782 white male licensed private pesticide applicators enrolled in the Agricultural Health Study in 1993-1997. Applicators provided information on lifetime pesticide use and 23 neurologic symptoms typically associated with pesticide intoxication. An indicator of more symptoms (> or = 10 vs. < 10) during the year before enrollment was associated with cumulative lifetime days of insecticide use: odds ratios (95% confidence intervals) were 1.64 (1.36-1.97) for 1-50 days, 1.89 (1.58-2.25) for 51-500 days, and 2.50 (2.00-3.13) for > 500 days, compared with never users. A modest association for fumigants [> 50 days, 1.50 (1.24-1.81)] and weaker relationships for herbicides [> 500 days, 1.32 (0.99-1.75)] and fungicides [> 50 days, 1.23 (1.00-1.50)] were observed. Pesticide use within the year before enrollment was not associated with symptom count. Only associations with insecticides and fumigants persisted when all four pesticide groups were examined simultaneously. Among chemical classes of insecticides, associations were strongest for organophosphates and organochlorines. Associations with cumulative exposure persisted after excluding individuals who had a history of pesticide poisoning or had experienced an event involving high personal pesticide exposure. These results suggest that self-reported neurologic symptoms are associated with cumulative exposure to moderate levels of fumigants and organophosphate and organochlorine insecticides, regardless of recent exposure or history of poisoning.

Environmental Health Perspectives. 2005 Jul;113(7):877-82. PMID: 16002376

Comment: *While based on an analysis of self-reported data, this study supports the association of neuropsychologic symptoms, such as depression, with "cumulative lifetime exposure" to frequently used classes of pesticides. Health care and mental health workers should include questions about pesticide exposure when taking medical history for psychological as well as physical problems. – J.A.S.*

DEPRESSION AND PESTICIDE EXPOSURES IN FEMALE SPOUSES OF LICENSED PESTICIDE APPLICATORS IN THE AGRICULTURAL HEALTH STUDY COHORT

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Objective: This nested case-control study evaluated the association between depression and pesticide exposure among women.

Methods: The study population included 29,074 female spouses of private pesticide applicators enrolled in the Agricultural Health Study between 1993 and 1997. Cases were women who had physician-diagnosed depression requiring medication. Lifetime pesticide use was categorized as never mixed/applied pesticides, low exposure (up to 225 days), high exposure (>225 days), and a history of diagnosed pesticide poisoning.

Results: After adjustment for state, age, race, off-farm work, alcohol, cigarette smoking, physician visits, and solvent exposure, depression was significantly associated with a history of pesticide poisoning (odds ratio [OR] = 3.26; 95% confidence interval [CI] = 1.72-6.19) but not low (OR = 1.09; CI = 0.91-1.31) or high (OR = 1.09; 95% CI = 0.91-1.31) cumulative pesticide exposure.

Conclusion: *Pesticide poisoning may contribute to risk of depression.*

Journal of Occupational and Environmental Medicine. 2006 Oct;48(10):1005-13. PMID: 17033500

Comment: *This study underscores that mental illness can be caused or exacerbated by a single event of pesticide poisoning as well as long-term exposure, as noted in the spouses' depressive symptoms resulting from "cumulative lifetime exposure" (see previous study). This study also establishes the importance of taking an environmental exposure history when treating patients diagnosed with depression. Again, questions concerning pesticide use and exposure gain added significance. –J.A.S.*

HEALTH EFFECTS OF DIAZINON ON A FAMILY

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There is increasing evidence of permanent sequalae from acute organophosphate poisoning. We report on accidental diazinon overexposure with acute organophosphate poisoning through cutaneous absorption and inhalation followed by persistent neurological effects. In addition, we observed skeletal and endocrine effects likely attributable to the diazinon poisoning. A family of seven was exposed to diazinon in June 1999 over a two-day period. The pesticide company mistakenly used diazinon to heavily spray the inside of the home instead of permethrin. The applicator applied the pesticide over the entire surface of the floor, carpeting, furniture, and clothing in closets to eradicate an infestation of fleas. Acute symptoms in the family members included headaches, nausea, skin irritation, runny nose, and vomiting. The family was first evaluated at 3 months and then 3 years after the acute poisoning. There were persisting neurological symptoms of memory loss, decreased concentration, irritability, and personality changes of varying degrees in all family members. Objective neurological findings of impaired balance, reaction time, color vision, slotted pegboards and trials making were present in the three older children who could be tested. Neuropsychological evaluation revealed evidence of organic brain dysfunction in all seven family members. Bone growth difficulties are present in four of five children. One child has delayed menarche.

Journal of Toxicology. 2004;42(5):579-91. PMID: 15462149

Comment: *This study is indicative of the potential long-term neuropsychological effects of pesticide poisoning. Home owners are often falsely reassured that the products used by pest control companies are "safe." In fact, it is against federal law (Federal Insecticide, Fungicide, and Rodenticide Act) for a pest control company or pesticide manufacturer to claim that any pesticide is "safe." Health care and mental health providers need to educate their patients about the hazards of pesticides and safer alternatives. While pesticides can cause a variety of acute symptoms, the seriousness of the neuropsychological effects three years later (decreased concentration and memory, mood swings, and personality changes) impacted this family's personal, social, and family development. –J.A.S.*

SUICIDE AND EXPOSURE TO ORGANOPHOSPHATE INSECTICIDES: CAUSE OR EFFECT?

London L, Flisher AJ, Wesseling C, Mergler D, Kromhout H.

Occupational and Environmental Health Research Unit, School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa.

Background: Suicide using pesticides as the agent is recognized as a major cause of pesticide poisoning.

Methods: A literature review of mortality and morbidity studies related to suicide among pesticide-exposed populations, and of human and animal studies of central nervous system toxicity related to organophosphate (OP) pesticides was performed.

Results: Suicide rates are high in farming populations. Animal studies link OP exposure to serotonin disturbances in the central nervous system, which are implicated in depression and suicide in humans. Epidemiological studies conclude that acute and chronic OP exposure is associated with affective disorders. Case series and ecological studies also support a causal association between OP use and suicide.

Conclusions: OPs are not only agents for suicide. They may be part of the causal pathway. Emphasizing OPs solely as agents for suicide shifts responsibility for prevention to the individual, reducing corporate responsibility and limiting policy options available for control.

American Journal of Industrial Medicine, 2005 Apr;47(4):308-21. PMID: 15776467

Comment: *This literature review further implicates that pesticides, in this case organophosphates, can cause severe depression resulting in suicide. While it is well known that pesticides are a poison of choice in suicide, the authors' review of science and public policy indicate that there is a need to shift responsibility back to the pesticide industry in its production of pesticides that may cause affective disorders. A thought-provoking call for further study of suicide as a result of pesticide-implicated depression. –J.A.S.*

MOTOR INHIBITION AND LEARNING IMPAIRMENTS IN SCHOOL-AGED CHILDREN FOLLOWING EXPOSURE TO ORGANOPHOSPHATE PESTICIDES IN INFANCY

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Despite the critical role of acetylcholinesterase (AChE) in cortical function and development, no long-term studies have been conducted in humans on the long-term sequelae of the disruption of the cholinergic system in early childhood. We report a neuropsychological assessment of healthy school-aged children, who had been hospitalized in infancy following exposure to organophosphate pesticides, compared with children exposed to other toxins such as kerosene, and age- and sex-matched non-exposed children. Although overall, the children seem to have overcome the acute one-time exposure incident, and they all attend regular schools, a finer assessment of specific cognitive abilities indicates they are impaired compared with the matched controls. Specifically, the children who had been exposed to organophosphate pesticides had a deficit in inhibitory motor control. Children with pesticide or kerosene poisoning had a retrieval deficit on the acquisition phase of a verbal learning task.

Pediatric Research, 2006 Jul; 60(1):88-92. PMID: 16788088

Comment: *Limiting factors for this study were its small size, and tester knowledge as to which children had been exposed. However, this study is part of a growing body of research linking pesticides to poor school performance and aggressive behavior. In 1998, Elizabeth Guillette, Ph.D, associate research scientist at the University of Florida, conducted a comparison study of preschool children in two communities with similar genetic backgrounds, diets, cultural patterns and social behaviors in the Yaqui Valley of Mexico. (An Anthropological Approach to the Evaluation of Preschool Children Exposed to Pesticides in Mexico; Environmental Health Perspectives, Volume 6, #106, June 1998) The children of the pesticide-intensive agrarian region were compared to children living in the foothills, where pesticide use is avoided. In comparison, functionally, the exposed children demonstrated decreases in stamina, gross and fine eye-hand coordination, 30-minute memory, the ability to draw a person and increased aggressive behavior. This study provides a basis for additional long term studies in a diagnostic category (ADHD) affecting many children. –R.B., J.A.S.*

IMPACT OF PRENATAL CHLORPYRIFOS EXPOSURE ON NEURODEVELOPMENT IN THE FIRST 3 YEARS OF LIFE AMONG INNER-CITY CHILDREN

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Objective: The purpose of this study was to investigate the impact of prenatal exposure to chlorpyrifos on 3-year neurodevelopment and behavior in a sample of inner-city minority children.

Methods: As part of an ongoing prospective cohort study in an inner-city minority population, neurotoxicant effects of prenatal exposure to chlorpyrifos were evaluated in 254 children through the first 3 years of life. This report examined cognitive and motor development at 12, 24, and 36 months (measured with the Bayley Scales of Infant Development II) and child behavior at 36 months (measured with the Child Behavior Checklist) as a function of chlorpyrifos levels in umbilical cord plasma.

Results: Highly exposed children (chlorpyrifos levels of >6.17 pg/g plasma) scored, on average, 6.5 points lower on the Bayley Psychomotor Development Index and 3.3 points lower on the Bayley Mental Development Index at 3 years of age compared with those with lower levels of exposure. Children exposed to higher, compared with lower, chlorpyrifos levels were also significantly more likely to experience Psychomotor Development Index and Mental Development Index delays, attention problems, attention-deficit/hyperactivity disorder problems, and pervasive developmental disorder problems at 3 years of age.

Conclusions: The adjusted mean 36-month Psychomotor Development Index and Mental Development Index scores of the highly and lower exposed groups differed by only 7.1 and 3.0 points, respectively, but the proportion of delayed children in the high-exposure group, compared with the low-exposure group, was 5 times greater for the Psychomotor Development Index and 2.4 times greater for the Mental Development Index, increasing the number of children possibly needing early intervention services.

Pediatrics. 2006 Dec;118(6):e1845-59. Epub 2006 Nov 20. PMID: 17116700

Comment: *Most notable in this study is the relationship between chlorpyrifos and behavioral disorders. The report indicates that children who came in contact with chlorpyrifos were significantly more likely to have both attention problems and ADHD. 36-month olds with prenatal exposures to chlorpyrifos had odds ratios of 11.3 for having attention problems, 6.5 for having ADHD problems, and*

5.4 for having PDD problems. ADHD impacts around two million children in the United States and causes inattention, impulsivity, and hyperactivity. Although chlorpyrifos was outlawed from residential use in 2001, it continues to be used intensively in agriculture for corn, wheat, and soy. A study led by an Emory University researcher found that chlorpyrifos can also enter children's bodies through dietary exposure. This study serves to remind us that early childhood exposure may have long lasting effects. Minimizing or preventing such exposure must be our society's plan. We do not want this type of article to be written about other pesticides in the future. It is a particularly heinous scenario when alternate pest control methodologies are available. We need to ensure that Maryland's day care centers follow the lead of the state's Integrated Pest Management-in-Schools law, which requires schools to use non-chemical pest prevention and management and only consider pesticides as a last resort. – R.B., L.K.G.

CANCER

HOUSEHOLD EXPOSURE TO PESTICIDES AND RISK OF CHILDHOOD ACUTE LEUKAEMIA

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Objectives: To investigate the relation between childhood acute leukaemia and household exposure to pesticides.

Methods: The study included 280 incident cases of acute leukaemia and 288 controls frequency matched on gender, age, hospital, and ethnic origin. The data were obtained from standardized face to face interviews of the mothers with detailed questions on parental occupational history, home and garden insecticide use, and insecticidal treatment of pediculosis. Odds ratios were estimated using unconditional regression models including the stratification variables parental socioeconomic status and housing characteristics.

Results: Acute leukaemia was observed to be significantly associated with maternal home insecticide use during pregnancy (OR = 1.8, 95% CI 1.2 to 2.8) and during childhood (OR = 1.7, 95% CI 1.1 to 2.4), with garden insecticide use (OR = 2.4, 95% CI 1.3 to 4.3), and fungicide use (OR = 2.5, 95% CI 1.0 to 6.2) during childhood. Insecticidal shampoo treatment of pediculosis was also associated with childhood acute leukaemia (OR = 1.9, 95% CI 1.2 to 3.3).

Conclusion: The results reported herein support the hypothesis that various types of insecticide exposure may be a risk factor for childhood acute leukaemia. The observed association with insecticidal shampoo treatment of pediculosis, which has never been investigated before, requires further study.

Occupational and Environmental Study, 2006 Feb;63(2):131-4. PMID: 16421392

Comment: *There are a great many factors in the cascade of events from pesticide exposure to the development of childhood leukemia, not least is to understand why some children are affected and others are not and why most childhood leukemia is lymphocytic. For example: Are the different and rarer forms of leukemia equally associated with pesticide exposure? Are some pesticides more potent than others in this association? Do the "inert" (proprietary ingredients) have a significant role to play? What are the stepwise molecular and genetic changes that result in the leukemia? Are there many pathways to the same leukemic phenotype? –R.L.H.*

BRAIN TUMORS AND EXPOSURE TO PESTICIDES: A CASE-CONTROL STUDY IN SOUTHWESTERN FRANCE

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Objectives: Brain tumors are often disabling and rapidly lethal; their etiology is largely unknown. Among potential risk factors, pesticides are suspected. We examined the relationship between exposure to pesticides and brain tumors in adults in a population-based case-control study in southwestern France.

Methods: Between May 1999 and April 2001, 221 incident cases of brain tumors and 442 individually matched controls selected from the general population were enrolled. Histories of occupational and environmental exposures, medical and lifestyle information were collected. A cumulative index of occupational exposure to pesticides was created, based on expert review of life-long jobs and tasks. Separate analyses were performed for gliomas and meningiomas.

Results: A non-statistically significant increase in risk was found for brain tumors when considering all types of occupational exposure to pesticides (OR=1.29, 95% Confidence Interval=0.87-1.91) and slightly higher but still non-statistically significant when considering gliomas separately (OR=1.47, 95%CI=0.81-2.66). In the highest quartile of the cumulative index, a significant association was observed for brain tumors (OR=2.16, 95%CI=1.10-4.23), and for gliomas (OR=3.21, 95%CI=1.13-9.11), but not for meningiomas. Concerning environmental exposure to pesticides, a significant increase in risk was also observed with treatment of home plants (OR=2.24, 95%CI=1.16-4.30).

Conclusions: These data suggest that a high level of occupational exposure to pesticides might be associated with an excess in risk of brain tumors, and especially of gliomas.

Occupational and Environmental Medicine. 2007 May 30; [Epub ahead of print]. PMID: 17537748

Comment: *Although the incidence of primary brain tumors seems to have stabilized in the U.S. since 1991 this has not been the case in France over the interval from 1980 to 2000. Previous studies have implicated exposure to pesticides as a possible environmental factor particularly in farm workers. This large, carefully defined and case-controlled study from a grape growing region (Bordeaux) revealed that at higher pesticide exposure levels a significant risk was seen for brain tumors in general and gliomas in particular. In these vineyards, 80% of the pesticides used are fungicides but without any further breakdown as to the specific agents that caused the exposure which only allowed the subjects to be classified as users or not. Another interesting finding was the significant relationship of the use of pesticides on house plants to the incidence of brain tumors. Continued study is warranted in order to more fully dissect out the various factors involved in these relationships of pesticide exposure to the development of brain tumors. -R.L.H.*

FONOFOS EXPOSURE AND CANCER INCIDENCE IN THE AGRICULTURAL HEALTH STUDY

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Background: The Agricultural Health Study (AHS) is a prospective cohort study of licensed pesticide applicators from Iowa and North Carolina enrolled 1993–1997 and followed for incident cancer through 2002. A previous investigation in this cohort linked exposure to the organophosphate fonofos with incident prostate cancer in subjects with family history of prostate cancer.

Objectives: This finding along with findings of associations between organophosphate pesticides and cancer more broadly led to this study of fonofos and risk of any cancers among 45,372 pesticide applicators enrolled in the AHS.

Methods: Pesticide exposure and other data were collected using self-administered questionnaires. Poisson regression was used to calculate rate ratios (RRs) and 95% confidence intervals (CIs) while controlling for potential confounders.

Results: Relative to the unexposed, leukemia risk was elevated in the highest category of lifetime (RR = 2.24; 95% CI, 0.94-5.34, ptrend = 0.07) and intensity-weighted exposure-days (RR = 2.67; 95% CI, 1.06–6.70, ptrend = 0.04), a measure that takes into account factors that modify pesticide exposure. Although prostate cancer risk was unrelated to fonofos use overall, among applicators with a family history of prostate cancer, we observed a significant dose–response trend for lifetime exposure-days (ptrend = 0.02, RR highest tertile vs. unexposed = 1.77, 95% CI, 1.03–3.05; RR interaction = 1.28, 95% CI, 1.07–1.54). Intensity-weighted results were similar. No associations were observed with other examined cancer sites.

Conclusions: Further study is warranted to confirm findings with respect to leukemia and determine whether genetic susceptibility modifies prostate cancer risk from pesticide exposure.

Environmental Health Perspectives. 2006 Dec;114(12):1838-42. PMID: 17185272

Comment: *Although overall prostate cancer was not related to fonofos exposure there was a significant dose-response relationship among applicators with a family history of prostate cancer. In contrast, risk of leukemia was related to its use and was increased with an increase in intensity-weighted exposure-days. With further study, perhaps these observations can be related to specific leukemia types. – R.L.H.*

ASTHMA HISTORY, OCCUPATIONAL EXPOSURE TO PESTICIDES AND THE RISK OF NON-HODGKIN'S LYMPHOMA

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Department of Preventive Medicine, College of Medicine, Korea University, Seoul.

We previously reported that, although asthma did not increase the risk of non-Hodgkin's lymphoma (NHL), the risk from pesticide exposures was higher among asthmatics than that among nonasthmatics. To further evaluate this finding, we analyzed data from a population-based case-control study of NHL conducted in Iowa, Detroit, Los Angeles and Seattle. Cases (n = 668) diagnosed with NHL from 1998 to 2000 and controls (n = 543) randomly selected from the same geographical areas as that of the cases were included in this analysis. Odds ratios (OR) for the risk of NHL from potential occupational exposure to pesticides tended to be higher among asthmatics (OR = 1.7; 95% CI 0.3-9.1) when compared with that among nonasthmatics (OR = 0.9; 95% CI 0.6-1.5). The risks of NHL associated with pesticide exposure were also higher among asthmatics who had history of hospitalization (OR = 2.1; 95% CI 0.2-29.0) or daily medication for asthma (OR = infinite) than those among asthmatics who did not have such histories. Our results support the previous finding that the risk of NHL from pesticide exposure may be greater among asthmatics.

International Journal of Cancer, 2006 Jun 15;118(12):3174-6. PMID: 16395708

Comment: *If supported by future studies, this paper raises some interesting questions about the generally accepted relationship between pesticide exposure and the development of non-Hodgkin's lymphoma. Is the relationship due to the asthma patients' altered immune status? Is it an exposure issue related to the impairment of the movement of the respiratory mucus blanket? Are there changes in the ability to detoxify the causative agent? Could it be related to the agents used to treat asthma (e.g. corticosteroids)? –R.L.H.*

ATOPY, EXPOSURE TO PESTICIDES AND RISK OF NON-HODGKIN LYMPHOMA

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Pesticide exposure has been associated with non-Hodgkin lymphoma (NHL) risk in a number of studies, and two recent studies suggest that the increased risk may be confined to those with a history of asthma. We examined the interaction between occupational pesticide exposure and atopy on risk of NHL in an Australian population-based case-control study. Incident cases (n = 694) were diagnosed in New South Wales or the Australian Capital Territory between 2000 and 2001 and controls (n = 694) were randomly selected from electoral rolls and frequency-matched to cases by age, sex and State of residence. Occupational pesticide exposure was determined by an expert occupational hygienist's assessment of job-specific questionnaires administered by telephone. History of atopy (asthma, hay fever, eczema, and food allergy) was self-reported. Logistic regression models included the three matching variables, ethnicity and sun exposure. The OR for NHL with substantial pesticide exposure and any history of asthma was 3.07 (95% CI 0.55-17.10) and with substantial pesticide exposure and no asthma history it was 4.23 (95% CI 1.76-10.16). The p-value for interaction was 0.29. A similar pattern of risk was observed for each of the pesticide subtypes; for asthma at various times of life; for hay fever, eczema, food allergy and any atopy, in men only and for follicular lymphomas only. Although this study had limited power, the findings do not suggest modification of the association between pesticide exposure and NHL risk by asthma or atopic disease more generally.

International Journal of Cancer. 2007 May 15;120(10):2271-4. PMID: 17290390

Comment: *In contrast to the study above, this study (although of limited power) failed to find any significant additional risk for patients with a history of asthma for the risk of the development of non-Hodgkin's lymphoma following pesticide exposure. In addition, other forms of atopy (hay fever, eczema, food allergy) also failed to add additional risk to that of the pesticide exposure alone. Curiously, the risks were actually less with the history of asthma and other forms of atopy, possibly suggesting some protective effect against pesticide exposure. If anything, this probably is revealing of the unusual results often seen in small studies of limited statistical power. – R.L.H.*

AGRICULTURAL EXPOSURES AND GASTRIC CANCER RISK IN HISPANIC FARM WORKERS IN CALIFORNIA

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Previous studies have indicated that farm workers may be at increased risk of gastric cancer. Meta-analyses, ecological, case-control, and cohort studies suggest that some aspects of the agricultural environment may be implicated in the elevated risk. Hispanic farm workers in California are exposed to a multitude of potentially toxic substances in the work site, including excessive sunlight, fertilizers, diesel fumes, and pesticides. A previous analysis of a cohort of California farm workers who had been members of a farm labor union, the United Farm Workers of America (UFW), found a proportionate cancer incidence ratio for stomach cancer of 1.69 when using the California Hispanic population as the standard. The aim of the current study was to further evaluate associations between gastric cancer and the types of crops and commodities UFW members cultivate and the associated pesticide use as recorded by the California Department of Pesticide Regulation (DPR). We conducted a nested case-control study of gastric cancer embedded in the UFW cohort and identified 100 cases of newly diagnosed gastric cancer between 1988 and 2003. We identified 210 control participants matched on age, gender, ethnicity, and who were known to be alive and resident in California up to the date of the cases' diagnosis. Both stratified analyses and unconditional logistic regression were used to calculate adjusted odds ratios (OR) and 95% confidence intervals (95% CI). Work in the citrus industry was associated with increased gastric cancer (OR ¼ 2.88; 95% CI ¼ 1.02–8.12) although no other specific crops or commodities were associated with this disease. Working in areas with high use of the phenoxyacetic acid herbicide 2,4-D was associated with gastric cancer (OR ¼ 1.85; 95% CI ¼ 1.05–3.25); use of the organochlorine insecticide chlordane was also associated with the disease (OR ¼ 2.96; 95% CI ¼ 1.48–5.94). Gastric cancer was associated with use of the acaricide propargite and the herbicide tri.urin (OR ¼ 2.86; 95% CI ¼ 1.56–5.23 and 1.69, 95% CI ¼ 0.99–2.89, respectively). Gastric cancer in California Hispanic farm workers is associated with work in the citrus

fruit industry and among those who work in fields treated with 2,4-D, chlordane, propargite, and trifliuin. These findings may have larger public health implications especially in those areas of the country where these pesticides are heavily used and where they may be found in the ambient atmosphere.

Environmental Research. 2007 Jun;104(2):282-9. Epub 2006 Dec 29. PMID: 17196584

Comment: *Relationships to gastric cancer reported in this study included working with citrus crops but not with other crops, and the pesticides 2,4D, chlordane, propargite and trifliuin. The authors suggest that larger public health problems may yet be discovered where these pesticides are used in quantities that would put them in higher concentration in the air and the environment. – R.L.H.*

RESIDENTIAL INSECTICIDE USE AND RISK OF NON-HODGKIN'S LYMPHOMA

Colt JS, Davis S, Severson RK, Lynch CF, Cozen W, Camann D, Engels EA, Blair A, Hartge P.

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Previous studies have linked non-Hodgkin's lymphoma (NHL) with occupational exposure to insecticides, but residential use is largely unexplored. In this population-based case-control study, we examined NHL risk and use of insecticides in the home and garden. We identified NHL cases, uninfected with HIV, diagnosed between 1998 and 2000 among women and men ages 20 to 74 years in Iowa and the metropolitan areas of Los Angeles, Detroit, and Seattle. Controls were selected using random digit dialing or Medicare files. Computer-assisted personal interviews (1,321 cases and 1,057 controls) elicited data on insecticide use at each home occupied since 1970. Insecticide levels were measured in dust taken from used vacuum cleaner bags (682 cases and 513 controls). We previously reported a positive association with dichlorodiphenyldichloroethylene levels in carpet dust residues. Here, we focus on insecticides that were commonly used after 1970, the time period covered by our questionnaire. People whose homes were treated for termites had elevated NHL risk (odds ratio, 1.3; 95% confidence interval, 1.0-1.6). Risk was modestly, although not significantly, elevated in all but one study center and in all sexes and races. The elevation in risk was restricted to people whose homes were treated before the 1988 chlordane ban. There was a significant trend of increasing risk with increasing levels of alpha-chlordane residues in dust (P(trend) = 0.04) and a marginally significant trend for gamma-chlordane (P(trend) = 0.06). We found no evidence of associations for insects overall, for specific types of insects other than termites, or for elevated residues of other insecticides. We concluded that chlordane treatment of homes for termites may increase residents' NHL risk.

Cancer Epidemiology, Biomarkers and Prevention. 2006 Feb; 15(2):251-7. PMID: 16492912

Comment: *See page 14 (left column).*

PERSISTENT ORGANOCHLORINE CHEMICALS IN PLASMA AND RISK OF NON-HODGKIN'S LYMPHOMA

De Roos AJ, Hartge P, Lubin JH, Colt JS, Davis S, Cerhan JR, Severson RK, Cozen W, Patterson DG Jr, Needham LL, Rothman N.

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Polychlorinated biphenyls (PCB) have been suspected as possible contributors to increasing non-Hodgkin's lymphoma incidence during the latter half of the 20th century based on their toxicologic properties and provocative epidemiologic reports. We investigated PCBs and other organochlorines and risk of non-Hodgkin's lymphoma in a population-based case-control study in the United States. Congeners of PCBs (including coplanar congeners), dioxins, furans and pesticides or pesticide metabolites were measured in plasma of 100 untreated cases and 100 control subjects. We used a multiple imputation procedure to fill in missing values of levels determined to be below the detection limits. Risks of non-Hodgkin's lymphoma associated with each analyte were estimated using conditional logistic regression for the continuous measure, exposure quartiles, trend across quartile categories, and exposures above the 95th percentile. Certain PCB congeners were associated with increased risk of non-Hodgkin's lymphoma, including coplanar PCBs 156, 180, and 194, with odds ratios for the highest versus lowest quartile ranging from 2.7 to 3.5, and significant trends. Each of the furan congeners was associated with risk of non-Hodgkin's lymphoma, as were total furans, with 3.5-fold increased risk for the highest versus lowest quartile and a significant trend across quartiles (P = 0.006). The toxic equivalency quotient (TEQ), a summed metric that weights congeners by their dioxin-like potency, was associated with non-Hodgkin's lymphoma, with 35% increased risk per 10 TEQ pg/g lipid (95% confidence interval, 1.02-1.79). Our results add to existing literature, which suggests that exposure to organochlorines contributes to non-Hodgkin's lymphoma risk; these risks were most apparent for certain PCBs and furans.

Cancer Research. 2005 Dec 1;65(23):11214-26. PMID: 16322272

Comment: *See page 14 (left column).*

ORGANOCHLORINES IN CARPET DUST AND NON-HODGKIN LYMPHOMA

Colt JS, Severson RK, Lubin J, Rothman N, Camann D, Davis S, Cerhan JR, Cozen W, Hartge P.

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Background: The incidence of non-Hodgkin lymphoma (NHL) has risen over the past several decades. Reasons for this increase are largely unexplained.

Methods: In this population-based case-control study, we examined NHL risk and exposure to organochlorine compounds using concentrations in carpet dust as an exposure indicator. We identified NHL cases, uninfected with HIV, diagnosed between 1998 and 2000 among women and men ages 20-74 years in Iowa, Los Angeles County, and the Detroit and Seattle metropolitan areas. Controls were selected using random-digit-dialing or Medicare files. Organochlorine concentrations were measured in vacuum bag dust from 603 white cases and 443 white controls who had owned most of their carpets for at least 5 years.

Results: NHL risk was elevated if any of the polychlorinated biphenyl (PCB) congeners (PCBs 105, 138, 153, 170, or 180) was detected (odds ratio = 1.5; 95% confidence interval = 1.2-2.0). Risk was elevated in the top tertile of PCB 180 (1.7; 1.1-2.6) and in the top 2 tertiles of total PCBs (middle tertile, 1.6 [1.1-2.4]; top tertile 1.5 [1.0-2.2]). There was a positive trend in risk with increasing PCB 180 levels (P trend = 0.03). NHL risk was elevated if dichlorodiphenyldichloroethylene (DDE) was detected (1.3; 1.0-1.7), but only among men. A positive, but not monotonic, dose-response relationship was observed for DDE (P trend = 0.02).

Conclusions: Our findings suggest an increased risk of NHL associated with exposure to PCBs, with evidence of greater effects for PCB 180. There is also some evidence of an association with DDE.

Epidemiology, 2005 Jul;16(4):516-25. PMID: 15951670

Comment: *These three papers continue in different and novel ways to explore the association of non-Hodgkin's lymphoma with pesticide exposure. Crucial to the further development of an understanding of this relationship is the recognition that non-Hodgkin's lymphoma is not a single disease but a category of convenience that includes at least 30 or more discrete diseases that differ in many fundamental ways. These differences include T or B cell origin, genetic differences, surface immunochemical differences, cytology and morphology. The frequency of the different lymphomas, their age distribution and symptoms are quite varied. They also differ in their responsiveness to treatment and their aggressiveness and hence in the survival of the individuals affected. Altogether they are a very challenging and confusing group of diseases. It would be remarkable if this diversity were not reflected in their relationship to exposure to pesticides. It will be very important to try to dissect out which of these lymphomas are most influenced by pesticide exposure. This diversity is also inherent in the rubric of "pesticide exposure" which also encompasses many different agents, doses, duration and frequency as well as host differences including sex, age and individual genetic differences.*

Untangling all of this will be a serious challenge and may not even be possible considering the relative rarity of some of these lymphomas. We may have to be content to appreciate the overall epidemiologic association and continue to try to reduce exposure to pesticides in general. –R.L.H.

GENETIC POLYMORPHISMS AND SUSCEPTIBILITY TO CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Acute lymphoblastic leukemia (ALL) is the most common form of pediatric cancer. Although exposure to environmental agents appears to predispose individuals to this disease, little attention has been paid to the role of genetic susceptibility to environmental exposures in the etiology of childhood ALL. The enzymes GSTM1, GSTT1, GSTP1, CYP1A1, and CYP2E1 are involved in the bioactivation and detoxification of a variety of xenobiotics present in food, organic solvents, tobacco smoke, drugs, alcoholic drinks, pesticides, and environmental pollutants. Polymorphisms in the genes coding for these enzymes have been associated with increased susceptibility to different cancers, including hematologic malignancies. To investigate whether these polymorphisms represent risk-modifying factors for childhood ALL, a study was conducted involving 113 Brazilian patients of childhood ALL and 221 controls with similar ethnic backgrounds. The data revealed that carriers of the rare GSTP1 Val allele were at higher risk of ALL (odds ratio [OR] = 2.7; 95% confidence interval [CI] = 1.1-6.8; P = 0.04). No difference was found in the prevalence of the GSTM1 and GSTT1 null genotypes between ALL patients and the controls, and no association was found between CYP1A1*2 and CYP2E1*3 variants and ALL. However, when the mutant CYP1A1 and CYP2E1 alleles were considered together with the GSTM1 and GSTP1 risk-elevating genotypes, the risk of ALL was increased further (OR = 10.3; 95% CI = 1.0-111.8; P = 0.05), suggesting a combined effect. These results imply that genetic variants of xenobiotic metabolizing genes influence the risk of developing childhood ALL.

Environmental and Molecular Mutagenesis. 2004;43(2):100-9. PMID: 14991750

Comment: *Genetic-environment interactions are now well established. This may be true with the association between pesticides and*

ALL. Studies such as this may not only explain the reason for the association, but may also show us the route to better prevention through identifying those at unique risk. –L.K.G.

CHILD AND MATERNAL HOUSEHOLD CHEMICAL EXPOSURE AND THE RISK OF ACUTE LEUKEMIA IN CHILDREN WITH DOWN'S SYNDROME: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP

Alderton LE, Spector LG, Blair CK, Roesler M, Olshan AF, Robison LL, Ross JA.

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Compared with the general pediatric population, children with Down's syndrome have a much higher risk of acute leukemia. This case-control study was designed to explore potential risk factors for acute lymphoblastic leukemia and acute myeloid leukemia in children with Down's syndrome living in the United States or Canada. Mothers of 158 children with Down's syndrome and acute leukemia (97 acute lymphoblastic leukemia, 61 acute myeloid leukemia) diagnosed between January 1997 and October 2002 and mothers of 173 children with Down's syndrome but without leukemia were interviewed by telephone. Positive associations were found between acute lymphoblastic leukemia and maternal exposure to professional pest exterminations (odds ratio = 2.25, 95% confidence interval: 1.13, 4.49), to any pesticide (odds ratio = 2.18, 95% confidence interval: 1.08, 4.39), and to any chemical (odds ratio = 2.72, 95% confidence interval: 1.17, 6.35). Most of the associations with acute myeloid leukemia were nonsignificant, and odds ratios were generally near or below 1.0. This exploratory study suggests that household chemical exposure may play a role in the development of acute lymphoblastic leukemia in children with Down's syndrome.

American Journal of Epidemiology. 2006 Aug 1;164(3):212-21. Epub 2006 Jun 7. PMID: 16760223

Comment: *This is another study showing a correlation between pesticide exposure and ALL. It is possible that pesticides have contributed to the steady increase incidence of ALL over the past 30 years. -L.K.G.*

REVIEW AND META-ANALYSIS OF RISK ESTIMATES FOR PROSTATE CANCER IN PESTICIDE MANUFACTURING WORKERS

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Purpose: The purpose of the present paper is to review cohort studies that examined the occurrence of prostate cancer in pesticide manufacturing workers in order to undertake a qualitative and quantitative evaluation of the risk as well as to assess the level of epidemiological evidence for each class of chemical compounds.

Methods: Following a systematic literature search, relative risk (RR) estimates for prostate cancer were extracted from 18 studies published between 1984 and 2004. All studies were summarized and evaluated for homogeneity and publication bias. As no significant heterogeneity was detected, combined RR estimators were calculated using a fixed effect model. Meta-analyses were performed both on the whole set of data and for each chemical class separately.

Results: The meta-rate ratio estimate for all studies was 1.28 [95% confidence interval (CI) 1.05-1.58]. After stratification by specific chemical class, consistent increases in the risk of prostate cancer were found in all groups but statistical significance was found only for accidental or non-accidental exposure to phenoxy herbicides contaminated with dioxins and furans. There was no obvious indication of publication bias.

Conclusion: The overall meta-analysis provides additional quantitative evidence consistent with prior reviews focusing on other groups exposed to pesticides (farmers, pesticide applicators). The results again point to occupational exposure to pesticides as a possible risk factor for prostate cancer but the question of causality remains unanswered. Epidemiological evidence did not allow identifying a specific pesticide or chemical class that would be responsible for the increased risk but the strongest evidence comes from workers exposed to phenoxy herbicides possibly in relation with dioxin and/or furan contamination.

Cancer Causes and Controls. 2006 May;17(4):353-73. PMID: 16596288

Comment: *The authors of this review conclude that there remains a "possible risk factor for prostate cancer" with pesticide exposure but as with most of these relationships between cancer and pesticides causality will be very difficult to define and surely will depend on the specifics of the agent, the exposure and the genetics of the host. – R.L.H.*

THE ASSOCIATION BETWEEN RESIDENTIAL PESTICIDE USE AND CUTANEOUS MELANOMA

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Occupational pesticide exposure has been linked to cutaneous melanoma in epidemiological studies. We studied the association between cutaneous melanoma and the residential use of

pesticides. This is a case-control study of cutaneous melanoma (287 incident cases; 299 controls). Data on pesticide use was obtained with a standardized interview. An increased risk of melanoma was found for high use (4 times annually) of indoor pesticides (odds ratio (OR)=2.18; 95% confidence intervals (CI) 1.07-4.43) compared to low use (1 times annually), after adjustment for sex, age, education, sun exposure and pigmentary characteristics. Subjects exposed for 10 years or more had two and a half times the risk (OR=2.46; 95% CI 1.23-4.94) of those exposed for less than 10 years. A dose response was observed for the intensity of pesticides use (p(trend)=0.027). The results indicate that residential pesticide exposure may be an independent risk factor for cutaneous melanoma.

European Journal of Cancer. 2007 Apr;43(6):1066-75. Epub 2007 Feb 28. PMID: 17331713

Comment: *Here is yet another malignancy that has been associated with exposure to the residential use of pesticides with a dose-response effect. If this holds up with additional studies and can be linked to the specific pesticides used (and their "inert" ingredients) we may have a way to impact the steadily rising incidence of melanoma which up to now has been thought to be largely due to UV exposure caused by depletion of the ozone layer. – R.L.H.*

PULMONARY

PESTICIDES AND OTHER AGRICULTURAL FACTORS ASSOCIATED WITH SELF-REPORTED FARMER'S LUNG AMONG FARM RESIDENTS IN THE AGRICULTURAL HEALTH STUDY

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Background: Farmer's lung, or hypersensitivity pneumonitis, is an important contributor to respiratory morbidity among farmers.

Methods: Using the 1993-7 enrollment data from the Agricultural Health Study, we conducted a cross-sectional study of occupational risk factors for farmer's lung among ~50,000 farmers and farm spouses in Iowa and North Carolina using hierarchical logistic regression controlling for age, state, and smoking status. Participants provided information on agricultural exposures, demographic characteristics, and medical history via self-administered questionnaires. Approximately 2% of farmers (N=481) and 0.2% of spouses (N=51) reported doctor-diagnosed farmer's lung during their lifetime. We assessed farmers and spouses separately due to different information on occupational exposure history. Only pesticide exposures represented lifetime exposure history, all other farm exposures represented current activities at enrollment.

Results: Among farmers, handling silage (OR=1.41, 95%CI=1.10,1.82), high pesticide exposure events (OR=1.75, 95%CI=1.39,2.21), and ever use of organochlorine (OR=1.34, 95%CI=1.04,1.74) and carbamate pesticides (OR=1.32, 95%CI=1.03,1.68) were associated with farmer's lung in mutually-adjusted models. The insecticides DDT, lindane, and aldicarb were positively associated with farmer's lung among farmers. Current animal exposures, while not statistically significant, were positively associated with farmer's lung, particularly for poultry houses (OR=1.55, 95%CI=0.93, 2.58) and dairy cattle (OR=1.28, 95%CI=0.86,1.89). The occupational data were more limited for spouses; however, we saw similar associations for dairy cattle (OR=1.50, 95%CI=0.72, 3.14) and organochlorine pesticides (OR=1.29, 95%CI=0.64, 2.59).

Conclusion: While historic farm exposures may contribute to the observed associations with pesticides, these results suggest that organochlorine and carbamate pesticides should be further evaluated as potential risk factors for farmer's lung.

Occupational and Environmental Medicine. 2007 May;64(5):334-41. Epub 2006 Dec 20. PMID: 17182642

Comment: *This study shows odds ratios for developing 'Farmers Lung' to be as high for pesticides as for the handling of silage. As this syndrome is likely to be a hypersensitivity phenomenon, it is not surprising to find a multitude of triggers. While the association of historical pesticide use and the development of the syndrome is not proof of causation, it is highly suggestive. While we await further studies to refine the relationship between pesticide use and the development of farmers lung, it would be prudent to add questions about pesticide use to the history of wheezing adults who work in agriculture. If exposures are present, physicians should advise patients of the possible link and help them look for lowered exposure through change in job or improved use of personal protection devices. -L.K.G.*

ASSOCIATION OF ALLERGIC RHINITIS WITH PESTICIDES USE AMONG GRAPE FARMERS IN CRETE, GREECE

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Department of Social Medicine, Faculty of Medicine, University of Crete, Heraklion, Crete, Greece.

Study objective: The aim of this study was to explore the association of allergic rhinitis with pesticides use among grape farmers in Crete.

Subjects and methods: We conducted a cross-sectional study of 120 grape farmers and 100 controls at the Malevisi region in Northern Crete. The protocol consisted of a questionnaire, skin prick tests for sixteen common allergens, measurement of specific IgE antibodies against eight allergens, and spirometry before and after bronchodilatation.

Results: Grape farmers who used pesticides had higher prevalence rates of allergic rhinitis symptoms (OR, 3.0; 95%CI, 1.4-6.2) compared with grape farmers who reported no current use of pesticides and control subjects. Logistic regression models controlling for age, sex, and smoking status showed that six of the twelve predefined groups of major pesticides were significantly related with allergic rhinitis symptoms. The highest risks were observed for paraquat and other bipyridyl herbicides (OR, 2.2; 95%CI, 1.0-4.8), dithiocarbamate fungicides (OR, 2.5; 95%CI, 1.1-5.3), and carbamate insecticides (OR, 3.0; 95%CI, 1.4-6.5). A factor analysis of pesticides used, identified three distinct factors. The most common factor was that of "multiple pesticide use" that included 9 pesticides and that was significantly associated with allergic rhinitis (OR, 1.5; 95% CI, 1.0-2.3). Odds ratios were higher when allergic rhinitis was defined using both questionnaire data on symptoms and atopy.

Conclusions: Occupational exposure to multiple agricultural chemicals could be related to allergic rhinitis in grape farmers.

Occupational and Environmental Medicine. 2007 Jun;64(6):417-21. Epub 2006 Dec 20.PMID: 17182637

Comment: *Pesticides have been known as allergens for some people for a long time. This article suggests the phenomena may be more widespread. This reaction may be similar to the disease known as irritant-induced asthma or occupational asthma. For practitioners, it suggests another cause for adult-onset allergic rhinitis and offers the possibility of alleviation or prevention for some patients through exposure control. –L.K.G.*

OTHER RESEARCH

IMPACT OF PERMETHRIN-TREATED BED NETS ON MALARIA, ANEMIA, AND GROWTH IN INFANTS IN AN AREA OF INTENSE PERENNIAL MALARIA TRANSMISSION IN WESTERN KENYA

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As part of a community-based, group-randomized, controlled trial of insecticide-treated bed nets (ITNs) in an area with intense malaria transmission in western Kenya, a birth cohort (n = 833) was followed monthly until the age of 24 months to determine the potential beneficial and adverse effects of reduced malaria exposure during pregnancy and infancy. Malaria transmission and morbidity were comparable pre-intervention. The ITNs reduced malaria attack rates (force of infection) in infancy by 74%, and delayed the median time-to-first parasitemia (4.5 to 10.7 months; $P < 0.0001$). The incidence of both clinical malaria and moderate-severe anemia (hemoglobin level <7 g/dL) were reduced by 60% ($P < 0.001$ for both). Protective efficacy was greatest in infants less than three months old and similar in older infants and one-year-old children. Efficacy was lowest in the dry season. Infants from ITN villages experienced better height and weight gain. In areas of intense perennial malaria transmission, ITNs substantially reduce exposure to malaria and subsequent malaria-associated morbidity in children less than 24 months old. Reduced malaria exposure during infancy did not result, with continued ITN use, in increased malaria morbidity in one-year-old children.

The American Journal of Tropical Medicine and Hygiene. 2003 Apr;68(4 Suppl):68-77. PMID: 12749488

Comment: *See p.18 (right column).*

INSECTICIDE-TREATED NETS

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Insecticide-treated nets (ITNs) are the most powerful malaria control tool to be developed since the advent of indoor residual spraying (IRS) and chloroquine in the 1940s, and as such they have been an important component of global and national malaria control policies since the mid-1990s. Yet a decade later, coverage is still unacceptably low: only 3% of African children are currently sleeping under an ITN, and only about 20% are sleeping under any kind of net. This review charts the scientific, policy and programmatic progress of ITNs over the last 10 years. Available evidence for the range of programmatic delivery mechanisms used at country level is presented alongside the key policy debates that together have contributed to the evolution of ITN delivery strategies over the past decade. There is now global consensus around a strategic framework for scaling up ITN usage in Africa, which recognizes a role for both the public sector (targeting vulnerable groups to promote equity) and the private sector (sustainable supply). So, while

progress with increasing coverage to date has been slow, there is now global support for the rapid scale-up of ITNs among vulnerable groups by integrating ITN delivery with maternal and child health programmes (and immunization in particular), at the same time working with the private sector in a complementary and supportive manner to ensure that coverage can be maintained for future generations of African children.

Advances in Parasitolology. 2006;61:77-128. PMID: 16735163

Comment: *See next column.*

PERMETHRIN-TREATED BED NETS (MOSQUITO NETS) PREVENT MALARIA IN GAMBIAN CHILDREN

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The incidence of clinical attacks of malaria was significantly less in Gambian children aged 1-9 years who slept in villages where all the bed nets (mosquito nets) were treated with permethrin than in children who slept in control villages with placebo-treated nets. Significant differences in changes in spleen size and in packed cell volume were also observed between the 2 groups during the course of a rainy season. No side effect was noted. Treatment of bed nets with insecticide is a form of malaria control that is well suited to community participation and can readily be incorporated into primary health care programmes. Insecticide-treated nets may be more effective in areas of seasonal or low intensity transmission than in areas with heavy perennial challenge.

Transactions of the Royal Society of Tropical Medicine and Hygiene. 1988;82(6):838-42. PMID: 2908286

Comment: *See next column.*

DO UNTREATED BED NETS PROTECT AGAINST MALARIA?

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Bed nets are thought to offer little, if any, protection against malaria, unless treated with insecticide. There is also concern that the use of untreated nets will cause people sleeping without nets to receive more mosquito bites, and thus increase the malaria risk for other community members. Regular retreatment of nets is therefore viewed as critical for malaria control. However, despite good uptake of nets, many control programmes in Africa have reported low re-treatment rates. We investigated whether untreated bed nets had any protective benefit (in October and November 1996) in The Gambia where nets, although widely used, are mostly untreated. Cross-sectional prevalence surveys were carried out in 48 villages and the risk of malaria parasitaemia was compared in young children sleeping with or without nets. Use of an untreated bed net in good condition was associated with a significantly lower prevalence of Plasmodium falciparum infection (51% protection [95% CI 34-64%], $P < 0.001$). This finding was only partly explained by differences in wealth between households, and children in the poorest households benefited most from sleeping under an untreated net (62% protection [14-83%], $P = 0.018$). There was no evidence that mosquitoes were diverted to feed on children sleeping without nets. These findings suggest that an untreated net, provided it is in relatively good condition, can protect against malaria. Control programmes should target the poorest households as they may have the most to gain from using nets.

Transactions of the Royal Society of Tropical Medicine and Hygiene. 2001 Sept-Oct; 95(5): 457-62. PMID: 11706649

Comment: *Insecticide treated nets (ITN) for the prevention of malaria in endemic areas has been widely studied and found to be efficacious. The first two articles are two of hundreds showing the effect of their use. The World Health Organization is supporting widespread use of these nets. Several studies have followed children looking for signs of pesticide toxicity. None has been found to date. In the face of increased growth because of lessened anemia, etc. finding minimal signs of toxicity may be unusually difficult.*

The pesticides being used are pyrethroids. They are marketed such that parents impregnate the nets themselves. This may lead to the highest exposure from the use of ITN's. Pyrethroids are known to exacerbate asthma in some people. Because of substantial efficacy, uncommon acute effects of pyrethroids may not limit their cost-effectiveness. The impact on death has been seen mainly in the first two years of life. Adequate long term studies on the side effects of the pesticides have not been published, however pyrethroids have been linked to cancer, Parkinson's disease and are suspected endocrine disruptors.

Early studies from about 20 years ago (third in this series) show the contrast of ITNs with untreated nets. Although a more recent study (fourth in this series) indicate that untreated nets in good condition can also be effective in reducing malaria, there is little research comparing the difference in efficacy between ITN and untreated nets made with the same material in the same condition.

The exposure dose to the person using the net night after night for extended periods should also be studied, such as to babies and young children, who may inadvertently ingest pesticides after mouthing the net or their hands after touching the net. As these agents have risks, we will just have to wait and watch. But in the areas of the world where malaria is an overwhelming problem, their use is significantly improving health. Whether their use will be significant for travelers from developed countries is yet to be determined. -L.K.G. and R.B.

ASSOCIATION BETWEEN SERUM CONCENTRATIONS OF PERSISTENT ORGANIC POLLUTANTS AND INSULIN RESISTANCE AMONG NONDIABETIC ADULTS: RESULTS FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 1999-2002

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Objective: We reported strong relations between serum concentrations of persistent organic pollutants (POPs), especially organochlorine (OC) pesticides or nondioxin-like polychlorinated biphenyls (PCBs), and prevalence of diabetes in a U.S population with background exposure to POPs. Here, we investigated POPs and insulin resistance, a frequent pathogenic precursor of type 2 diabetes.

Research design and methods: Serum POPs and homeostasis model assessment of insulin resistance (HOMA-IR) were investigated cross-sectionally in 749 nondiabetic participants aged > or = 20 years. Nineteen POPs in five subclasses were selected, detectable in > or = 60% of participants.

Results: Among subclasses, OC pesticides were most strongly associated with HOMA-IR. Adjusted geometric means of HOMA were 3.27, 3.36, 3.48, and 3.85 (P for trend <0.01) across quartiles of OC pesticides. The relationship strengthened with increasing HOMA-IR percentile: adjusted odds ratios comparing the highest versus lowest POPs quartile were 1.8 for being > or = 50th percentile of HOMA-IR, 4.4 for being > or = 75th percentile, and 7.5 for being > or = 90th percentile. Associations with elevated HOMA-IR appeared to be specific to oxychlordane and trans-nonachlor but also were found for two nondioxin-like PCBs. No HOMA-IR associations were seen in the other three POP subclasses. The association between OC pesticides and HOMA-IR tended to strengthen as waist circumference increased, with no apparent association in the lowest quartile of OC pesticide concentrations.

Conclusions: These findings, coupled with those concerning diabetes prevalence, suggest that OC pesticides and nondioxin-like PCBs may be associated with type 2 diabetes risk by increasing insulin resistance, and POPs may interact with obesity to increase the risk of type 2 diabetes.

Diabetes Care. 2007 Mar;30(3):622-8. PMID: 17327331

Comment: *This article shows a remarkable association between organochlorine pesticides and insulin resistance. As a society, we have reduced our exposure to this group of compounds, but they persist and we all carry them in our bodies. What would strengthen this association is a mechanism of action for this effect of the pesticide. Others will, we hope, examine this association. Unfortunately, if true, there is no therapy that would be effective although loss of weight would lower the total body burden of pesticides. Stay tuned. –R.L.H.*

TOXIC SERUM FACTOR LONG AFTER SINGLE EXPOSURE TO ORGANOPHOSPHATE; A NEW APPROACH FOR BIOMONITORING

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One of the major limitations of current methods of biological detection of exposure to hazardous environmental agents is their inability to detect long-term exposures. In the current study we examined the potential of a new bioassay based on the hypothesis that serum of exposed individuals contains a toxic factor(s) produced by an affected cell/tissue. The procedure included exposure of neuronal PC12 cell cultures to sera of rats treated once with the organophosphate chlorpyrifos. Samples taken 4 weeks after chlorpyrifos exposure reduced nerve growth factor (NGF)-induced neurite outgrowth by 40%. This effect lasted 6 weeks after treatment, whereas motor activity and cholinesterase activity returned to normal levels within 1 week. These results demonstrate the potential of the proposed method to detect environmental exposures long after they have occurred.

Archives of Toxicology. 2006 May;80(5):269-74. Epub 2005 Oct 20. PMID: 16237519

Comment: *This interesting paper uses an indirect method to demonstrate a persistent effect after pesticide exposure. An indicator cell line continued to respond to the sera of rats exposed to a pulse of the organophosphate chlorpyrifos up to six weeks after the exposure whereas the rats had returned to baseline in one week. The authors postulate the induction, release and persistence of a toxic factor(s) that could be detected by their assay in the blood. If this observation can be confirmed and generalized it may prove to be a useful way to complement more direct assays of the presence of pesticides in the body and also provide insight into the time course, mechanism and cell targets of the toxic exposure. -R.L.H.*

UNIDENTIFIED INERT INGREDIENTS IN PESTICIDES: IMPLICATIONS FOR HUMAN AND ENVIRONMENTAL HEALTH

Cox C, Surgan M.

Northwest Coalition for Alternatives to Pesticides, Eugene, Oregon, USA.

Background: By statute or regulation in the United States and elsewhere, pesticide ingredients are divided into two categories: active and inert (sometimes referred to as other ingredients, adjuvants, or coformulants). Despite their name, inert ingredients may be biologically or chemically active and are labeled inert only because of their function in the formulated product. Most of the tests required to register a pesticide are performed with the active ingredient alone, not the full pesticide formulation. Inert ingredients are generally not identified on product labels and are often claimed to be confidential business information.

Objectives: In this commentary, we describe the shortcomings of the current procedures for assessing the hazards of pesticide formulations and demonstrate that inert ingredients can increase the toxicity of and potential exposure to pesticide formulations.

Discussion: Inert ingredients can increase the ability of pesticide formulations to affect significant toxicologic end points, including developmental neurotoxicity, genotoxicity, and disruption of hormone function. They can also increase exposure by increasing dermal absorption, decreasing the efficacy of protective clothing, and increasing environmental mobility and persistence. Inert ingredients can increase the phytotoxicity of pesticide formulations as well as the toxicity to fish, amphibians, and microorganisms.

Conclusions: Pesticide registration should require full assessment of formulations. Evaluations of pesticides under the National Environmental Policy Act, the Endangered Species Act, and similar statutes should include impact assessment of formulations. Environmental monitoring for pesticides should include inert ingredients. To enable independent research and risk assessment, inert ingredients should be identified on product labels.

Environmental Health Perspectives. 2006 Dec;114(12):1803-6. PMID: 17185266

Comment: *In addition to the possibilities mentioned by the authors for unwanted and adverse actions by "inert" ingredients, their impact on humans might also include allergic reactions. Full disclosure of the formulation of pesticides is logical and desirable. Then, we have to consider such a change in regulation for other compounds. Even your poison control center may not know what is included as 'inert' ingredients. –L.K.G.*

AN INTERVENTION TO REDUCE RESIDENTIAL INSECTICIDE EXPOSURE DURING PREGNANCY AMONG AN INNER-CITY COHORT

Williams MK, Barr DB, Camann DE, Cruz LA, Carlton EJ, Borjas M, Reyes A, Evans D, Kinney PL, Whitehead RD Jr, Perera FP, Matsoanne S, Whyatt RM.

Columbia Center for Children's Environmental Health, Mailman School of Public Health, Columbia University, New York, New York 10032, USA.

Background: We previously reported widespread insecticide exposure during pregnancy among inner-city women from New York City. Here we report on a pilot intervention using integrated pest management (IPM) to reduce pest infestations and residential insecticide exposures among pregnant New York City African-American and Latina women (25 intervention and 27 control homes).

Methods: The IPM consisted of professional cleaning, sealing of pest entry points, application of low-toxicity pesticides, and education. Cockroach infestation levels and 2-week integrated indoor air samples were collected at baseline and one month post-intervention. The insecticides detected in the indoor air samples were also measured in maternal and umbilical cord blood collected at delivery.

Results: Cockroach infestations decreased significantly ($p = 0.016$) after the intervention among intervention cases but not control households. Among the intervention group, levels of piperonyl butoxide (a pyrethroid synergist) were significantly lower in indoor air samples after the intervention ($p = 0.016$). Insecticides were detected in maternal blood samples collected at delivery from controls but not from the intervention group. The difference was significant for trans-permethrin ($p = 0.008$) and of borderline significance ($p = 0.1$) for cis-permethrin and 2-isopropoxyphenol (a propoxur metabolite).

Conclusion: To our knowledge, this is the first study to use biologic dosimeters of prenatal pesticide exposure for assessing effectiveness of IPM. These pilot data suggest that IPM is an effective strategy for reducing pest infestation levels and the internal dose of insecticides during pregnancy.

Environmental Health Perspectives. 2006 Nov;114(11):1684-9.PMID:17107853

Comment: *Integrated pest management is effective in controlling urban pests. This is another study that confirms the efficacy of this approach which relies primarily on prevention and non-chemical strategies and only considers least toxic pesticides as a last resort. This study adds the biomonitoring of the people involved. Physicians may confidently urge patients to contract with pest-control companies that will approach pest control in this manner. It is reassuring that hospitals and elder care facilities participating in MPN's IPM in Health Care Facilities pilot project are embracing this approach. –L.K.G.*

PESTICIDES IN THE NEWS

Press Release from the Indiana University School of Medicine, May 7, 2007.

PREMATURE BIRTHS MAY BE LINKED TO SEASONAL LEVELS OF PESTICIDES AND NITRATES IN SURFACE WATER

INDIANAPOLIS — The growing premature birth rate in the United States appears to be strongly associated with increased use of pesticides and nitrates, according to work conducted by Paul Winchester, M.D., professor of clinical pediatrics at the Indiana University School of Medicine. He reports his findings May 7 at the Pediatric Academic Societies' annual meeting, a combined gathering of the American Pediatric Society, the Society for Pediatric Research, the Ambulatory Pediatric Association and the American Academy of Pediatrics.

Dr. Winchester and colleagues found that preterm birth rates peaked when pesticides and nitrates measurements in surface water were highest (April-July) and were lowest when nitrates and pesticides were lowest (Aug.-Sept.).

More than 27 million U.S. live births were studied from 1996-2002. Preterm births varied from a high of 12.03% in June to a low of 10.44% in September. The highest rate of prematurity occurred in May-June (11.91%) and the lowest for Aug-Sept (10.79%) regardless of maternal age, race, education, marital status, alcohol or cigarette use, or whether the mother was an urban, suburban or rural resident. Pesticide and nitrate levels in surface water were also highest in May-June and lowest in August–September, according to the U.S. Geological Survey.

For the past four years, Dr. Winchester and colleagues have focused attention on the outcomes of pregnancy in Indiana and the United States in relation to environmental pesticides and nitrates in surface and drinking water. Last year at the Pediatric Academic Societies' annual meeting, Dr. Winchester reported that birth defects peak in Indiana and in the United States as a whole during April through July, the same months as pesticides and nitrates reach their maximum concentrations in surface water. This year's presentation expands upon that work.

"A growing body of evidence suggests that the consequence of prenatal exposure to pesticides and nitrates as well as to other environmental contaminants is detrimental to many outcomes of pregnancy. As a neonatologist, I am seeing a growing number of birth defects and preterm births, and I think we need to face up to environmental causes," said Dr. Winchester, who is also director of Newborn Intensive Care Services at St. Francis Hospital in Indianapolis.

"Preterm births in the United States vary month to month in a recurrent and seasonal manner. Pesticides and nitrates similarly vary seasonally in surface water throughout the U.S. Nitrates and pesticides can disrupt endocrine hormones and nitric oxide pathways in the developing fetus," he said.

"I believe this work may lay the foundation for some of the most important basic and clinical research and public health initiatives of our time. To recognize that what we put into our environment has potential pandemic effects on pregnancy outcome and possibly on child development is a momentous observation, which hopefully will help transform the way humanity cares for its world," said James Lemons, M.D., Hugh McK. Landon Professor of Pediatrics at the IU School of Medicine. Dr. Lemons is director of the section of neonatal-perinatal medicine at the IU School of Medicine and heads the Riley Hospital for Children of Clarian Health's section of neonatal-perinatal medicine.

Collaborating with Dr. Winchester on this study were Akosua Boadiwaa Adu-Boahene and Sarah L. Kosten of the IU School of Medicine, Alex K. Williamson of the U.S. Geological Survey, and Ying Jun, Ph.D. of the University of Cincinnati. The work was funded by the Division of Neonatology, Department of Pediatrics of the IU School of Medicine.

From Environmental Law at Maryland (Winter/Spring 2007), a newsletter from the University of Maryland Environmental Law Program.

MDA SHOULD PROVIDE BETTER GUIDANCE ON PESTICIDE USE IN SCHOOLS

By Corianne Iacovelli and Kerry E. Rodgers

The Maryland Department of Agriculture has a new Secretary, Roger Richardson, but it still needs new guidance manuals for its Integrated Pest Management-in-Schools program. Nearly eight years after the General Assembly passed Maryland's Integrated Pest Management-in-Schools law ("IPM-in-Schools"), the Department's guidance manuals fail to accurately reflect the law's requirement that pesticides be used in public schools only as a last resort. The manuals are supposed to interpret the law and instruct school pest managers and administrators as to the proper way to control pests. Unfortunately, the current manuals present the schools' legal responsibilities in a misleading way, causing Maryland's schoolchildren to be unnecessarily exposed to toxic pesticides and inducing false reliance on the protection of this public health law.

Maryland's IPM-in-Schools law, enacted in 1999, requires public schools to implement IPM programs that minimize pesticide use and lower the risk to human health and the environment associated with pesticide application. Pesticide exposure can cause health effects such as cancer, nerve damage, and asthma, and children are especially vulnerable during growth and development. IPM combines different methods of pest control, such as surveillance for pests using traps, good sanitation, and

caulking. When non-toxic options are unreasonable or have been exhausted, pest managers can then consider the use of pesticides.

While the law deemed pesticides a last resort, the legislature realized that schools might not be able to completely eliminate the use of pesticides and required notice of their application. At the beginning of the school year, schools must notify all parents, guardians, and staff of their IPM programs. This notice must explain the school's IPM program, list any pesticides that could potentially be used in the school building or on school grounds, and include a statement that product labels or a safety data sheet is available for review by a parent, guardian, staff member, or student. The notice must also identify the school's designated contact person who keeps information on the IPM program, pest control practices and pesticide application. During the year, schools must send a similar notice to parents or guardians of newly enrolled students and to new staff members.

In addition, the law provides for notice regarding any pesticide application that occurs during the school year. Elementary schools must give all parents, guardians, and staff written notice at least 24 hours prior to a pesticide application or within 24 hours after an emergency application. Middle and high schools must notify those parents, guardians, and staff who requested to be put on a notification list by phone, direct contact, or written notice.

Despite revisions in 2006, the Department's manuals continue to inaccurately reflect the law and contain information that frustrates the legislature's intent to minimize the use of pesticides in schools. Generally, the manuals present IPM as an optional method of pest control, fail to incorporate statutory language, and contain ambiguous statements regarding IPM implementation and legal obligations.

Some manuals confuse readers by suggesting that pesticides are acceptable in situations other than where they are the last resort, or that pesticides are a necessary part of an IPM program. A growing number of schools around the country have proven that it is possible to prevent and manage pests without the use of chemical pesticides.

Other manuals suggest that IPM is an alternative to pesticide application. By representing IPM as an alternative, rather than the law, in a guide written for pest managers, the Department undermines the IPM-in-Schools law. As a result, pest managers lack adequate guidance as to the proper role of pesticides in public schools and pesticides are used too often, that is, illegally, in public schools.

With a new Administration and a new Secretary of Agriculture, it is time for the manuals to be revised so that they properly implement the IPM-in-Schools law. Maryland's public school children have a right to be free from unwarranted pesticide use and the risks pesticides pose to their health. The public has a right to accurate guidance from its government.

Kerry E. Rodgers directs the Environmental Law Clinic at the University of Maryland School of Law, where she is a Visiting Associate Professor of Law. Her e-mail address is krodgers@law.umaryland.edu. Corianne Iacovelli is a Student Attorney in the Environmental Law Clinic, which is seeking better IPM-in-Schools guidance on behalf of the Maryland Pesticide Network. Reprinted from Environmental Law at Maryland (Winter/Spring 2007), published by the University of Maryland Environmental Law Program.

The guidance manuals are available at http://www.mda.state.md.us/, by entering "IPM schools" in the search box. For more information, contact your school's designated Contact Person or the Maryland Department of Agriculture's Pesticide Regulation Section at (410) 841-5710.

Excerpted from a May 3, 2007 Pesticide Action Network North America press release.

WORLD HEALTH ORGANIZATION AFFIRMS COMMITMENT TO DDT REDUCTION IN MALARIA CONTROL

Dakar, Senegal

During the Third Conference of Parties to the Stockholm Convention this week in Dakar, Senegal, the Director of the World Health Organization Office on Public Health and Environment Dr. Maria Neira stated categorically that WHO strongly supports the Stockholm Convention, and is committed to reducing reliance on DDT in malaria control.

The Stockholm Convention is an international treaty calling for the phase-out of Persistent Organic Pollutant (POPs) chemicals. DDT is among the original 12 chemicals listed by the treaty. The Convention, also known as the "POPs Treaty," has been adopted by 143 countries and is administered by the UN Environment Programme (UNEP). Scientific studies link DDT to miscarriages, failure to breastfeed, male infertility, abnormalities in sexual organs, developmental delays in children, and is listed by U.S. EPA as a "probable" carcinogen. DDT is transported globally by wind and water, concentrating in the polar regions where it builds up in marine mammals and other traditional foods of indigenous communities. DDT and its breakdown products, which are also linked to health risks, persist in the environment for decades.

WHO's Dr. Neira addressed a large audience of government officials from around the world at a WHO/UNEP event in Dakar entitled, "Reducing Reliance on DDT While Strengthening Malaria Control." She affirmed that WHO's goal is to reduce and eventually eliminate use of DDT, in accordance with the Stockholm Convention. She stressed that this has been the case since the Convention came into existence, and the WHO position on DDT has not changed.

Dr. Neira also confirmed the agency's awareness of negative health effects associated with DDT, and that WHO is "very

much concerned with health consequences [resulting from] use of DDT." She said that "WHO is committed to making sure alternatives [to DDT] are soon available" and ensuring that member states comply and report on their use of DDT.

WHO and UNEP announced that since the signing of the Stockholm Convention, use of DDT has doubled. Many countries still apply the chemical with a blanket spray, rather than selectively as required by WHO guidelines, due to the severe lack of financial and technical resources in many countries with malaria problems.

A UNEP speaker emphasized that Integrated Vector Management should be the centrepiece of efforts to reduce DDT, with the use of other pesticides as a last option in cases where non-chemical controls are not sufficient. Dr. Lucien Manga of WHO African Regional office said WHO has a clear policy of using Integrated Vector Management programs to control malaria, and that this approach combines engagement with local communities; knowledge of the local factors that influence disease transmission; and use of a range of interventions that in combination "need to demonstrate the effectiveness of alternatives in their own country."

WHO spokespersons also stressed the need for a "global business plan to develop new alternatives" and "to strengthen collaboration south to south."

The workshop also heard from Dr. Enrique Loyola of the Pan American Health Organization about a malaria control project in Mexico that greatly reduced malaria without using DDT, achieving a 30% reduction at the village level, and a 50% reduction at the national level. Methods included public education, planting trees with mosquito repellent properties near homes and clearing away vegetation that might harbor mosquitoes, plastering homes with mosquito repelling calcium hydroxide (lime), personal hygiene measures, cleaning canals and removing algae that serves as a mosquito refuge, and the use of larvicides such as Bt (Bacillus thuringiensis). Mexico no longer uses DDT for vector control, and is now seeking to reduce the use of other chemicals in vector management.

Excerpted from Beyond Pesticides Daily News, Nov. 13, 2006.

NEW LEAST TOXIC BED BUG PRODUCT HITS MARKET

Bed bugs have made a comeback of epic proportions in the United States and around the world. Reports of growing resistance to pesticides and evidence of toxicity of conventional bed bug products has led to the production of new least toxic bed bug products.

For example, the company K4 Products, L.L.C., has released a new least-toxic product called EcoBugFree for Bed Bugs, which claims to kill bed bugs on contact. The product qualifies as an EPA exempt minimum risk pesticide, and therefore is considered a low-risk product.

Bedbugs are tiny reddish-brown insects that live in cracks and crevices in bed frames and adjacent walls or in mattress seams. They usually feed on blood at night, while their host sleeps. Human reactions to bed bug bites can include swelling and pain. Bed bugs are easily transported from one host to another by riding on clothing or bedding to public places where they transfer to another person.

Signs of a bed bug infestation include a pungent odor, and blood or fecal spots on pillow casings and sheets. If bed bugs are suspected, search out eggs and adult bedbugs in the cracks and spaces in the bed frame and along the baseboard. As with any pest problem, first investigate the possible cause of the infestation, which may be a nearby bird's nest or bat nesting area. Getting rid of the source helps end infestations. Caulk and paint the openings and cracks in bed frames and surrounding area to close up any hiding places.

A good short-term emergency technique involves setting up a barrier so that the bugs cannot get on a bed. Place the legs of the bed in containers filled with soapy water, and make sure that no part of the bed is touching the wall. Also, thoroughly clean sheets and blankets using an enzyme cleaner or borax. Steam clean furniture and replace infested mattresses and other bedding. Insecticidal soaps and silica aerogels provide other least-toxic controls.

Excerpted from Beyond Pesticides Daily News, Nov. 2, 2006.

ANTIBACTERIAL AGENT FOUND TO BE AN ENDOCRINE DISRUPTOR AT LOW LEVELS

A study in the journal Aquatic Toxicology Canadian found that the anti-bacterial agent triclosan interferes with the thyroid hormone in frogs, affecting the timing of their metamorphosis from tadpoles to adults. This study is the first demonstration of low-level impacts of triclosan on thyroid hormone function and raises further questions about triclosan's risks to humans and the environmental.

The study – The Bactericidal Agent Triclosan Modulates Thyroid Hormone-Associated Gene Expression and Disrupts Postembryonic Anuran Development – shows that exposure to as little as 0.15 micrograms/L of triclosan causes an earlier than normal metamorphosis from tadpole to frog, with effects on the tadpole brain and tail. Results also indicate that low levels of triclosan can potentially affect the human thyroid gland, which plays a role in development, body temperature and metabolism.

Triclosan, marketed widely to protect children from germs, is found in hundreds of products, including antibacterial soaps, deodorants, toothpastes, cosmetics, fabrics and plastics. Research shows that triclosan is no more effective than washing with regular soap and water, and the ubiquitous nature of the chemical is

leading to antibacterial resistance problems. Triclosan is so common that is has made its way into the human body; it's has been found in umbilical cords and breast milk.

The Canadian Paediatric Society has urged parents to stop buying antibacterial products, and instead use traditional soap and water to wash toys, hands or household items. The American Medical Association and Association for Professionals in Infection Control have said there's no evidence that antibacterial soaps prevent infections in homes. In October 2005, the Nonprescription Drugs Advisory Committee, which advises US FDA, voted 11-1 that antibacterial soaps and washes were no more effective than regular soap and water in fighting infections. Shortly after, Beyond Pesticides and 14 other public health and environmental advocacy groups petitioned FDA to ban triclosan for all non-medical uses. As of yet, the agency has failed to respond to the petition.

A 2006 study by the Johns Hopkins Bloomberg School of Public Health found that after people flush antibacterial products down the drain about 75 percent of triclocarban and triclosan compounds survive treatment at sewage plants and ends up in waterways and sludge spread on agricultural fields, and may end up on produce.

Excerpted from the Baltimore Sun, May 14, 2007.

BREAST CANCER LINKED TO CHEMICALS

More than 200 chemicals – many found in urban air and everyday consumer products – caused breast cancer in animal tests, according to a compilation of scientific report. In a publication of the American Cancer Society, researchers said that reducing exposure to the compounds could prevent many women from developing the disease.

The research team from five institutions analyzed a growing body of evidence that links environmental contaminants to breast cancer, the leading killer of U.S. women in their late 30s to early 50s. Experts say that family history and genes are responsible for a small percentage of breast cancer cases but that environmental or lifestyle factors such as diet are probably involved in the vast majority.

"Overall, exposure to mammary gland carcinogens is widespread," researchers from institutions in the Boston area, Los Angeles and Buffalo, N.Y., wrote in a special supplement to the journal Cancer. "These compounds are widely detected in human tissues and in environments, such as homes, where women spend time."

The scientists said there is insufficient data to estimate the number of breast cancer cases linked to chemical exposure. But because the disease is so common and the chemicals so widespread, "the public health impacts of reducing exposures would be profound even if the true relative risks are modest. If even a small percentage is due to preventable environmental factors, modifying these factors would spare thousands of women."

The three reports and a commentary were compiled by researchers from the Silent Spring Institute, a women's environmental health institute in Newton, Mass.; Harvard's Medical School and School of Public Health; the Roswell Park Cancer Institute, and the University of Southern California's Keck School of Medicine. Silent Spring Institute Executive Director Julia Brody led the team.

They named 216 chemicals that induce breast tumors in animals. Of those, people are highly exposed to 97, including industrial solvents, pesticides, dyes, gasoline and diesel exhaust compounds, cosmetics ingredients, hormones, pharmaceuticals, radiation and a chemical in chlorinated water.

Excerpted from Beyond Pesticides Daily News, January 27, 2007.

TOXIC EFFECTS OF PESTICIDES AMPLIFIED WHEN COMBINED

A new report finds significant harmful effects of pesticide mixtures on frogs, even though levels of the individual pesticides were thought not to cause harm and were 10 to 100 times below EPA standards. This finding, published January 23, 2007 by University of California Berkley professor Tyrone Hayes in the online version of the journal Environmental Health Perspectives, suggests that current efforts to assess health risks of chemicals in isolation may significantly undermine their danger.

Frogs treated with the mixture of pesticides, all commonly found in agricultural runoff, were, on average, 10 to 12 percent smaller than the untreated control group. Nearly 70% of the treated frogs became infected by a common pathogen that the untreated group fought off. They also developed holes, or plaques, in their thymus. High levels of corticosterone, a hormone similar to one found in humans, were also found. Corticosterone is associated with stress and known to decrease growth and slow development. In a related paper also published by Dr. Hayes on Jan. 27, 2006, these chemicals, and atrazine in particular, switched testosterone to estrogen, causing the testes of exposed male frogs to produce eggs instead of sperm. Effects were seen in frogs at concentrations of 0.1 parts per billion, a level far below any health threshold.

Dr. Shanna Swan a professor at the University of Rochester, has also found that pesticide concentrations as low as 0.1 ppb may cause problems in humans as well. In particular, she found a link between this concentration and low fertility in men. As a reference, the urine of a farm worker contains 2,400 parts per billion of some of these compounds.

Safety tests performed by the US EPA and FDA study only one compound in isolation. By ignoring the real-world interactions between different chemicals, the safety reports may be significantly underestimating the danger these chemicals cause. Though it may be more difficult to replicate real-world environments in studies, it is important to do so in order to fully understand the implications chemicals may have on human health and the environment.

Amphibians are declining at alarming rates across the globe, and many scientists believe that industrial chemicals and pesticides may be partially to blame. Numerous scientific studies have definitively linked pesticide use with significant developmental, neurological and reproductive effects on amphibians. Also, recent studies by Dr. Tyrone Hayes at the University of California demonstrated that atrazine is an endocrine disruptor that chemically castrates and feminizes male amphibians.

Additionally, a study by Penn State University researcher Joseph Kiesecker found that wild tadpoles exposed to low-level agricultural chemicals along with the deformity causing parasite trematode were five times more likely to develop leg deformities than frogs only exposed to the trematode. The presence of the pesticides is thought to weaken the frog's immune system, thereby making them more susceptible to infection by the parasites.

Excerpted from a Maryland Pesticide Network press release, May 15, 2007.

PESTICIDES IN THE CHESAPEAKE BAY WATERSHED PROJECT LAUNCHED

On May 14, 2007, Maryland Pesticide Network partnered with the Johns Hopkins Center for a Livable Future to establish the first working group to assess existing data on pesticides in the Chesapeake Bay watershed, to examine known and potential implications, and to identify strategies for reducing the volume and impacts of pesticides in the Chesapeake. In the Fall 2007, MPN will publish a white paper to communicate recommendations based on our research and suggestions from the working groups. Chesapeake Bay stakeholders and MPN will continue to meet to develop a strategy and timeline for implementing goals over the next two years. Stakeholders include scientists, public health experts, waterkeepers, watermen, government agency representatives, policymakers, representatives of environmental organizations, and others.

The Chesapeake Bay watershed is periled by various anthropogenic stressors. One such stressor is pesticides, an important but sometimes overlooked risk to aquatic life and the health of local residents. Whereas nutrient overloading rightfully captures most of the attention today, recent reports indicate that pesticides—which are designed to kill target organisms—frequently occur throughout the Chesapeake watershed and exceed water quality benchmarks. Evidence shows that many pesticides may be toxic to aquatic life, wildlife or humans.

Even at low levels, toxic effects from pesticides can place additional stress on resident microbiota, plants, fish and other wildlife, further threatening the largest and most biologically diverse estuary in the United States. Some pesticides also bioaccumulate in larger fish or contribute to adverse reproductive effects, such as the occurrence of eggs in male fish.

Pesticide contamination of drinking water and edible fish can also harm people who live in the Chesapeake region. Although existent drinking water standards are rarely exceeded, according to recent studies, comprehensive data are still lacking and risks of potential health impacts from low-level exposure to pesticides remain unknown. Vulnerable populations, such as infants and the elderly presumably are most at risk due to their weak immune responses and increased susceptibility. Those who depend on private wells serving less than 25 people also have an increased risk of exposure to pesticides in their drinking water because of a lack of government oversight.

Excerpted from Environmental Science & Technology Science News, Sept. 6, 2006.

EFFECTIVENESS OF TRUCK-MOUNTED SPRAYING AGAINST WEST NILE QUESTIONED

A new study shows that truck-mounted spraying does not reduce the transmission of West Nile Virus. The study, *Efficacy of Resmethrin Aerosols Applied from the Road for Suppressing Culex Vectors of West Nile Virus*, was funded in part by the Centers for Disease Control and the National Institutes of Health, and led by the Harvard School of) Public Health (Michael R. Reddy, et. al.).

The authors stated, "Although numerous field trials have demonstrated that insecticidal aerosols are lethal to caged mosquitoes (Mount 1998), few have monitored their impact on mosquitoes in nature." Their study was based on typical spray application of the pyrethroid pesticide, resmethrin, in a suburban area of eastern Massachusetts.

The authors said the treatments did not decrease the reproductive activity of the adult mosquitoes. They concluded: "We find that ULV applications of resmethrin had little or no impact on the Culex vectors of WNV, even at maximum permitted rates of application, [and] such insecticidal aerosols, delivered from the road, may not effectively reduce the force of transmission of WNV."

Excerpted from Environmental News Service, Dec.14, 2006.

EUROPEAN PARLIAMENT ADOPTS STRICTER CHEMICALS LAW

The European Parliament has approved regulations for hazardous chemicals that oblige producers to register all chemical substances produced or imported above a total quantity of one metric ton per year. Many are chemicals used in everyday products such as cosmetics, toys and building materials.

The most hazardous substances, such as those that are very persistent and those that accumulate up the food chain, will not be authorized if safer alternatives exist. Producers will have to submit a substitution plan to replace these toxic chemicals with safer ones. When no alternative exists, producers must

present a research plan aimed at finding one. The substitution measure covers about 3,000 of the most hazardous chemical substances.

The regulations, known as REACH (Registration, Evaluation, Authorization and Restriction of Chemicals), replaces 40 legislative texts that now govern chemicals in the European Union. European Parliament President Josep Borrell said, "This vote, on one of the most complex texts in the history of the EU, sets up an essential piece of legislation to protect public health and the environment from the risks of chemical substances, without threatening European competitiveness. It offers EU citizens true protection against the multitude of toxic substances in everyday life in Europe."

Environmental and consumer groups say the REACH does not go far enough. REACH, which takes effect in June 2007, transfers the burden of proof regarding testing and evaluation of the risks of chemicals from the authorities to industry.

"Major loopholes in REACH will still allow many chemicals that can cause serious health problems, including cancer, birth defects and reproductive illnesses, to continue being used in manufacturing and consumer goods," said a joint statement by Friends of the Earth Europe, Women in Europe for a Common Future, Greenpeace Europe, Eurocoop, the Health & Environment Alliance, and the European Environmental Bureau, which represents 143 member organizations in 31 countries.

"Further concessions exempt companies which import and manufacture chemicals in volumes below 10 tons a year – 60% of chemicals covered by REACH – from the requirement to provide any meaningful safety data," the groups said.

U.S. environmental organizations say they will use REACH to lobby for stricter controls on hazardous chemicals in the United States. Daryl Ditz, senior policy advisor at the Center for International Environmental Law, based in Washington, DC, said, "To protect the health of Americans and the competitiveness of U.S. companies, we must now overhaul our own laws on toxic chemicals."

Excerpted from the Montreal Gazette, April 4, 2006.

QUEBEC STRENGTHENS PESTICIDE BAN

A new era in pesticide use has begun in Quebec with the banning of many domestic products that have chemicals considered toxic to humans and the environment. The third and final phase of Quebec's Pesticide Management Code, first introduced in March 2003, has gone into effect. With its ban on 20 active ingredients, 210 lawn-care products are now off the market, giving Quebec the toughest standards in North America.

Home gardeners may no longer use such popular herbicides as Green Cross Killex, C-I-L Tri-Kill and Weedex that contain 2,4-D to rid lawns of dandelions and other weeds. Insecticides such as Sevin that include Carbaryl are also banned.

The move was hailed by concerned physicians and environmentalists. The Canadian Association of Physicians for the Environment, based in Toronto, said the code makes Quebec a leader in protecting human and animal health. "This bold action ... sets a standard for excellence that other governments ignore at their peril," said Warren Bell, an association board member.

Michel Gaudet, president of the Coalition for Alternatives to Pesticides, said that Quebec law is now in line with 2,4-D prohibitions in effect in Denmark, Norway and Sweden. "Sweden prohibited 2,4-D in 1977 and 12 years later they noted the increase in some of their cancers started to go down," he said.

PESTICIDE INJURY REPORTING – DID YOU KNOW IT'S MANDATORY!

Effective March 1, 2004 Maryland regulation (Code of Maryland Regulation 10.06.01) requires that health care providers (physician, physicians assistant, chiropractor, nurse practitioner, nurses, medical examiner, clinic, nursing home or any other licensed health care provider) and hospitals submit a report of diagnosed or suspected cases of pesticide related illness to the Commissioner of Health in Baltimore City or the health officer in the county where provider cares for that person.

To report online, go to www.cha.state.md.us/oeh/html/pesticide.html

QUESTIONS ABOUT PESTICIDE ILLNESS REPORTING?

Contact Clifford S. Mitchell, MS, MD, MPH, Director,
Environmental Health Coordination Program,
Maryland Department of Health and Mental Hygiene (DHMH)
cmitchell@dhmh.state.md.us

BIOMONITORING TESTS FOR DIAGNOSING PESTICIDE-RELATED ILLNESS: MARYLAND DHMH LABORATORY TESTING

Upon physician request, the Maryland Department of Health and Mental Hygiene laboratories Administration Division of Environmental Chemistry conducts biomonitoring testing for 11 organochlorines, 6 organophosphates, pyrethroid metabolite and heavy metals. For information on specific tests and how and when to submit a patient's urine sample contact Ms. Deborah Miller-Tuck, Director, Toxic Organics Program at 410.767.4388 or millertuck@dhmh.state.md.us.

DIAGNOSING PESTICIDE INJURY

For information on taking a pesticide exposure history go to: www.mdpestnet.org/history.pdf.

For a brief overview of diagnosing and treating pesticide injuries go to: www.mdpestnet.org/diagnostreatmnt.pdf, and www.mdpestnet.org/diagnostreatchart.pdf.

For the on-line version of US EPA Office of Pesticides Program's handbook on "Recognition and Management of Pesticide Poisonings" go to: www.epa.gov/oppfead1/safety/healthcare/handbook/handbook.

WHY REPORT SUSPECTED PESTICIDE-RELATED INJURIES TO MPN?

We need your help. The goal of MPN's collection of data on suspected pesticide injury in the state is to develop a yearly report to be shared with health care providers, county health officers and policy makers. As a non-government organization, we have the ability to compile this critical information and make it readily and regularly available to you on an ongoing basis. MPN's reporting system only requires the patient's initials, year of birth and zip code to account for and avoid duplication of reporting. Reporting this information should only take several minutes and is critical in conducting more accurate impact analysis of pesticide exposure. Your assistance is greatly appreciated! Please also report suspected injury to: www.mdpestnet.org/pesticide_injury_report.

ABOUT THE MARYLAND PESTICIDE NETWORK

The Maryland Pesticide Network (MPN) is a grassroots coalition of organizations in Maryland dedicated to protecting health and the environment from the hazards of pesticides and promoting safer solutions for healthy living. Founded in 1994, MPN's diverse membership includes health care provider, consumer, environmental, parent, labor, agricultural and religious organizations.

The impact of pesticide use is a complex issue about which we will never have perfect knowledge. Therefore, the coalition's work is based on the precautionary principle, that, "When an activity raises threats of harm to human health or their environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically."

One aspect of MPN's mission is to educate health care providers on how to prevent, diagnose, treat and report pesticide injuries.

MEMBER ORGANIZATIONS

American Academy of Pediatrics, MD Chapter; AFL-CIO, MD; American Lung Association, MD Chapter; Audubon Naturalist Society; Assateague Coastal Trust; Baltimore Physicians for Social Responsibility; Rachel Carson Council; Chemical Sensitivity Disorders Association; Chesapeake Bay Foundation; Clean Up Coalition; Clean Water Action-MD; Federated Garden Clubs of MD; Leukemia and Lymphoma Society-MD Chapter; MD Organic Food and Farmers Association; MCS Referral and Resources; MD Nurses Association; MD Assoc. of School Health Nurses; MD Interfaith Coalition for the Environment; MD League of Women Voters; MD League of Conservation Voters; Environment Maryland; MD State Teachers Association; MD PTA-Howard County Chapter; Beyond Pesticides; Sierra Club-MD Chapter.

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Ruth Berlin, L.C.S.W.-C, has been a practicing psychotherapist and a teacher in the field for the past 35 years. She was the co-founder and co-director of the Family Group Institute, San Francisco and associate faculty at the University of San Francisco Medical School. Ruth also co-founded and is the former co-director of InnerSource: A Center for Psychotherapy and Healing, in Annapolis, MD. She is the founder and executive director of the Maryland Pesticide Network.

Richard L. Humphrey, M.D., has been on the faculty and staff of the Johns Hopkins (JH) University School of Medicine, the JH Hospital and the JH Bloomberg School of Public Health for more than 45 years. Dr. Humphrey founded and directed the Multiple Myeloma and Plasma Cell Disease Research and Treatment Program at Johns Hopkins and was also the Director of the Immunology laboratory in the Department of pathology until his partial retirement in 1999.

Lawrence A. Plumlee, M.D., served as a research investigator in physiology at the Walter Reed Army Institute of Research and as medical science adviser in the office of research of the U.S. Public Health Service's Consumer Protection and Environmental Health Service, and at the U.S. Environmental Protection Agency. Dr. Plumlee was also Assistant Professor of Behavioral Biology at Hopkins. Presently he is editor of The Environmental Physician and President of the Chemical Sensitivity Disorders Association.

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Cover Photo: Courtesy of USDA

"When an activity raises threats of harm to human health or their environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically."

— *Precautionary Principle*

MPN

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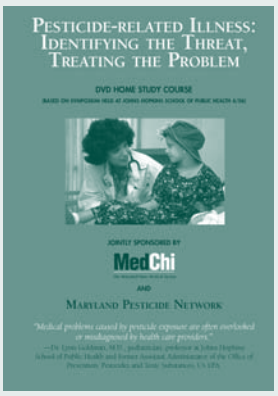

This course was originally a one-day symposium co-sponsored by MedChi, the Maryland State Medical Society and the Maryland Pesticide Network and co-partnered with the MidAtlantic Public Health Training Center; Johns Hopkins School of Public Health; Johns Hopkins Education and Research Center for Occupational Safety and Health; Johns Hopkins Center for Public Health Preparedness and the Institute for Johns Hopkins Nursing. It was held at the Johns Hopkins School of Public Health in April, 2006, and was designed by experts in the field to enable health care providers to more accurately diagnose, treat, report and prevent acute and chronic pesticide-related illness. It is a great tool for educating health care providers.

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of MedChi, The Maryland State Medical Society and the Maryland Pesticide Network. MedChi is accredited by the ACCME to provide continuing medical education for physicians. MedChi designates this educational activity for a maximum of 5.0 AMA PRA Category 1 credits™. Physicians should claim credit commensurate with the extent of their participation in the activity.

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