

PESTICIDES AND PUBLIC HEALTH: CRITICAL LITERATURE ON HUMAN HEALTH 2001-2005



MPN
MARYLAND PESTICIDE NETWORK

“Particular uncertainty exists regarding the long-term health effects of low-dose pesticide exposures. Current surveillance systems are inadequate to characterize potential exposure problems related either to pesticide usage or pesticide-related illnesses.”

— The American Medical Association’s Council on Scientific Affairs, 1997

Dear Health Care Provider:

Welcome to *Pesticides and Public Health: Critical Literature on Human Health 2001-2005*, a publication designed to keep the medical community up to date about this salient issue.

Most of us are carrying multiple toxic pesticides in our bodies, according to the CDC's Third National Report on Human Exposure to Environmental Chemicals released on July 21, 2005. About 90% of the study's sample group had 5 to 16 of the 21 pesticides in their bodies. The average levels in children were more than 4 times the levels considered acceptable by the EPA for 6-11 year-olds and more than 3 times the "acceptable" level for 12-19 year-olds.

The EPA estimates there are 300,000 acute pesticide-related illnesses each year in the United States. There are likely many more that go unreported or are misdiagnosed. Although further research is needed, existing epidemiological studies link pesticides to a wide range of acute as well as chronic illnesses, which include cancers, neurological and behavioral problems, reproductive dysfunctions, developmental disabilities, immune system disorders, and asthma and other respiratory diseases. Thus, pesticide illness may not be apparent until years after exposure.

In Maryland, there are 510,000 adults and 151,000 children who have a history of asthma. Childhood asthma in Maryland has increased 160% in the past twenty years. Some experts believe that increasing exposure to air pollution, including pesticides, contributes to these trends.

Nearly 100 pesticides are considered probable or likely carcinogens and nearly 90 pesticides are considered possible or suggestive human carcinogens by the EPA. Certain pesticides are linked to various cancers even at low-dose exposures. Research shows that certain pesticides may cause or promote non-Hodgkin's lymphoma, soft tissue sarcomas, lung cancer, childhood leukemia, and brain and nervous system tumors. Recent research also implicates pesticides in other chronic diseases such as Parkinson's and Lewy Body disease.

While the EPA registers pesticides for use, registration does not equal safety. The EPA states, "By their very nature, most pesticides create some risk of harm to humans, animals or the environment because they are designed to kill or otherwise adversely affect living organisms." In fact, it is against federal law to claim that any pesticide is safe. The U.S. General Accounting Office has repeatedly told Congress that, "The general public receives limited and misleading information on pesticide hazards and is misled on pesticide safety by pesticide applicator statements characterizing pesticides as 'safe' or 'harmless.'" Pesticide residues may be present hours, days and even months after an application, creating the potential for long-term exposure.

In light of the new Maryland Department of Health and Mental Hygiene regulations mandating pesticide injury reporting (see page 17 for more information), pesticide injury is a medical problem practitioners need to be informed about.

In May 2003 we distributed *Pesticides and Public Health: A Kit for Health Care Providers* to you and 17,000 of your colleagues in Maryland. The "kit" helps health practitioners to diagnose and treat pesticide injuries. Please return the enclosed order form if you would like to receive an additional health care provider kit, additional copies of this periodical, or copies of our resource guide for your patients—*Pesticides: The Risks, Prevention and Healthier Choices*.

We look forward to your feedback and to continuing to provide you with useful information on this critical subject.

Respectfully,

The Maryland Pesticide Network Health Care Provider Committee

Lorne K. Garrettson, M.D. (Chair)

Richard L. Humphrey, M.D.

Lawrence A. Plumlee, M.D.

JoAnn Schropp, R.N., M.S.N.

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RECENT RESEARCH (2001-2005)

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

Comments following each abstract are provided by pediatrician and medical toxicologist, Lorne K. Garrettson (LKG), M.D. Chair of Maryland Pesticide Network's health care provider committee; committee member, oncologist Richard L. Humphrey (RLH), M.D. and committee member JoAnn Schropp (JAS), R.N., M.S.N. (For biographical information, see page 18, "MPN Health Care Provider Committee Members.")

I. FETAL AND PEDIATRIC EFFECTS OF PESTICIDES

STUDIES

RELATION BETWEEN PESTICIDE EXPOSURE AND INTRAUTERINE GROWTH RETARDATION

Levario-Carrillo M, Amato D, Ostrosky-Wegman P, Gonzalez-Horta C, Corona Y, Sanin LH.

Unidad de Investigacion Medica en Epidemiologia Clinica, Hospital de Ginecologia y Obstetricia IMSS, Av. Division del Norte 2300 CH 44-228, Colonia Altavista, CP 31320 Chihuahua, Mexico.

The increased use of organophosphorus insecticides in agriculture and their widespread existence in the environment poses a potential health hazard. To determine the relationship between exposure to pesticides and intrauterine growth retardation (IUGR), live newborns from singleton pregnancies, with (n = 79) and without (n = 292) IUGR were studied. During the gestational period the mothers were living in agricultural communities in the state of Chihuahua, Mexico. Exposure to agrochemical products was evaluated. A significant association between the history of positive exposure to pesticides (i.e. the women themselves or their newborns who showed acetylcholinesterase activity levels lower than 20%) and the presence of IUGR was found. The proportions of exposure in the cases were 18% and 8% in the control group; the adjusted OR (fat free mass, anti-cytomegalovirus antibodies and placental weight) was 2.33 (p = 0.04).

Chemosphere. 2004 Jun;55(10):1421-7 PMID 15081785

Comment: This study was done with the unique situation of differential exposures in a population that has similar demographics. The results are compelling in that there is an association between pesticide exposure and growth retardation. —LKG

EXPOSURE TO INDOOR PESTICIDES DURING PREGNANCY IN A MULTIETHNIC, URBAN COHORT

Berkowitz GS, Obel J, Deych E, Lapinski R, Godbold J, Liu Z, Landrigan PJ, Wolff MS. Department of Community and Preventive Medicine, Mount Sinai School of Medicine, New York, New York 10029-6574, USA.

Evidence is growing that indoor pesticide exposure is of considerable magnitude in the United States and that pesticide concentrations may be especially high in urban areas. Of particular concern is exposure of pregnant women because animal data suggest that exposure to pesticides during pregnancy and early life may impair neurodevelopment in the offspring. To investigate the relationship between prenatal exposure to indoor pesticides and infant growth and development, we are conducting a prospective, multiethnic cohort study of mothers and infants delivered at Mount Sinai Hospital in New York City. This article provides data on pesticide exposure based on questionnaire items and analysis of maternal urinary metabolite levels among 386 women. Both the questionnaire and laboratory data revealed that exposure to indoor pesticides was considerable. The proportion of women estimated from questionnaire data as having been exposed during pregnancy to indoor pesticides (approximately 70%) was somewhat lower than the 80-90% of American households who reportedly used pesticides in previous surveys, but some of the latter surveys included both indoor and outdoor pesticide use. Urinary metabolite levels of 3,5,6-trichloro-2-pyridinol (TCPy; median = 11.3 micro g/g creatinine), phenoxybenzoic acid (PBA; median = 19.3 micro g/g creatinine), and pentachlorophenol (PCP; median = 7.3 micro g/g creatinine) were higher than those reported in other studies of adults in the United States. Furthermore, no associations were evident between the pesticide questionnaire data and the urinary metabolites. Assessments of sociodemographic and building characteristics with questionnaire data and the metabolite levels revealed no consistent trends. Significant temporal variations were observed for urinary PBA but not TCPy or PCP. The temporal variations for PBA were consistent with seasonal spraying of pyrethroid pesticides. These data underscore the need to assess the potentially adverse effects of pesticide exposure on fetuses and infants and the importance of finding alternative methods for pest management to reduce pesticide exposures.

Environ Health Perspect. 2003 Jan;111(1):79-84.
PMID: 12515682

Comment: This study documents, by biomarker assay, that exposure to pesticides in the urban community is large. Other studies by this group have documented the cost of this exposure to the fetuses of the community. —LKG

IN UTERO PESTICIDE EXPOSURE, MATERNAL PARAOXONASE ACTIVITY, AND HEAD CIRCUMFERENCE

Berkowitz GS, Wetmur JG, Birman-Deych E, Obel J, Lapinski RH, Godbold JH, Holzman IR, Wolff MS. Department of Community and Preventive Medicine, Mount Sinai School of Medicine, Box 1172, One Gustave L. Levy Place, New York, NY 10029-6574, USA.

Although the use of pesticides in inner-city homes of the United States is of considerable magnitude, little is known about the potentially adverse health effects of such exposure. Recent animal data suggest that exposure to pesticides during pregnancy and early life may impair growth and neurodevelopment in the offspring. To investigate the relationship among prenatal pesticide exposure, paraoxonase (PON1) polymorphisms and enzyme activity, and infant growth and neurodevelopment, we are conducting a prospective, multi-ethnic cohort study of mothers and infants delivered at Mount Sinai Hospital in New York City. In this report we evaluate the effects of pesticide exposure on birth weight, length, head circumference, and gestational age among 404 births between May 1998 and May 2002. Pesticide exposure was assessed by a prenatal questionnaire administered to the mothers during the early third trimester as well as by analysis of maternal urinary pentachlorophenol levels and maternal metabolites of chlorpyrifos and pyrethroids. Neither the questionnaire data nor the pesticide metabolite levels were associated with any of the fetal growth indices or gestational age. However, when the level of maternal PON1 activity was taken into account, maternal levels of chlorpyrifos above the limit of detection coupled with low maternal PON1 activity were associated with a significant but small reduction in head circumference. In addition, maternal PON1 levels alone, but not PON1 genetic polymorphisms, were associated with reduced head size. Because small head size has been found to be predictive of subsequent cognitive ability, these data suggest that chlorpyrifos may have a detrimental effect on fetal neurodevelopment among mothers who exhibit low PON1 activity.

Environ Health Perspect. 2004 Mar;112(3):388-91
PMID: 14998758

Comment: Similar to the study from Mexico, this study shows an effect on fetal brain growth from pesticide exposure in utero. Such effects have the possibility of causing the greatest long-term deficits in the child. —LKG

MULTIPATHWAY ORGANOPHOSPHORUS PESTICIDE EXPOSURES OF PRESCHOOL CHILDREN LIVING IN AGRICULTURAL AND NONAGRICULTURAL COMMUNITIES

Lu C, Kedan G, Fisker-Andersen J, Kissel JC, Fenske RA. Department of Environmental and Occupational Health Sciences, School of Public Health and Community Medicine, University of Washington, Box 357234, Health Sciences Building, Room F-225A, Seattle, WA 98195, USA.

Environmental measurements of organophosphorus (OP) pesticides were conducted in the homes of 13 children, who lived either in the Seattle metropolitan area or in the agricultural region of Washington State, to ascertain exposure through multiple pathways. Each home was sampled for two 24-hour periods during two seasons, summer and fall. Samples included 24-h indoor air, drinking water, soil, house dust, and hand and toy wipes and 24-h duplicate diets. At least one OP pesticide was found in each of the matrices sampled except for drinking water. Half of the indoor air samples contained detectable levels of chlorpyrifos or diazinon. Detectable levels of diazinon and azinphosmethyl in house dust were found in most of the agricultural homes, whereas only diazinon was found in the Seattle homes in the summer. Quantifiable chlorpyrifos and azinphosmethyl were found on either agricultural children's hands or their toys. These findings suggest different exposure pathways for children living in agricultural and non-agricultural regions.

Environ Res. 2004 Nov;96(3):283-9. PMID: 15364595

Comment: Pesticides can enter the body through multiple paths. Exposure prevention is therefore complex and will best be targeted to specific groups. —LKG

PRENATAL INSECTICIDE EXPOSURES AND BIRTH WEIGHT AND LENGTH AMONG AN URBAN MINORITY COHORT

Whyatt RM, Rauh V, Barr DB, Camann DE, Andrews HF, Garfinkel R, Hoepner LA, Diaz D, Dietrich J, Reyes A, Tang D, Kinney PL, Perera FP. Columbia Center for Children's Environmental Health, Mailman School of Public Health, Columbia University, New York, New York 10032, USA. rmw5@columbia.edu

We reported previously that insecticide exposures were widespread among minority women in New York City during pregnancy and that levels of the organophosphate chlorpyrifos in umbilical cord plasma were inversely associated with birth weight and length. Here we expand analyses to include additional insecticides (the organophosphate diazinon and the carbamate propoxur), a larger sample size ($n = 314$ mother-newborn pairs), and insecticide measurements in maternal personal air during pregnancy as well as in umbilical cord plasma at delivery. Controlling for potential confounders, we found no association between maternal personal air insecticide levels and birth weight, length, or head circumference. For each log unit increase in cord plasma chlorpyrifos levels, birth weight decreased by 42.6 g [95% confidence interval (CI), -81.8 to -3.8, $p = 0.03$] and birth length decreased by 0.24 cm (95% CI, -0.47 to -0.01, $p = 0.04$). Combined measures of (ln)cord plasma chlorpyrifos and diazinon (adjusted for relative potency) were also inversely associated with birth weight and length ($p < 0.05$). Birth weight averaged 186.3 g less (95% CI, -375.2 to -45.5) among newborns with the highest compared with lowest 26% of exposure levels ($p = 0.01$). Further, the associations between birth weight and length and cord plasma chlorpyrifos and diazinon were highly significant ($p < \text{or} = 0.007$) among newborns born before the 2000-2001 U.S. Environmental Protection Agency's regulatory actions to phase out residential use of these insecticides. Among newborns born after January 2001, exposure levels were substantially lower, and no association with fetal growth was apparent ($p > 0.8$). The propoxur metabolite 2-isopropoxyphenol in cord plasma was inversely associated with birth length, a finding of borderline significance ($p = 0.05$) after controlling for chlorpyrifos and diazinon. Results indicate that prenatal chlorpyrifos exposures have impaired fetal growth among this minority cohort and that diazinon exposures may have contributed to the effects. Findings support recent regulatory action to phase out residential uses of the insecticides.

Environ Health Perspect. 2004 Jul;112(10):1125-32 PMID: 15238288

Comment: Growth is not necessarily an indicator of significant injury. However, it is a red flag and caution must be exercised until long range studies can be done. —LKG

REVIEWS

PESTICIDES

Weiss B, Amler S, Amler RW. Department of Environmental Medicine, University of Rochester School of Medicine and Dentistry, Rochester, New York 14642, USA.

Pesticides are a broad group of heterogeneous chemicals that have a significant public health benefit by increasing food production productivity and decreasing food-borne and vector-borne diseases. However, depending on the agent and the exposure, they may pose health risks. Because of their behavior, acute accidental toxic exposures occur more commonly in children. Because of the dietary habits and greater intake of foods per kilogram in children and because some infants are breastfed, there is also concern about the effects on them of low-level environmental exposures. In the absence of direct conclusive evidence, consistent and relevant observations have led some investigators to infer that chronic low-dose exposure to certain pesticides might pose a potential hazard to the health and development of infants and children. Other investigators have concluded that such inferences can be neither supported nor refuted at the present time. The pediatrician has a role to play in recognizing the symptoms of acute exposure and to be able to provide appropriate treatment. It is essential to study whether there are subtle neurologic effects that may result from low-level pesticide exposures in individual patients.

Pediatrics. 2004 Apr;113(4 Suppl):1030-6. PMID: 15060196

Comment: Authors have considerable experience with environmental issues in children. This review is part of a broader group of environmental topics in a Supplement to Pediatrics. —LKG

PESTICIDES IN CHILDREN

Reigart JR, Roberts JR. Department of Pediatrics, Medical University of South Carolina, Charleston, South Carolina, USA.

Children are exposed to a wide range of pesticides, including insecticides, herbicides, fungicides, and rodenticides. They differ from adults in their exposures and responses to exposures. Acute and chronic toxicity are discussed, and important chronic effects, such as carcinogenesis, endocrine disruption, and neurodevelopment effects are reviewed. The state of laws and regulations are also discussed. Recommendations are made to pediatricians regarding treatment and advising families regarding avoidance of pesticide exposures and their effects.

Pediatr Clin North Am. 2001 Oct;48(5):1185-98, ix. PMID: 11579668

Comment: A thorough review by a long-time student of pesticide toxicology. —LKG

II. PULMONARY DISEASES

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 counter-matched 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 (p trend = 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.

Environ Health Perspect. 2004 May;112(6):760-5.
PMID: 15121522

Comment: Early childhood exposures are increasingly identified as associated with disease occurring later in childhood. Pesticides are among those agents usually found as associated, as in this article. All of the triggers identified in this article are those that we can reduce or eliminate. Caution demands that these avoidance steps be initiated now. The mechanisms of action of all these triggers will need to be further elucidated. —LKG

CHEMICAL PREDICTORS OF WHEEZE AMONG FARMER PESTICIDE APPLICATORS IN THE AGRICULTURAL HEALTH STUDY.

Hoppin JA, Umbach DM, London SJ, Alavanja MC, Sandler DP. Epidemiology Branch and Biostatistics Branch, National Institute of Environmental Health Sciences/NIH, Research Triangle Park, NC 27709-2233, USA.

Pesticides may contribute to respiratory symptoms among farmers. Using the Agricultural Health Study, a large cohort of certified pesticide applicators in Iowa and North Carolina, we explored the association between wheeze and pesticide use in the past year. Self-administered questionnaires contained items on 40 currently used pesticides and pesticide application practices. A total of 20,468 applicators, ranging in age from 16 to 88 years, provided complete information; 19% reported wheezing in the past year. Logistic regression models controlling for age, state, smoking, and history of asthma or atopy were used to evaluate associations between individual pesticides and wheeze. Among pesticides suspected to contribute to wheeze, paraquat, three organophosphates (parathion, malathion, and chlorpyrifos), and one thiocarbamate (S-ethyl-dipropylthiocarbamate [EPTC]) had elevated odds ratios (OR). Parathion had the highest OR (1.5, 95% confidence interval [CI] 1.0, 2.2). Chlorpyrifos, EPTC, paraquat, and parathion demonstrated significant dose-response trends. The herbicides, atrazine and alachlor, but not 2,4-D, were associated with wheeze. Atrazine had a significant dose-response trend with participants applying atrazine more than 20 days/year having an OR of 1.5 (95% CI 1.2, 1.9). Inclusion of crops and animals into these models did not significantly alter the observed OR. These associations, though small, suggest an independent role for specific pesticides in respiratory symptoms of farmers.

Am J Respir Crit Care Med. 2002 Mar 1;165(5):683-9. PMID: 11874814

Comment in: Am J Respir Crit Care Med. 2002 Mar 1;165(5):563-4.

Comment: Most will not remember which pesticides to ask about in the history of wheezing workers. However, this article supports the idea that these agents are associated with wheeze and that generic questions about workplace activities are appropriate. —LKG

PESTICIDE SPRAYING FOR WEST NILE VIRUS CONTROL AND EMERGENCY DEPARTMENT ASTHMA VISITS IN NEW YORK CITY, 2000

Karpati AM, Perrin MC, Matte T, Leighton J, Schwartz J, Barr RG. Division of Disease Control, New York City Department of Health and Mental Hygiene, New York, NY, USA.

Pyrethroid pesticides were applied via ground spraying to residential neighborhoods in New York City during July–September 2000 to control mosquito vectors of West Nile virus (WNV). Case reports link pyrethroid exposure to asthma exacerbations, but population-level effects on asthma from large-scale mosquito control programs have not been assessed. We conducted this analysis to determine whether widespread urban pyrethroid pesticide use was associated with increased rates of emergency department (ED) visits for asthma. We recorded the dates and locations of pyrethroid spraying during the 2000 WNV season in New York City and tabulated all ED visits for asthma to public hospitals from October 1999 through November 2000 by date and ZIP code of patients' residences. The association between pesticide application and asthma-related emergency visits was evaluated across date and ZIP code, adjusting for season, day of week, and daily temperature, precipitation, particulate, and ozone levels. There were 62,827 ED visits for asthma during the 14-month study period, across 162 ZIP codes. The number of asthma visits was similar in the 3-day periods before and after spraying (510 vs. 501, $p = 0.78$). In multivariate analyses, daily rates of asthma visits were not associated with pesticide spraying (rate ratio = 0.92; 95% confidence interval, 0.80–1.07). Secondary analyses among children and for chronic obstructive pulmonary disease yielded similar null results. This analysis shows that spraying pyrethroids for WNV control in New York City was not followed by population-level increases in public hospital ED visit rates for asthma.

Environ Health Perspect. 2004 Aug; 112(11): 1183-7
PMID: 15289164

Comment: Pyrethroids are likely antigens that can cause allergic reactions in sensitive individuals. It is reassuring that population spraying as shown in this study is not associated with measurable increases in asthma attacks. However, in the individual patient, the use of this group of pesticides needs to be considered in assessing the control of allergic triggers. —LKG

A CASE CONTROL ETIOLOGIC STUDY OF SARCOIDOSIS ENVIRONMENTAL AND OCCUPATIONAL RISK FACTORS

Lee S. Newman, Cecile S. Rose, Eddy A. Bresnitz, Milton D. Rossman, Juliana Barnard, Margaret Frederick, Michael L. Terrin, Steven E. Weinberger, David R. Moller, Geoffrey McLennan, Gary Hunninghake, Louis DePalo, Robert P. Baughman, Michael C. Iannuzzi, Marc A. Judson, Genell L.

Knatterud, Bruce W. Thompson, Alvin S. Teirstein, Henry Yeager, Jr., Carol J. Johns [{}dagger] , David L. Rabin, Benjamin A. Rybicki and Reuben Cherniack the ACCESS Research Group.* National Jewish Medical and Research Center and University of Colorado Health Sciences Center, Denver, Colorado; New Jersey Department of Health and Senior Programs, Trenton, New Jersey; University of Pennsylvania and Medical College of Pennsylvania-Hahnemann University Medical Centers, Philadelphia, Pennsylvania; Clinical Trials and Surveys Corp., and Johns Hopkins University School of Medicine, Baltimore, Maryland; Beth Israel Deaconess Medical Center, Boston, Massachusetts; University of Iowa College of Medicine, Iowa City, Iowa; Mount Sinai Medical Center, New York, New York; University of Cincinnati Medical Center, Cincinnati, Ohio; University of South Carolina, Charleston, South Carolina; Georgetown University Medical Center, Washington, DC; and Case Western Reserve University-Henry Ford Health Sciences Center, Detroit, Michigan

Past research suggests that environmental factors may be associated with sarcoidosis risk. We conducted a case control study to test a priori hypotheses that environmental and occupational exposures are associated with sarcoidosis. Ten centers recruited 706 newly diagnosed patients with sarcoidosis and an equal number of age-, race-, and sex-matched control subjects. Interviewers administered questionnaires containing questions regarding occupational and nonoccupational exposures that we assessed in univariable and multivariable analyses. We observed positive associations between sarcoidosis and specific occupations (e.g., agricultural employment, odds ratio [OR] 1.46, confidence interval [CI] 1.13–1.89), exposures (e.g., insecticides at work, OR 1.52, CI 1.14–2.04, and work environments with mold/mildew exposures [environments with possible exposures to microbial bioaerosols], OR 1.61, CI 1.13–2.31). A history of ever smoking cigarettes was less frequent among cases than control subjects (OR 0.62, CI 0.50–0.77). In multivariable modeling, we observed elevated ORs for work in areas with musty odors (OR 1.62, CI 1.24–2.11) and with occupational exposure to insecticides (OR 1.61, CI 1.13–2.28), and a decreased OR related to ever smoking cigarettes (OR 0.65, CI 0.51–0.82). The study did not identify a single, predominant cause of sarcoidosis. We identified several exposures associated with sarcoidosis risk, including insecticides, agricultural employment, and microbial bioaerosols.

American Journal of Respiratory and Critical Care Medicine
Vol 170. pp. 1324-1330, (2004) PMID: 15347561

Comment: Associations alone do not make the case. We must await an explanation of the biological plausibility of this observed association. It is intriguing that pesticides may be linked to this disease which has defied explanation for so long. —LKG

III. CANCER

STUDIES

PESTICIDES AND LUNG CANCER RISK IN THE AGRICULTURAL HEALTH STUDY COHORT

Alavanja MC, Dosemeci M, Samanic C, Lubin J, Lynch CF, Knott C, Barker J, Hoppin JA, Sandler DP, Coble J, Thomas K, Blair A. Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, MD 20892, USA. alavanjm@mail.nih.gov.

The authors examined the relation between 50 widely used agricultural pesticides and lung cancer incidence in the Agricultural Health Study, a prospective cohort study of 57,284 pesticide applicators and 32,333 spouses of farmer applicators with no prior history of lung cancer. Self-administered questionnaires were completed at enrollment (1993-1997). Cancer incidence was determined through population-based cancer registries from enrollment through December 31, 2001. A lung cancer standardized incidence ratio of 0.44 (95% confidence interval: 0.39, 0.49) was observed overall, due in large part to a low cigarette smoking prevalence. Two widely used herbicides, metolachlor and pendimethalin (for low-exposed groups to four higher exposure categories: odds ratio (OR) = 1.0, 1.6, 1.2, 5.0; $p(\text{trend}) = 0.0002$; and OR = 1.0, 1.6, 2.1, 4.4; $p(\text{trend}) = 0.003$, respectively), and two widely used insecticides, chlorpyrifos and diazinon (OR = 1.0, 1.1, 1.7, 1.9; $p(\text{trend}) = 0.03$; and OR = 1.0, 1.6, 2.7, 3.7; $p(\text{trend}) = 0.04$, respectively), showed some evidence of exposure response for lung cancer. These excesses could not be explained by previously identified lung cancer risk factors. The usage levels in this cohort are considerably higher than those typically experienced by the general population. An excess risk among spouses directly exposed to pesticides could not be evaluated at this time.

Am. J Epidemiol. 2004 Nov 1;160(9):876-85.
PMID: 15496540.

Comment: This article comes from a very experienced group of investigators at the National Cancer Institute who have a very large scale prospective cohort of subjects known as the Agricultural Health Study. From this data base a number of very important relationships are being discovered. In this study, exposure intensity to two widely used herbicides and two widely used insecticides is associated with the occurrence of lung cancer.—RLH

CANCER INCIDENCE AMONG PESTICIDE APPLICATORS EXPOSED TO ATRAZINE IN THE AGRICULTURAL HEALTH STUDY

Rusiecki JA, De Roos A, Lee WJ, Dosemeci M, Lubin JH, Hoppin JA, Blair A, Alavanja MC. Occupational and

Environmental Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Rockville, MD 20892-7240, USA.

BACKGROUND: Atrazine is the most heavily applied agricultural pesticide for crop production in the United States. Both animal and human studies have suggested that atrazine is possibly carcinogenic, but results have been mixed. We evaluated cancer incidence in atrazine-exposed pesticide applicators among 53,943 participants in the Agricultural Health Study, a prospective cohort study of licensed pesticide applicators in Iowa and North Carolina. **METHODS:** We obtained detailed pesticide exposure information using a self-administered questionnaire completed at the time of enrollment (1993-1997). Cancer incidence was followed through December 31, 2001. We used adjusted Poisson regression to calculate rate ratios (RRs) and 95% confidence intervals (CIs) of multiple types of cancer among atrazine exposed applicators. $P(\text{trend})$ values were calculated using atrazine exposure as a continuous variable, and all statistical tests were two-sided. Two exposure metrics were used: quartiles of lifetime days of exposure and quartiles of intensity-weighted lifetime days of exposure. **RESULTS:** 36,513 (68%) applicators reported ever using atrazine; exposure was not associated with overall cancer incidence. Comparisons of cancer incidence in applicators with the highest atrazine exposure and those with the lowest exposure, assessed by lifetime days (RR(LD)) and intensity-weighted lifetime days (RR(IWLD)) of exposure yielded the following results: prostate cancer, RR(LD) = 0.88, 95% CI = 0.63 to 1.23, $P(\text{trend}) = .26$, and RR(IWLD) = 0.89, 95% CI = 0.63 to 1.25, $P(\text{trend}) = .35$; lung cancer, RR(LD) = 1.91, 95% CI = 0.93 to 3.94, $P(\text{trend}) = .08$, and RR(IWLD) = 1.37, 95% CI = 0.65 to 2.86, $P(\text{trend}) = .19$; bladder cancer, RR(LD) = 3.06, 95% CI = 0.86 to 10.81, $P(\text{trend}) = .18$, and RR(IWLD) = 0.85, 95% CI = 0.24 to 2.94, $P(\text{trend}) = .71$; non-Hodgkin lymphoma, RR(LD) = 1.61, 95% CI = 0.62 to 4.16, $P(\text{trend}) = .35$, and RR(IWLD) = 1.75, 95% CI = 0.73 to 4.20, $P(\text{trend}) = .14$; and multiple myeloma, RR(LD) = 1.60, 95% CI = 0.37 to 7.01, $P(\text{trend}) = .41$, and RR(IWLD) = 2.17, 95% CI = 0.45 to 10.32, $P(\text{trend}) = .21$. **CONCLUSIONS:** Our analyses did not find any clear associations between atrazine exposure and any cancer analyzed. However, further studies are warranted for tumor types in which there was a suggestion of trend (lung, bladder, non-Hodgkin lymphoma, and multiple myeloma).

J Natl Cancer Inst. 2004 Sep 15;96(18):1375-82. PMID: 15367570.

Comment: From the same investigators discussed previously, a study of atrazine was reported. Atrazine, the most widely used insecticide in agriculture, has been suspected of being a carcinogen. This paper reports the authors' failure to find a convincing association between the overall cancer incidence and atrazine exposure. However, when specific cancers were separately analyzed, P value trends were suggestive for lung, bladder, NHL and multiple myeloma and were felt to justify further study.—RLH

USE OF AGRICULTURAL PESTICIDES AND PROSTATE CANCER RISK IN THE AGRICULTURAL HEALTH STUDY COHORT

Alavanja MC, Samanic C, Dosemeci M, Lubin J, Tarone R, Lynch CF, Knott C, Thomas K, Hoppin JA, Barker J, Coble J, Sandler DP, Blair A. Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, MD 20892, USA. alavanjm@mail.nih.gov.

The authors examined the relation between 45 common agricultural pesticides and prostate cancer incidence in a prospective cohort study of 55,332 male pesticide applicators from Iowa and North Carolina with no prior history of prostate cancer. Data were collected by means of self-administered questionnaires completed at enrollment (1993-1997). Cancer incidence was determined through population-based cancer registries from enrollment through December 31, 1999. A prostate cancer standardized incidence ratio was computed for the cohort. Odds ratios were computed for individual pesticides and for pesticide use patterns identified by means of factor analysis. A prostate cancer standardized incidence ratio of 1.14 (95% confidence interval: 1.05, 1.24) was observed for the Agricultural Health Study cohort. Use of chlorinated pesticides among applicators over 50 years of age and methyl bromide use were significantly associated with prostate cancer risk. Several other pesticides showed a significantly increased risk of prostate cancer among study subjects with a family history of prostate cancer but not among those with no family history. Important family history-pesticide interactions were observed.

Am J Epidemiol. 2003 May 1;157(9):800-14.
PMID 12727674

Comment: This paper from the same NIH group looks at the relationship of prostate cancer to pesticide exposure and concludes that the use of chlorinated pesticides by applicators over the age of 50 and the use of methyl bromide are significant risk factors. In addition, an important role for a positive family history of prostate cancer was observed for several other pesticides. This is an important observation confirming that not all individuals exposed to a specific agent will respond in the same way. Some are more susceptible than others. Why this is so - at a genetic and molecular level - will become an increasingly important research question. —RLH

INTERACTION BETWEEN GENETIC POLYMORPHISM OF CYTOCHROME P450-1B1 AND ENVIRONMENTAL POLLUTANTS IN BREAST CANCER RISK

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Cytochrome P450 1B1 (CYP1B1) is implicated in the activation of potentially carcinogenic xenobiotics and oestrogens. The polymorphism of the CYP1B1 gene at codon 432 (Val->Leu) is associated with change in catalytic function. In a case-series study of breast cancer patients, we investigated the interaction between this polymorphism and environmental exposure. The women carrying the Val CYP1B1 allele and who had lived near to a waste incinerator for more than 10 years had a higher risk of breast cancer than those never exposed with the Leu/Leu genotype (odds ratio of interactions (ORi)=3.26, 95% confidence interval (CI) 1.20-8.84). Also, the Val CYP1B1 allele increased the susceptibility to breast cancer for women exposed during their life to agricultural products used in farming (ORi = 2.18, 95% CI 1.10-4.32). These xenobiotics, mainly organochlorine hydrocarbons, are known to bind to the aromatic hydrocarbon receptor (AhR), and to induce the expression of CYP1B1 enzyme. The excess risk for exposed women with a Val CYP1B1 homo/heterozygous genotype could result from a higher exposure to activated metabolites of pesticides or dioxin-like substances. Also, a higher induction of CYP1B1 enzyme by xenobiotics could increase the formation of genotoxic catechol-oestrogens among exposed women carrying the Val CYP1B1 allele. Our results suggested that the Val CYP1B1 allele increases the susceptibility to breast cancer in women exposed to waste incinerator or agricultural pollutants.

Eur J Cancer Prev. 2004 Feb;13(1):83-6. PMID 15075793

Comment: This very interesting study analyzes the possible interaction between a polymorphism of cytochrome P450 1B1 and exposure to potentially carcinogenic xenobiotics and estrogens in the development of breast cancer. This enzyme has been implicated in the activation of these carcinogens with the val/val or val/leu alleles being more effective in this activation than the leu/leu allotype. Women who had the val/val or val/leu genotype and who lived near a waste incinerator for more than 10 years or were exposed to agents used in agriculture were two to three times more likely to develop breast cancer than women who had the leu/leu allele. If supported by additional studies, this work reveals the importance of the specific genetic make up of the individual exposed to a given environmental toxin or carcinogen in determining the risk of cancer development. As more such relationships are discovered the true magnitude of the risk of exposure to such agents as it relates to specific individuals may be revealed to be very significant. —RLH

ASSOCIATION BETWEEN AGENT ORANGE AND PROSTATE CANCER: A PILOT CASE-CONTROL STUDY.

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OBJECTIVES: To estimate in a pilot study the risk of being diagnosed with prostate cancer after exposure to Agent Orange in a clinical population of military veterans. Prostate cancer is the most common cancer diagnosed in American men and the second leading cause of cancer deaths. An association between Agent Orange and prostate cancer has been suggested by epidemiologic studies.

METHODS: A case-control study was conducted at the Department of Veterans Affairs Medical Center in Ann Arbor, Michigan. Cases of pathologically diagnosed prostate cancer were identified and age matched in a 1:3 ratio with controls. Exposure to Agent Orange was assessed by reviewing the administrative portion of the computerized medical records. A subanalysis of the cases was conducted to examine the clinical features of prostate cancer in men reporting exposure to Agent Orange versus those who did not report exposure.

RESULTS: A total of 47 military veterans with prostate cancer and 142 control men without prostate cancer were selected. After adjusting for age and race, men with prostate cancer were approximately two times more likely to report previous exposure to Agent Orange (odds ratio 2.06; 95% confidence interval 0.81 to 5.23). **CONCLUSIONS:** The results from this pilot study suggest exposure to Agent Orange is associated with an increased risk of prostate cancer. Additional study in larger populations is necessary to confirm and to quantify this association more accurately.

Urology. 2004 Apr;63(4):757-60; discussion 760-1.
PMID: 15072895

Comment: Agent Orange, a 1:1 mixture of 2,4-dichlorophenoxyacetic acid and 2,4,5-trichlorophenoxyacetic acid was widely used as a defoliant in Vietnam. It was contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin a member of the complex family of compounds known as the dioxins. Dioxins are known carcinogens. In this small study there was a two fold greater risk of developing prostate cancer if there had been previous exposure to Agent Orange. Although it is a limited study about which there can be some caveats, it is interesting because it highlights that an unsuspected contaminant in a product may actually be the harmful agent whereas the "active" agents may be playing a limited role in causing harm. —RLH

DIFFERENTIAL EFFECTS OF GLYPHOSATE AND ROUNDUP ON HUMAN PLACENTAL CELLS AND AROMATASE

Richard S, Moslemi S, Sipahutar H, Benachour N, Seralini GE. Laboratoire de Biochimie et Biologie Moléculaire, USC-INCR, Université de Caen, Caen, France.

Roundup is a glyphosate-based herbicide used worldwide, including on most genetically modified plants that have been designed to tolerate it. Its residues may thus enter the food chain, and glyphosate is found as a contaminant in rivers. Some agricultural workers using glyphosate have pregnancy problems, but its mechanism of action in mammals is questioned. Here we show that glyphosate is toxic to human placental JEG3 cells within 18 hr with concentrations lower than those found with agricultural use, and this effect increases with concentration and time or in the presence of Roundup adjuvants.

Surprisingly, Roundup is always more toxic than its active ingredient. We tested the effects of glyphosate and Roundup at lower nontoxic concentrations on aromatase, the enzyme responsible for estrogen synthesis. The glyphosate-based herbicide disrupts aromatase activity and mRNA levels and interacts with the active site of the purified enzyme, but the effects of glyphosate are facilitated by the Roundup formulation in microsomes or in cell culture. We conclude that endocrine and toxic effects of Roundup, not just glyphosate, can be observed in mammals. We suggest that the presence of Roundup adjuvants enhances glyphosate bioavailability and/or bioaccumulation.

Environ Health Perspect. 2005 Jun;113(6):716-20
PMID: 15929894

Comment: Also pointing to the importance of the role of "inert" chemicals in a product's formulation as a potential hazard, this report is very interesting. The authors conducted an in-vitro study using a human placental cell line (JEG3) that they exposed to glyphosate and Roundup which is a major glyphosate-based commercial product. In their studies, Roundup was "surprisingly...always more toxic than its active ingredient." This emphasizes that supposedly "inert" ingredients, often proprietary and hence not revealed, that are intended as adjuvants to enhance dispersal, spreading (surfactants), cell penetration and persistence—all of which are treated as diluents for regulatory purposes—may in fact also be the agents for toxic effects. Sometimes these "inert" chemicals may act synergistically with other chemicals found in the product or in the environment. —RLH

EPIGENETIC TRANSGENERATIONAL ACTIONS OF ENDOCRINE DISRUPTORS AND MALE FERTILITY

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Transgenerational effects of environmental toxins require either a chromosomal or epigenetic alteration in the germ line. Transient exposure of a gestating female rat during the period of gonadal sex determination to the endocrine disruptors vinclozolin (an antiandrogenic compound) or methoxychlor (an estrogenic compound) induced an adult phenotype in the F1 generation of decreased spermatogenic capacity (cell number and viability) and increased incidence of male infertility. These effects were transferred through the male germ line to nearly all males of all subsequent generations examined (that is, F1 to F4). The effects on reproduction correlate with altered DNA methylation patterns in the germ line. The ability of an environmental factor (for example, endocrine disruptor) to reprogram the germ line and to promote a transgenerational disease state has significant implications for evolutionary biology and disease etiology.

Comment: In this important study, the authors demonstrate that vinclozolin (a fungicide widely used in the wine industry) and methoxychlor (a pesticide substitute for DDT) cause heritable fertility problems in rats. Both of these agents are known endocrine disruptors. The striking new finding of this work is the demonstration that the impaired fertility effect is passed down at least four subsequent generations. The mechanism is not clear but seems correlated with altered DNA methylation in the germ line. If confirmed by future studies, this represents a new and very troubling way that endocrine disruptors can wreak havoc. —RLH

REVIEWS

THE EPIDEMIOLOGY OF PESTICIDE EXPOSURE AND CANCER: A REVIEW.

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Cancer is a multifactorial disease with contributions from genetic, environmental, and lifestyle factors. Pesticide exposure is recognized as an important environmental risk factor associated with cancer development. The epidemiology of pesticide exposure and cancer in humans has been studied globally in various settings. Insecticides, herbicides, and fungicides are associated with hemopoietic cancers, and cancers of the prostate, pancreas, liver, and other body systems. The involvement of pesticides in breast cancer has not yet been determined. In developing countries, sufficient epidemiologic research and evidence is lacking to link pesticide exposure

with cancer development. Agricultural and industrial workers are high-risk groups for developing cancer following pesticide exposure. Children of farm workers can be exposed to pesticides through their parents. Maternal exposure to pesticides can pose a health risk to the fetus and the newborn. The organophosphates are most the commonly used compounds, but the organochlorines are still permitted for limited use in developing countries. Pesticide exposure, independently or in synergism with modifiable risk factors, is associated with several types of cancer.

Rev Environ Health. 2005 Jan-Mar;20(1):15-38.
PMID: 15835496

ENVIRONMENTAL AND GENETIC RISK FACTORS FOR CHILDHOOD LEUKEMIA: APPRAISING THE EVIDENCE.

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Childhood leukemia is the most common cause of malignancy under the age of 15, representing an annual incidence rate of 43 cases per million in the United States. Confirmed clinical and epidemiologic associations explain less than 10% of disease incidence, leaving 90% of cases with an unclear etiology. To effectively study leukemia in children, one must recognize that this disease has a multifactorial causal mechanism and a heterogeneous biological composition. In addition, the timing of environmental exposures and genetic changes related to disease risk must be considered. This review of both environmental and genetic risk factors for childhood leukemia evaluates the current published literature and synthesizes the available knowledge. Furthermore, attention is directed to expected sources of new advances and the compelling current issues that need to be addressed before further progress can be made. We discuss parental occupational exposures, air pollution, other chemical exposures such as household solvents and pesticides, radiation, dietary factors, immunological factors, socioeconomic status, and genetic susceptibility. We hope to provide the reader with an understanding of the challenge and promise that characterizes the current and future directions in childhood leukemia research.

Cancer Invest. 2005;23(1):60-75. PMID: 15779869

Comment: These two recent reviews are recommended and will be found useful for those who would like to examine in a broader way the current state of our knowledge on these important topics. —RLH

EMERGING LINKS BETWEEN CHRONIC DISEASE AND ENVIRONMENTAL EXPOSURE: NON-HODGKIN'S LYMPHOMA

Readers who are interested in further information about the possible relationship of pesticides to Non-Hodgkin's Lymphoma are encouraged to obtain a copy of a recent review by distinguished authors in the field which is made available by Physicians for Social Responsibility. It is one of a series entitled: "Emerging Links between Chronic Disease and Environmental Exposure: Non-Hodgkin's Lymphoma", May, 2003. Contact: Physicians for Social Responsibility, 1875 Connecticut Ave., NW, Suite 1012, Washington, DC 20009; Phone: 202-667-4260; Fax: 202-667-4201; www.psr.org

IV. ENDOCRINE EFFECTS

RISK FACTORS FOR FEMALE INFERTILITY IN AN AGRICULTURAL REGION.

Greenlee AR, Arbuckle TE, Chyou PH. Marshfield Clinic Research Foundation, Marshfield, WI 54449, USA.

BACKGROUND: Recent studies have suggested that agricultural occupations or exposure to pesticides may impair female fertility. **METHODS:** The Fertility Risk Factor Study retrospectively examined agricultural and residential exposures and the risk of female infertility. Cases and controls (N = 322 each) came from women who sought treatment at a large group medical clinic in Wisconsin. Women and their male partners provided information on health, occupational and lifestyle exposures in response to a telephone interview during 1997-2001.

RESULTS: Mixing and applying herbicides 2 years before attempting conception was more common among infertile women (odds ratio [OR] = 27; 95% confidence interval [CI] = 1.9-380), as was the use of fungicides (OR = 3.3; CI = 0.8-13). Residing on a farm, ranch or in a rural area during this time period was protective of female fertility. Households supplied with central Wisconsin groundwater were at less risk for infertility than households using municipal sources (OR = 0.6; CI = 0.4-0.9). Behavioral risk factors included alcohol consumption (OR = 1.8; 1.2-2.5), smoking (1.6; 0.9-2.9), passive smoke exposure (1.8; 1.2-2.5), steady weight gain in adult life (3.5; 2.0-6.1), and having a male partner over the age of 40 (4.5; 1.2-16.3). Drinking 3 or more glasses of milk per day was protective of female fertility (0.3; 0.1-0.7). **CONCLUSION:** These results suggest that certain agricultural, residential and lifestyle choices may modify the risk of female infertility.

Epidemiology. 2003 Jul;14(4):429-36. PMID: 12843768

Comment: While any difference between herbicides is not delineated by this study, the enormous odds ratio makes one take notice. Endocrine effects of many pesticides have been seen in lower animals. This study is compelling enough to add appropriate questions to fertility histories everywhere. —LKG

V. RETINAL DEGENERATION

RETINAL DEGENERATION AND OTHER EYE DISORDERS IN WIVES OF FARMER PESTICIDE APPLICATORS ENROLLED IN THE AGRICULTURAL HEALTH STUDY

Kirrane EF, Hoppin JA, Kamel F, Umbach DM, Boyes WK, Deroos AJ, Alavanja M, Sandler DP. Coda, Inc., Durham, NC 27709, USA.

Retinal degeneration is the leading cause of visual impairment in older adults. An association between retinal degeneration and fungicide use was observed previously among farmer pesticide applicators in the Agricultural Health Study, a large study of farm families from Iowa and North Carolina. The objective of this investigation was to determine whether wives of these farmer pesticide applicators were at increased risk of retinal degeneration. Self-reported cross-sectional data obtained via questionnaire between 1993 and 1997 from 31,173 wives were used. Associations of specific pesticides and groups of pesticides based on function (fungicides, herbicides, insecticides, and fumigants) or chemical structure (organophosphates, organochlorines, and carbamates) with eye disorders were evaluated using logistic and hierarchical logistic regression analyses. Self-reported retinal degeneration was associated with the wife's fungicide use (odds ratio = 1.9, 95% confidence interval: 1.2, 3.1) after adjustment for age and state of residence. Specific fungicides that appeared to drive this association were maneb or mancozeb and ziram. No associations between pesticide use and other eye disorders were found. Although these findings for retinal degeneration are based solely on self-reported disease, they are consistent with those reported for farmer pesticide applicators. These findings suggest that exposure to some fungicides and other pesticides may increase the risk of retinal degeneration and warrant further investigation.

Am J Epidemiol. 2005 Jun 1;161(11):1020-9. PMID: 15901622

Comment: The fungicides which drive this association are commonly used in home and farm applications. This association needs confirmation and mechanistic studies but prudent advice may be to limit the exposure to these compounds by any person with genetic or other risk factors for retinal disease. —LKG

VI. GENE - ENVIRONMENT INTERACTION

CYP2D6 Polymorphism, Pesticide Exposure, and Parkinson's Disease

Elbaz A, Levecque C, Clavel J, Vidal JS, Richard F, Amouyel P, Alperovitch A, Chartier-Harlin MC, Tzourio C. National Institute of Health and Medical Research (INSERM) Unit 360, Hôpital de la Salpêtrière, 47 boulevard de l'Hôpital, 75651 Paris Cedex 13, France.

We performed a case-control study of Parkinson's disease (PD) in a population characterized by a high prevalence of pesticide exposure and studied the joint effect of pesticide exposure and CYP2D6. Although they are based on a small group of subjects with the joint exposure, our findings are consistent with a gene-environment interaction disease model according to which (1) pesticides have a modest effect in subjects who are not CYP2D6 poor metabolizers, (2) pesticides' effect is increased in poor metabolizers (approximately twofold), and (3) poor metabolizers are not at increased PD risk in the absence of pesticide exposure.

Ann Neurol. 2004 Mar;55(3):430-4. PMID: 14991823

Comment: These investigators have suggested, with this article, that there may be graded risk to pesticide exposure that is related to one's genetic make-up. With cigarettes there are some who are at greater risk of injury from exposure than others. The marker for that increased susceptibility is still ill-defined. We may be a long time from learning who is at greater risk with pesticides. As with cigarettes, the preventative action will need to be initiated before the biology is fully understood. —LKG

VII. ALTERNATIVES TO PESTICIDE USE

INTEGRATED PEST MANAGEMENT IN AN URBAN COMMUNITY: A SUCCESSFUL PARTNERSHIP FOR PREVENTION

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Pesticides, applied in large quantities in urban communities to control cockroaches, pose potential threats to health, especially to children, who have proportionately greater exposures and unique, developmentally determined vulnerabilities. Integrated pest management (IPM) relies on nonchemical tools—cleaning of food residues, removal of potential nutrients, and sealing cracks and crevices. Least toxic pesticides are used sparingly. To evaluate IPM's effectiveness, the Mount Sinai Children's Environmental Health and Disease Prevention Research Center, in partnership with two community health centers in East Harlem, New York City (NY, USA), undertook a prospective intervention trial. Families (n = 131) enrolled when mothers came to the centers for prenatal care. Household cockroach infestation was measured by glue traps at baseline and 6 months afterward. The intervention group received individually tailored IPM education, repairs, least-toxic pest control application, and supplies, with biweekly pest monitoring for 2 months and monthly for 4 months. The control group, residing in East Harlem and demographically and socioeconomically similar to the intervention group, received an injury prevention intervention. The proportion of intervention households with cockroaches declined significantly after 6 months (from 80.5 to 39.0%). Control group levels were essentially unchanged (from 78.1 to 81.3%). The cost, including repairs, of individually tailored IPM was equal to or lower than traditional chemically based pest control. These findings demonstrate that individually tailored IPM can be successful and cost-effective in an urban community.

Environ Health Perspect 111:1649-1653 (2003).

Comment: Other work from this group has shown the adverse effects on the fetus that heavy pesticide use can cause. This article clearly shows the efficacy of IPM, which avoids the significant risk of pesticide use. —LKG

VIII. INSECT REPELLANTS

STUDY

EXPOSURE OF CHILDREN TO DEET AND OTHER TOPICALLY APPLIED INSECT REPELLENTS

Menon KS, Brown AE. Department of Public and Community Health, University of Maryland, College Park, Maryland 20742, USA.

BACKGROUND: Use of topical repellents on children is common. Anecdotal reports suggest repellents may be applied inappropriately, but no studies characterizing the actual usage patterns and exposure of children have been reported.

METHODS: In the summer of 2002, a cross-sectional survey on the use patterns of repellents on children and possible associated effects was conducted in Maryland campgrounds. Information requested included products used, details of applications, post-application practices, and parents' decision-making process.

RESULTS: The study yielded 301 respondents. Deet was the most commonly used active ingredient (83.4%); aerosols were the most common formulation (42.5%). Over a third of subjects (38.9%) treated their children's clothing as well as their skin. Over half of the children did not remove the repellent before going to bed. More than a third of parents failed to read or follow label directions.

CONCLUSIONS: This study provides documentation of practices leading to undesirable exposure. Educational outreach to change parents' usage patterns is indicated.

Am J Ind Med. 2005 Jan;47(1):91-7. PMID: 15597352

Comment: While DEET is generally safe, excess use has caused serious consequences. It is worrisome, at least, that the population in the United States is as cavalier about the use of this compound as this article shows. Another effective repellent is picaridin. Although somewhat less effective than DEET and picaridin, oil of lemon eucalyptus and 2% soybean oil have insect repellent activity. —LKG

REVIEW

DEET-BASED INSECT REPELLENTS: SAFETY IMPLICATIONS FOR CHILDREN AND PREGNANT AND LACTATING WOMEN

Koren G, Matsui D, Bailey B. Division of Clinical Pharmacology and Toxicology, Hospital for Sick Children and University of Toronto, Toronto, Ont.

Reducing the risk of mosquito bites is currently the only way to reduce the risk of West Nile virus infection. Methods for avoiding mosquito bites include limiting the time spent outdoors at dawn and dusk, wearing protective clothing and using an insect repellent. Repellents containing DEET (N,N-diethyl-m-toluamide, also known as N,N-diethyl-3-methylbenzamide) are the most effective and most widely used. However, concerns have been raised over the risk of adverse toxic effects, especially in young children and pregnant and lactating women. In this article, we review the available evidence on the effectiveness and safety of DEET-based products. The evidence does not support increased risk in young children.

CMAJ. 2003 Aug 5;169(3):209-12 PMID: 12900480

Erratum in: CMAJ. 2003 Aug 19;169(4):283.

Comment in: CMAJ. 2004 Jan 6;170(1):14; author reply 14.

Comment: An exhaustive review by a highly regarded investigator finds that DEET, when used in recommended doses, does not pose an increased risk of side effects for children. Adverse effects when DEET is combined with pesticides in rodent studies will cause continued concern, especially in Maryland and other states, where synthetic pyrethroids are commonly used for mosquito control. —LKG

IX. ENVIRONMENTAL EFFECTS OF PESTICIDES

HERMAPHRODITIC, DEMASCULINIZED FROGS AFTER EXPOSURE TO THE HERBICIDE ATRAZINE AT LOW ECOLOGICALLY RELEVANT DOSES

Hayes TB, Collins A, Lee M, Mendoza M, Noriega N, Stuart AA, Vonk A. Laboratory for Integrative Studies in Amphibian Biology, Group in Endocrinology, Museum of Vertebrate Zoology, Department of Integrative Biology, University of California, Berkeley, CA 94720-3140, USA.

Atrazine is the most commonly used herbicide in the U.S. and probably the world. It can be present at several parts per million in agricultural runoff and can reach 40 parts per billion (ppb) in precipitation. We examined the effects of atrazine on sexual development in African clawed frogs (*Xenopus laevis*). Larvae were exposed to atrazine (0.01-200 ppb) by immersion throughout larval development, and we examined gonadal

histology and laryngeal size at metamorphosis. Atrazine (> or =0.1 ppb) induced hermaphroditism and demasculinized the larynges of exposed males (> or =1.0 ppb). In addition, we examined plasma testosterone levels in sexually mature males. Male *X. laevis* suffered a 10-fold decrease in testosterone levels when exposed to 25 ppb atrazine. We hypothesize that atrazine induces aromatase and promotes the conversion of testosterone to estrogen. This disruption in steroidogenesis likely explains the demasculinization of the male larynx and the production of hermaphrodites. The effective levels reported in the current study are realistic exposures that suggest that other amphibian species exposed to atrazine in the wild could be at risk of impaired sexual development. This widespread compound and other environmental endocrine disruptors may be a factor in global amphibian declines.

Proc Natl Acad Sci U S A. 2002 Apr 16;99(8):5476-80. PMID: 11960004

Comments: Important issues to emerge from this study were the low doses of atrazine used (concentrations considered safe in drinking water, or safe for limited human exposure); and the use of amphibians as environmental monitors or sentinels. Since the publication, the United States Environmental Protection Agency has re-registered atrazine. However, the European Union has refused to do so, in an effort to phase it out. Professor Hayes has continued his research with atrazine and has reported replications of his frog studies by other researchers that identify sexual development problems in goldfish, small mouth bass, salmon, alligators, and other species exposed to atrazine. —JS

The recent DCD-NCEH 3rd Biomonitoring report found no detectable atrazine in any group. While certainly reassuring for now, long term effects and thresholds for effects in humans haven't been determined. —LKG

X. EXPOSURE EPIDEMIOLOGY

ACUTE ILLNESSES ASSOCIATED WITH PESTICIDE EXPOSURE AT SCHOOLS.

Alarcon WA, Calvert GM, Blondell JM, Mehler LN, Sievert J, Propeck M, Tibbetts DS, Becker A, Lackovic M, Soileau SB, Das R, Beckman J, Male DP, Thomsen CL, Stanbury M. National Institute for Occupational Safety and Health, US Centers for Disease Control and Prevention, Cincinnati, Ohio 45226, USA. walarcon@cdc.gov

CONTEXT: Pesticides continue to be used on school property, and some schools are at risk of pesticide drift exposure from neighboring farms, which leads to pesticide exposure among students and school employees. However, information on the magnitude of illnesses and risk factors associated with these pesticide exposures is not available.

OBJECTIVE: To estimate the magnitude of and associated risk factors for pesticide related illnesses at schools.

DESIGN, SETTING, AND PARTICIPANTS: Analysis of surveillance data from 1998 to 2002 of 2593 persons with acute pesticide related illnesses associated with exposure at schools. Nationwide information on pesticide related illnesses is routinely collected by 3 national pesticide surveillance systems: the National Institute for Occupational Safety and Health's Sentinel Event Notification System for Occupational Risks pesticides program, the California Department of Pesticide Regulation, and the Toxic Exposure Surveillance System.

MAIN OUTCOME MEASURES: Incidence rates and severity of acute pesticide related illnesses.

RESULTS: Incidence rates for 1998-2002 were 7.4 cases per million children and 27.3 cases per million school employee full time equivalents. The incidence rates among children increased significantly from 1998 to 2002. Illness of high severity was found in 3 cases (0.1%), moderate severity in 275 cases (11%), and low severity in 2315 cases (89%). Most illnesses were associated with insecticides (n = 895, 35%), disinfectants (n = 830, 32%), repellents (n = 335, 13%), or herbicides (n = 279, 11%). Among 406 cases with detailed information on the source of pesticide exposure, 281 (69%) were associated with pesticides used at schools and 125 (31%) were associated with pesticide drift exposure from farmland.

CONCLUSIONS: Pesticide exposure at schools produces acute illnesses among school employees and students. To prevent pesticide related illnesses at schools, implementation of integrated pest management programs in schools, practices to reduce pesticide drift, and adoption of pesticide spray buffer zones around schools are recommended.

JAMA. 2005 Jul 27;294(4):455-65. PMID: 16046652

Comment: Maryland is one of the first states to implement an integrated pest management program for schools. While performance is inconsistent, (see page 15) it has served to reduce exposure for many of the State's children. This article suggests that we may need to expand the program to include buffer zones where agricultural pesticide application has the possibility of getting into schools. Drift control might be harder. This study shows that environmental exposure in schools does indeed pose a risk albeit one producing mild symptoms for the most part. There is still work to be done to get our children to a level of exposure that causes no harm. —LKG

RELEVANT NEWS

CDC: Most Americans Have Multiple Pesticides In Their Bodies

A Center for Disease Control and Prevention Third National Report on Human Exposure to Environmental Chemicals report released on July 21, 2005 says most Americans have multiple pesticides in their bodies. The report is the third in a series of bi-annual reports on statistically significant measurements of chemicals, or their metabolites, in the blood or urine of a representative cross section of Americans. The report includes information on 148 chemicals, including 43 pesticides. 3,097 individuals were tested for pesticides in their urine. 2,517 individuals were tested for pesticides in their blood. (http://www.cdc.gov/exposurereport/3rd/pdf/thirdreport_summary.pdf)

Scientists at Pesticide Action Network North America analyzed the report's pesticide data and found that 90% of those tested carried a mixture of pesticides in their bodies. Many of these chemicals have been associated with health effects such as cancer, birth defects and neurological problems. Their analysis of the CDC report found that:

- 21 pesticides were detected in 25% of the population tested. (Additional detail is available at www.panna.org)
- About 90% of the sample group had 5 to 16 of those 21 pesticides in their bodies.
- Six pesticides (or their metabolites) were found in 30% of the sample population.
- 76% had detectable levels of the synthetic pyrethroid permethrin, which is used in Maryland for mosquito control, and the organophosphate chlorpyrifos, which was recently phased out for residential use due to health concerns.
- The average levels in children were more than four times the levels considered acceptable by the U.S. EPA for children 6-11 years and more than three times the "acceptable" level for youth 12-19 years.

The CDC report acknowledges that there is widespread human exposure to synthetic pyrethroids and that more studies about the health effects are needed. However, there already is a growing body of research on this class of pesticides.

Synthetic pyrethroids are commonly used in lice treatments, agriculture and home and garden use, and are the poison of choice for ground applications in Maryland's mosquito control program. They are neurotoxic chemicals linked to cancer, respiratory problems such as asthma, Parkinson's disease, and endocrine disruption. The Maryland Department of Health and Mental Hygiene cautions: "People with existing respiratory problems, including asthma, allergies, and emphysema, are encouraged to stay indoors during spray events since pyrethroids may aggravate these conditions."

Organophosphates are widely used in agriculture, home and garden products, and mosquito control. In Maryland, the organophosphate Naled is applied aurally for mosquito control. Naled is classified by the EPA as a developmental and reproductive toxin. Organophosphates are neurotoxic chemicals and are now under review by the US EPA. Several organophosphates are already being phased out for residential use as a result of the EPA review, due to health concerns. Home use of chlorpyrifos was banned in 2001 because of concern over health effects in children, but an estimated 10 million pounds continues to be used in agricultural fields every year.

GULF WAR VETERANS' ILLNESS LINKED TO PESTICIDES

A federal panel of medical experts created by the Veterans Administration in 2002 has concluded that many 1991 Gulf War veterans are suffering from neurological damage caused from exposure to neurotoxic chemicals, including pesticides that inhibit the production of the enzyme acetylcholinesterase, necessary for the normal functioning of the central nervous system. The findings were reported in the *New York Times* on October 15, 2004 and in *Science* 306 (5693); 2004 Oct 1: 26-7.

U.S. FRESH WATER CONTAMINATED WITH PESTICIDES

The U.S. Geological Survey found that most of the nation's fresh water sources—especially those near agricultural and urban developments—are contaminated with low concentrations of chemicals. The study conducted by USGS found pesticides in 94 percent of all the water samples and in 90 percent of the fish samples, according to a May 22, 2004 *Science News* article.

Diazinon and malathion, which are insecticides commonly used on lawns and gardens, were found in nearly all of the sampled streams. Atrazine, metolachlor, alachlor, and cyanazine, which are herbicides, were found in streams in agricultural areas. Although concentrations of these chemicals in most areas were below the U.S. EPA's recommended limits, USGS found that such widespread contamination is cause for concern.

NEW NON-TOXIC TREATMENT FOR HEAD LICE

A paper published by the American Academy of Pediatrics in September 2004 details a new head lice treatment developed by dermatologist Dale Pearlman, M.D. The treatment uses no toxic chemicals and does not require nit removal. Instead, a lotion called Nuvo is used to suffocate the lice. Nuvo is dried on the scalp, left for eight hours, and then shampooed out. "Lice have portholes on the side of their bodies, which they breathe through. If you plug up all those portholes, they die," Dr. Pearlman told Reuters Health. The treatment is given once per week for up to three weeks.

Dr. Pearlman notes in the article that all of the ingredients in the lotion are "generally recognized as safe" by the U.S. Food

and Drug Administration, although it is not yet approved. Nuvo lotion contains stearyl alcohol, propylene glycol, sodium lauryl sulfate, cetyl alcohol, water and other ingredients. In two studies involving 133 children with head lice infestation, the cure rate was 96 percent. This success rate is equal to or better than conventional lice treatment shampoos, which contain insecticides such as permethrin, malathion, and lindane.

Permethrin is considered a possible carcinogen and a suspected endocrine disruptor. Endocrine disruptors interfere with normal hormone functions and are linked to breast and testicular cancers, birth defects, learning disorders, and other adverse health problems. Malathion may affect the central nervous system, the immune system, adrenal glands, liver and blood. Malathion is mutagenic in humans and other animals. Lindane is a carcinogen and may cause seizures or even death when absorbed through the skin in overdose. More than 500 cases of adverse impacts from products containing lindane have been reported.

Children are more susceptible to the harmful effects of pesticides because they have developing organ systems that are more vulnerable and less able to detoxify chemicals. Low levels of pesticide exposure can adversely affect a child's neurological, immune and endocrine systems.

MARYLAND SCHOOLS AND DEPARTMENT OF AGRICULTURE NOT COMPLYING WITH IPM-IN-SCHOOLS LAW

A significant number of Maryland schools and the state Department of Agriculture (MDA) are failing to fully implement a state law designed to minimize the use of pesticides in and around public schools—leaving students, staff and others at greater risk of suffering from the harmful effects of toxic chemicals, according to first-of-their kind reports released by the Maryland Pesticide Network (MPN) on September 22, 2004.

The state's Integrated-Pest Management-in-Schools (IPM) Law went into effect in September 2000. Its intent was to eliminate or significantly minimize the use of chemical pesticides that can be harmful to humans in and around Maryland public schools. The law also provides notification to parents/guardians and employees about pesticide use in their schools. Children and pregnant women—both prominent on school campuses—are particularly vulnerable to the effects of pesticides.

A two-year MPN survey assessed the law's implementation by querying school district pest control managers, teachers and Parent-Teacher Association presidents. A second MPN effort reviewed MDA's published guidelines for schools on implementing the law. MPN's major findings include:

- While some school districts are successfully implementing the law, the majority of school districts are not. Some schools are failing to follow mandated procedures for using non-toxic options first and pesticides only as a last resort. Some are failing to provide mandated notification when using pesticides.
- MDA guidelines, meant to help schools implement the law, are instead a major detriment to implementation because of

the degree to which they misrepresent the law. Thus, even school districts that follow the MDA guidelines are not in compliance with the law.

- MDA has declined to correct the guidelines, despite being advised to do so by the Maryland Attorney General's office.

Details and copies of the MPN Reports *Are We Passing the Grade? - Assessing MD Schools Compliance with IPM-In-Schools Law*, and *Are We Passing the Grade? — Maryland Department of Agriculture's failure to comply with the Integrated Pest Management-in-Schools Law* are available to download in PDF from Maryland Pesticide Network's website www.mdpestnet.org.

The law mandates that pesticides are only to be considered as an option when non-toxic options are unreasonable or have been exhausted, in order to a) minimize the use of pesticides and b) minimize the risk to human health and the environment associated with pesticide applications. The law requires universal notification of pesticide applications to elementary school children's parents/guardians and to employees, and notification of middle and high school student's parents/guardians and employees who sign up for notification at the beginning of the school year.

PESTICIDES AND TERRORISM: EXPERTS CALL FOR NEW CHEMICAL ATTACK ANTIDOTES

From : Manchester Online (Manchester Evening News, G.B.); Friday, 19th November 2004; <http://www.cwmg.org/men11.19.04.html>

Scientists need to develop new antidotes to prepare for possible terrorist chemical attacks in the West, researchers urge, according to the study in the British Medical Journal.

But despite the severity of the situation, neither the pharmaceutical industry nor the military have attempted to test new remedies to deal with the danger from organophosphates, according to experts from Canberra Hospital in Australia. Organophosphates are used in some pesticides, but have also been used in chemical weapons and nerve gas attacks, such as the sarin attack in Japan.

But despite the concerns, no new antidotes have been tested in clinical trials in the last 30 years.

The current treatment involves giving victims atropine and benzodiazepines, but these are only moderately effective. "Newer, more effective antidotes are needed," the researchers said. "The currently recommended antidotes are the tip of a therapeutic iceberg that could be mobilized."

The researchers said animal studies had revealed the potential for new treatments. "Information on these potential treatments has been available for years, but neither the military nor the pharmaceutical industry has attempted to test them or develop new drugs," they said. The researchers pointed out that every

year hundreds of thousands of people were dying from pesticide poisoning in the world's poorest countries.

They also said that given government concerns about having the means to respond to victims of chemical warfare and terrorist attacks, "the time is ripe to break this drug development impasse."

"HEALTHY HOSPITALS" REPORT SPURS GROUNDBREAKING PILOT PROJECT IN MARYLAND

Our most vulnerable populations—newborns, the sick and the elderly—are for the most part unknowingly exposed to pesticides used in hospitals and nursing homes. According to a 2003 report, "Healthy Hospitals: Controlling Pests Without Harmful Pesticides" published by Health Care Without Harm and Beyond Pesticides, few hospitals in the country are aware of this critical issue and most regularly use toxic pesticides that may put the health of patients and employees at greater risk. As the report states, "Hospital patients who have compromised immune and nervous systems, the elderly, infants and children and those who have an allergy or sensitivity to pesticides are particularly vulnerable to their toxic effects. Patients taking certain medications may also have heightened reactions to pesticides."

Patients and employees of hospitals and nursing homes are rarely notified about their exposure to pesticides. While it is important that health related facilities maintain environments free of pests that threaten health, it is also important that patients, their visitors and employees be protected from exposure to pesticides.

Fortunately, increasing numbers of health-related facilities are implementing Integrated Pest Management programs based on the understanding that pest control does not necessitate

the use of chemical pesticides. For example the VA policy for pest control is based on the understanding that no chemical controls are to be used where appropriate alternatives exist. "Pest management in health care facilities differs from control practices in other types of institutions," states the Department of Veterans Affairs. "The effect on patients in various stages of debilitation and convalescence, and in varied physical and attitudinal environments, requires that a cautious, conservative policy be adopted concerning all uses of pesticides." Massachusetts General Hospital opposes the use of pesticides in the workplace. San Francisco General Hospital only uses pesticides as a last resort and claims that other methods are tried first and almost always succeed. The Friends House in Maryland, whose facilities range from assisted living to full nursing home care have changed from a pesticide-reliant pest control program to a non-chemical approach.

Several states (Illinois, Maine, Massachusetts, New Jersey and Texas) require notification of pesticide use for certain types of pesticide applications made in health care facilities. Twenty states, including Maryland, require commercial applicators to post notification signs when pesticides are applied to lawns.

Based on the report's findings, the Maryland Pesticide Network, in partnership with Beyond Pesticides and in collaboration with Maryland Hospitals for a Healthy Environment and the University of Maryland School of Nursing Environmental Health Education Center, has launched an IPM in Health Care Facilities Program. The program includes surveying all Maryland hospitals and nursing homes to assess their current pest control practices and a one-year IPM pilot project with several preeminent Maryland healthcare facilities. The results of the survey and the pilot project will be published in a report in 2007.

PESTICIDE INJURY – MANDATORY REPORTING IN MARYLAND

Effective March 1, 2004 Maryland regulation (Code of Maryland Regulation 10.06.01) requires that health care providers (physician, physicians assistant, chiropractor, nurse practitioner, nurse, 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: <https://www.cha.state.md.us/oeht/html/hcp/hcp.cfm>

Questions about pesticide illness reporting?

Contact Dr. Marguerite Hawkins at the Maryland Department of Health and Mental Hygiene (DHMH): mhawkins@dhhm.state.md.us

WHY IT IS ALSO CRITICAL TO REPORT 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 report suspected injury to: www.mdpestnet.org. Click on the link to Pesticide Injury Reporting.

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/diagnostreatment.pdf and www.mdpestnet.org/diagnostreatchart.pdf
- For the on-line version of the U.S. EPA Office of Pesticides Program's handbook on "Recognition and Management of Pesticide Poisonings," do a general search on www.epa.gov by the title of that publication.

MARYLAND DHMH BIOMONITORING TESTING FOR DIAGNOSING PESTICIDE-RELATED ILLNESS

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 metabolites 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@dhhm.state.md.us

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 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; MD Public Interest Research Group; MD State Teachers Association; MD PTA-Howard County Chapter; Beyond Pesticides/National Coalition Against Misuse of Pesticides; Sierra Club-MD Chapter.

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MPN HEALTH CARE PROVIDER COMMITTEE MEMBERS

Lorne Garrettson, M.D., is Board Certified in Pediatrics and Medical Toxicology. He has served on the faculties of medicine at State University of New York at Buffalo, Virginia Commonwealth University and Emory University. He has been involved in the management of poison control centers and in the care of poisoned patients for 40 years and has run clinics for the diagnosis and care of lead poisoned children in Virginia and Georgia. Dr. Garrettson developed the Georgia Poison Center as a reference center for the public and professionals on issues of drugs in human breast milk. He has served on the editorial boards of the *Journal of Toxicology*, *Clinical Toxicology* and as chair of the Poison Prevention Subcommittee of the AAP Injury Prevention Committee and as Chair of the Section of Clinical Pharmacology and Therapeutics. He is the author of 75 articles and 13 chapters to textbooks dealing with lead poisoning, drug metabolism and other toxicologic topics. He currently serves as advisor to the Maryland Children's Environmental Health and Protection Advisory Committee and Montgomery County's Child Mortality Committee.

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. He has held appointments in the Department of Internal Medicine, Oncology and Pathology in the School of Medicine and Health Policy and Management in the School of Public Health. 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. Dr. Humphrey is the author or co-author of more than 70 published articles and 30 textbook chapters. Dr. Humphrey is on the Steering Committee of the Baltimore Chapter of Physicians for Social Responsibility and an Advisory Board member of the Center for a Livable Future. He remains active in teaching, research, mentoring students and fellows, and as an Attending in the Immunology Laboratory.

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.

Jo Ann Schropp, R.N., M.S.N. is a Psychiatric Nursing Clinical Instructor at Howard County Community College, Columbia, Maryland. She was a Mental Health Nursing Clinical Specialist at Anne Arundel Medical Center (AAMC) in Annapolis, Maryland, and also served as a consultant to the Inpatient Psychiatric Service. She worked extensively with the AAMC Cardiac Rehabilitation Service as an education and counseling resource for patients and their families and has also worked in the OB/GYN, Pediatric, and Public Health Nursing specialty areas.

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precautionary measures should be taken
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are not fully established scientifically.”*

— *Precautionary Principle*

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