

# Pesticides and Public Health

**CRITICAL LITERATURE ON HUMAN HEALTH**



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**MPN**  
MARYLAND PESTICIDE NETWORK

## ACKNOWLEDGEMENTS

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MPN is also grateful for the continued dedication of its Health Care Provider Committee in publishing the third edition of this Journal: Lorne Garrettson, M.D., Ruth Berlin, LCSW-C, Richard Lord Humphrey, M.D. and Lawrence Plumlee, M.D. Thanks to Ira Rifkin for his editorial assistance.

Spring 2009

Dear Health Care Provider:

Welcome to the third 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 issue, as well as relevant news. It is intended to assist you in understanding the impact of pesticides on public health so that you may be better-versed in diagnosing suspected pesticide-related illnesses and can better advise your patients and communities on why and how they should limit exposures, and on using safer and least-toxic alternatives.

While we generally think of pesticides in relationship to insect, rodent or landscape management, pesticides have many other uses. For example, registered pesticides are used as antimicrobials in soaps and other cosmetics and are also common ingredients in cleaning products. Common routes of exposure are air, water and food.

To date the acute and chronic synergistic effects of these daily exposures to multiple pesticides and other chemicals have yet to be examined by the US Environmental Protection Agency, and therefore are not considered in the pesticide registration process. Since the second edition of this Journal in Fall 2007, additional research indicates that adverse health effects are more likely as a result of combined pesticide exposures..

In April 2009, U.S. EPA launched its mandated evaluation of pesticides for their role as endocrine disruptors. Pesticide manufacturers are required to initially test 67 chemicals contained in their products to determine whether they disrupt the endocrine system. Endocrine disrupting pesticides have been linked to intersex fish in the Potomac River and lifelong health problems include certain cancers.

“Inert” ingredients that generally comprise the largest percentage of a pesticide product or formulation and can be more toxic than the active ingredient continue to be considered “trade secrets” and therefore remain undisclosed. Registration requirements for inerts remain less stringent than for active pesticide ingredients.

The body of research on the impact of pesticides on public health and the environment continues to grow. We reviewed hundreds of peer-reviewed studies published over the past 18 months for this edition (as we did for the first two editions) and only included those studies we decided are currently clinically relevant, bring understanding to the practice of medicine, or reveal emerging patterns of disease.

The News items included in this edition also represent what we believe to be the most valuable information available for health care providers.

We look forward to your feedback. Please let us know how we can better serve your needs by sending an email to [info@mdpestnet.org](mailto:info@mdpestnet.org). We also encourage you to contact us with any questions or other 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



**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

June 1, 2009

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 new web page, at <http://dhmh.md.gov/eh>. The page also describes how to report pesticide-related illness, including our downloadable 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. 32 for more information regarding mandatory injury reporting]*

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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 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 committee members Psychotherapist Ruth Berlin (R.B.), L.C.S.W.-C., Oncologist Richard L. Humphrey (R.L.H.), M.D., and Physician Lawrence A. Plumlee (L.A.P.), M.D. (For additional information, see page 34, MPN Health Care Provider Committee members.)

## RECENT RESEARCH

### ACUTE PESTICIDE POISONING

#### ACUTE PESTICIDE POISONING AMONG AGRICULTURAL WORKERS IN THE UNITED STATES, 1998-2005

Calvert GM, Karnik J, Mehler L, Beckman J, Morrissey B, Sievert J, Barrett R, Lackovic M, Mabee L, Schwartz A, Mitchell Y, Moraga-McHaley S. [jac6@cdc.gov](mailto:jac6@cdc.gov)

*American Journal of Industrial Medicine*. 2008 Dec; 51(12):883-98. PMID: 18666136

**Background:** Approximately 75% of pesticide usage in the United States occurs in agriculture. As such, agricultural workers are at greater risk of pesticide exposure than non-agricultural workers. However, the magnitude, characteristics and trend of acute pesticide poisoning among agricultural workers are unknown.

**Methods:** We identified acute pesticide poisoning cases in agricultural workers between the ages of 15 and 64 years that occurred from 1998 to 2005. The California Department of Pesticide Regulation and the SENSOR-Pesticides program provided the cases. Acute occupational pesticide poisoning incidence rates (IR) for those employed in agriculture were calculated, as were incidence rate ratios (IRR) among agricultural workers relative to non-agricultural workers.

**Results:** Of the 3,271 cases included in the analysis, 2,334 (71%) were employed as farmworkers. The remaining cases were employed as processing/packing plant workers (12%), farmers (3%), and other miscellaneous agricultural workers (19%). The majority of cases had low severity illness (N = 2,848, 87%), while 402 (12%) were of medium severity and 20 (0.6%) were of high severity. One case was fatal. Rates of illness among various agricultural worker categories were highly variable but all, except farmers, showed risk for agricultural workers greater than risk for non-agricultural workers by an order of magnitude or more. Also, the rate among female agricultural workers was almost twofold higher compared to males.

**Conclusion:** The findings from this study suggest that acute pesticide poisoning in the agricultural industry continues to be an important problem. These findings reinforce the need for heightened efforts to better protect farmworkers from pesticide exposure.

**Comment:** This author has studied agricultural pesticide poisoning for years and this is a new comprehensive study extending the detail of what has been known. It relies on new reporting techniques that capture more cases. It is noted that the pesticide injury rate for agricultural workers is 39 times higher than injury rates for all causes in all other industries! The precipitating causes of pesticide injury are pesticide wind drift, entering the field too soon after application, and not following instructions. Half a century ago, the famous pesticide toxicologist, Wayland J. Hayes, MD, made the observation that no one got poisoned who read the label. Nonetheless, this study shows the enormous risk taken by agricultural workers because of pesticides. This article is full of data on which pesticides, what region, and how severe the symptoms were for each group of compounds. – L.K.G.



#### PYRETHRIN AND PYRETHROID EXPOSURES IN THE UNITED STATES: A LONGITUDINAL ANALYSIS OF INCIDENTS REPORTED TO POISON CENTERS

Power LE, Sudakin DL.

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*Journal of Medical Toxicology*. 2007 Sep; 3(3):94-9. PMID: 18072143

**Introduction:** Citing the Food Quality Protection Act, the US Environmental Protection Agency (EPA) decided to phase out and eliminate organophosphate insecticide use in residential environments. The phase out process spanned from 2000 to 2005, and it may have resulted in increased consumer use of insecticides containing other active ingredients. This study utilized data from the national Poison Control Center to assess possible changes in exposure incidents involving pyrethrin and pyrethroid insecticides during the phase out of organophosphates from residential uses.

**Methods:** We extracted pyrethrin and pyrethroid insecticide exposure data from the American Association of Poison Control Centers Toxic Exposure Surveillance System (TESS) annual reports from 2000 to 2005. We examined pyrethrin and pyrethroid incidents by total exposures for each year, and we stratified exposures by age range, reason, number of cases treated in

a health care facility, and medical outcome. Cases were examined as a proportion of all insecticide exposures. We calculated the annual incidence rates for exposures involving pyrethrin and pyrethroid insecticides of the population served.

**Results:** Pyrethrin and pyrethroid exposures increased annually in number and as a percentage of all insecticide exposure incidents. The increase in cases was observed for all age categories and exposure reasons. A statistically significant correlation was observed between advancing years (2000-2005) and the number of pyrethrin and pyrethroid incidents ( $p < .01$ ). While the number of incidents treated in a health care facility increased annually during the study period, the proportion was constant ( $0.185 \pm 0.012$ ) over the six year period. During the study period, the incidence rate for pyrethrin and pyrethroid exposures increased each year. 44% of all medical outcomes data was recorded, and the majority of outcomes resulted in no symptoms (37%) or minor symptoms (53%).

**Conclusion:** TESS data showed a clear increase in cases involving pyrethrins and pyrethroids. The increase was temporally associated with the phase out of organophosphates from

residential uses. In the future, medical toxicologists and poison control center personnel should be prepared to respond to an increasing number of pyrethrin and pyrethroid insecticide exposures.

**Comment:** *The phase out of organophosphates for home uses is beneficial in two arenas. Firstly, these compounds are associated with significant acute poisoning risk. Secondly, they have been implicated in chronic disease from all ages of exposure. As the use of these compounds dropped, the pyrethroids rose in use. While these compounds are much less likely to cause acute symptoms (90% of cases reported here were either symptom free or had only minor symptoms), pyrethroids can cause irritation to eyes, skin and mucous membranes which probably accounts for the majority of minor complaints and may account for the sporadic and uncommon complaint of dyspnea. Thus, advice has been for those with existing medical conditions to avoid exposure. While pyrethroids have been linked to Parkinson's Disease and certain pyrethroids are considered possible carcinogens and endocrine disruptors, the long range toxicity of these compounds continues to be debated (see other articles in this Journal.) – L.K.G.*

## NEUROLOGICAL AND PSYCHOLOGICAL DISORDERS

### MOTOR NEURON DISORDER SIMULATING ALS INDUCED BY CHRONIC INHALATION OF PYRETHROID INSECTICIDES

Doi H, Kikuchi H, Murai H, Kawano Y, Shigeto H, Ohyagi Y, Kira J.

Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka, 812-8582, Japan.

*Neurology*. 2006 Nov 28; 67(10):1894-5. PMID: 17130437

Note: Case report without an abstract

**Comment:** *This short but well done case report tells of a woman who had a very high, daily exposure to four different pyrethroids over a 3 year period. The pyrethroids were used heavily in a small, closed room. Her first symptoms were common, acute symptoms known to be produced by pyrethroids but thought in the past to be entirely reversible. They included numbness of the tongue, nausea, and rhinitis. After 2 years, she developed weakness that progressed and included fasciculations. Slurred speech developed. Electromyography and physical examination were consistent with ALS. With cessation of exposure, signs and symptoms lessened but atrophy and fasciculations of the tongue persisted.*

*This case of unusual exposure harks back to several studies, mentioned below, that identified a link between agricultural insecticide exposure and sporadic cases of ALS. A gene has been identified that may be associated with slow removal of the compounds. This article and the two studies that follow clearly lead us to be more cautious. The diagnosis of ALS is now more complicated as it requires a*

*detailed exposure history. But, if the case report offers hope for some recovery in the sporadic case that comes from pyrethroid exposure, all cases may not be on a steady downhill course to death. – L.K.G.*



### EXPOSURE TO CHEMICALS AND METALS AND RISK OF AMYOTROPHIC LATERAL SCLEROSIS: A SYSTEMATIC REVIEW

Sutedja NA, Veldink JH, Fischer K, Kromhout H, Heederik D, Huisman MH, Wokke JH, Van Den Berg LH.

Department of Neurology and Julius Center for Health Sciences and Primary Care University Medical Center Utrecht; and the Institute for Risk Assessment Sciences, Division of Environmental Epidemiology, Utrecht, The Netherlands.

*Amyotrophic Lateral Sclerosis*. 2008 Nov 8: 1-20. PMID: 18991149. Epub.

Environmental exposure to chemicals and metals may contribute to the risk of sporadic amyotrophic lateral sclerosis (ALS). Two systematic reviews of the literature on these topics performed according to the well-established MOOSE guidelines are presented. Literature cited in MEDLINE, EMBASE, CINAHL, and Cochrane databases (up to March 2007) as well as references of relevant articles were screened for case-control or cohort studies investigating the associations between sporadic ALS and exposure to chemical agents or metals. Methodology of selected studies was appraised according to Armon's classification system for ALS risk factor studies as well as a newly developed classification system for quality of expo-

sure assessment. Seven of the 38 studies concerning exposure to chemicals and three of the 50 studies concerning exposure to metals fulfilled the validity criteria. In two independent studies meeting the validity criteria, a significant association with increased ALS risk was reported for exposure to pesticides. This systematic review demonstrated the difficulty in attaining a high level of evidence due to lack of high quality of methodological and exposure assessment components. Although pesticide exposure was identified as candidate risk factor, more well-designed studies are needed to provide a definitive answer about exogenous factors of ALS.

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## GENETIC SUSCEPTIBILITY TO ENVIRONMENTAL TOXICANTS IN ALS

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*American Journal of Medical Genetics Part B Neuropsychiatric Genetics*. 2007 Oct 5; 144B(7):885-90. PMID: 17503480

Environmental toxicants such as heavy metals, pesticides, and chemicals appear to be risk factors for sporadic amyotrophic lateral sclerosis (SALS). An impaired ability to break down these toxicants because of differences in detoxification genes could underlie some cases of this disease. We therefore examined the frequencies of single nucleotide polymorphisms (SNPs) in 186 SALS patients and 186 controls at the allele, genotype, and haplotype levels for the metallothionein (MT) family of genes, metal transcription factor-1 (MTF-1), and glutathione synthetase (GSS). Exposure to heavy metals, solvents/chemicals, and pesticides/herbicides was assessed by questionnaire, and gene-toxicant interactions were analyzed. An intronic SNP upstream of MT-1e differed in SALS patients and controls at the allele and genotype levels. Haplotypes covering MT-1 isoforms also differed between the two groups. Alleles and genotypes of one MTF-1 SNP differed in female SALS patients. One GSS haplotype interacted with both metals and solvents/chemicals to increase the risk of the disease. Differences in genes involved in handling toxicants, and interactions between toxicants and these genes, appear to be present in some patients with SALS. This suggests that impaired detoxification mechanisms play a role in SALS.

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## NEUROTOXICITY OF PESTICIDES: A BRIEF REVIEW

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*Frontiers in Bioscience*. 2008 Jan 1; 13:1240-9. PMID: 17981626

Pesticides are substances widely used to control unwanted pests such as insects, weeds, fungi and rodents. Most pesticides are not highly selective, and are also toxic to nontarget species, including humans. A number of pesticides can cause neurotoxicity. Insecticides, which kill insects by targeting their nervous system, have neurotoxic effect in mammals as well. This family of chemicals comprises the organophosphates, the carbamates, the pyrethroids, the organochlorines, and other compounds. Insecticides interfere with chemical neurotransmission or ion channels, and usually cause reversible neurotoxic effects that could nevertheless be lethal. Some herbicides and fungicides have also been shown to possess neurotoxic properties. The effects of pesticides on the nervous system may be involved in their acute toxicity, as in the case of most insecticides, or may contribute to chronic neurodegenerative disorders, most notably Parkinson's disease. This brief review highlights some of the main neurotoxic pesticides, their effects, and mechanisms of action.

**Comment:** *This short review might be useful for some. The chronic effects of pesticides are still less well defined than the acute. So, conclusions need to be couched in terms of uncertainty.* – L.K.G.

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## UPDATE IN THE EPIDEMIOLOGY OF PARKINSON'S DISEASE

Elbaz A, Moisan

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*Current Opinion in Neurology*. 2008 Aug; 21(4):454-60

**Purpose of Review:** In the past 18 months, several important studies on the epidemiology of Parkinson's disease have been published. In particular, large cohorts have identified sufficient incident patients with Parkinson's disease to study risk or protective factors of Parkinson's disease; one of the important recent events in the field is the publication of some of their findings.

**Recent Findings:** We will first review findings of descriptive studies on the frequency of the disease and its geographic or temporal distribution. We will then summarize the findings of analytical studies dealing with risk or protective factors in the fields of dietary and lifestyle factors (cigarette smoking, coffee and tea drinking, uric acid, dairy products), environmental exposures (pesticides, lead, manganese, welding), hormonal factors (oophorectomy), vascular risk factors (diabetes, hypertension, cholesterol level), pharmacoepidemiology (NSAIDs, statins), and familial aggregation.

**Summary:** Epidemiologic studies have consistently found that some exposures are inversely (e.g., cigarette smoking) or

positively associated with Parkinson's disease (e.g., pesticides), while their findings are, at the present time, less consistent for other exposures (e.g., NSAIDs, vascular risk factors). Finally, recent studies have investigated new research fields (e.g., hormonal factors, uric acid, pharmacoepidemiology) and additional data need to be collected.

**Comment:** *This review may be of interest to those concerned with Parkinson patients as it is comprehensive in its approach. Pesticides are just one of many factors besides heredity that have been associated with the disorder. This author attempts to put it all in a succinct review. – L.K.G.*

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### PARKINSON'S DISEASE AND RESIDENTIAL EXPOSURE TO MANEB AND PARAQUAT FROM AGRICULTURAL APPLICATIONS IN THE CENTRAL VALLEY OF CALIFORNIA

Sadie Costello, Myles Cockburn, Jeff Bronstein, Xinbo Zhang and Beate Ritz

*American Journal of Epidemiology.* 2009 169(8):919-926. PMID: 19270050

Evidence from animal and cell models suggests that pesticides cause a neurodegenerative process leading to Parkinson's disease (PD). Human data are insufficient to support this claim for any specific pesticide, largely because of challenges in exposure assessment. The authors developed and validated an exposure assessment tool based on geographic information systems that integrated information from California Pesticide Use Reports and land-use maps to estimate historical exposure to agricultural pesticides in the residential environment. In 1998–2007, the authors enrolled 368 incident PD cases and 341 population controls from the Central Valley of California in a case-control study. They generated estimates for maneb and paraquat exposures incurred between 1974 and 1999. Exposure to both pesticides within 500 m of the home increased PD risk by 75% (95% confidence interval (CI): 1.13, 2.73). Persons aged 60 years at the time of diagnosis were at much higher risk when exposed to either maneb or paraquat alone (odds ratio = 2.27, 95% CI: 0.91, 5.70) or to both pesticides in combination (odds ratio = 4.17, 95% CI: 1.15, 15.16) in 1974–1989. This study provides evidence that exposure to a combination of maneb and paraquat increases PD risk, particularly in younger subjects and/or when exposure occurs at younger ages.

**Comment:** *This is another study linking pesticides and Parkinson's Disease that is noteworthy as it looks at the synergistic effects of two pesticides. A combination of compounds seems worse than a single agent. This study underscores the need for further research on the synergistic effects of exposure to multiple chemicals which may increase the effect of each chemical. This is important since we are often exposed to more than one pesticide in the environment.*

*The study also suggests that the critical window of exposure may have occurred years before a diagnosis of Parkinson's was made. We must await further study to design targeted protective advice, but personal protective devices for applicators need to be rigorously promoted. Exposure must now be a consideration in the diagnosis of all new cases. –L.K.G.*

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### A COHORT STUDY OF PESTICIDE POISONING AND DEPRESSION IN COLORADO FARM RESIDENTS

Beseler CL, Stallones L., Department of Epidemiology, Department of Environmental, Agricultural and Occupational Health, College of Public Health, University of Nebraska Medical Center, Omaha (C.L.B.) and Colorado State University, Fort Collins (L.S.).

*Annals of Epidemiology.* 2008 Oct;18(10):768-74. PMID: 18693039

**Purpose:** Depressive symptoms have been associated with pesticide poisoning among farmers in cross-sectional studies, but no longitudinal studies have assessed the long-term influence of poisoning on depressive symptoms. The purpose of this study was to describe the associations between pesticide poisoning and depressive symptoms in a cohort of farm residents.

**Methods:** Farm operators and their spouses were recruited in 1993 from farm truck registrations using stratified probability sampling. The Center for Epidemiologic Studies-Depression scale was used to evaluate depression in participants using generalized estimating equations. Baseline self-reported pesticide poisoning was the exposure of interest in longitudinal analyses.

**Results:** Pesticide poisoning was significantly associated with depression in three years of follow-up after adjusting for age, gender, and marital status (odds ratio [OR] 2.59; 95% confidence interval [CI] 1.20-5.58). Depression remained elevated after adjusting for health, decreased income, and increased debt (OR 2.00; CI 0.91-4.39) and was primarily due to significant associations with the symptoms being bothered by things (OR 3.29; CI 1.95-5.55) and feeling everything was an effort (OR 1.93; CI 1.14-3.27).

**Conclusions:** Feeling bothered and that everything was an effort were persistently associated with a history of pesticide poisoning, supportive of the hypothesis that prolonged irritability may result from pesticide poisoning.

**Comment:** *See page 6 (right column)*

## DEPRESSION AND PESTICIDE EXPOSURES AMONG PRIVATE PESTICIDE APPLICATORS ENROLLED IN THE AGRICULTURAL HEALTH STUDY

Beseler CL, Stallones L, Hoppin JA, Alavanja MC, Blair A, Keefe T, Kamel F

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*Environmental Health Perspectives*. 2008 Dec; 116(12):1713-9. Epub 2008 Sep 9. PMID: 19079725

**Background:** We evaluated the relationship between diagnosed depression and pesticide exposure using information from private pesticide applicators enrolled in the Agricultural Health Study between 1993 and 1997 in Iowa and North Carolina.

**Methods:** There were 534 cases who self-reported a physician-diagnosed depression and 17,051 controls who reported never having been diagnosed with depression and did not feel depressed more than once a week in the past year. Lifetime pesticide exposure was categorized in three mutually exclusive groups: low (< 226 days, the reference group), intermediate (226-752 days), and high (> 752 days). Two additional measures represented acute high-intensity pesticide exposures: an unusually high pesticide exposure event (HPEE) and physician-diagnosed pesticide poisoning. Logistic regression analyses were performed relating pesticide exposure to depression.

**Results:** After adjusting for state, age, education, marital status, doctor visits, alcohol use, smoking, solvent exposure, not currently having crops or animals, and ever working a job off the farm, pesticide poisoning was more strongly associated with depression [odds ratio (OR) = 2.57; 95% confidence

interval (CI), 1.74-3.79] than intermediate (OR = 1.07; 95% CI, 0.87-1.31) or high (OR = 1.11; 95% CI, 0.87-1.42) cumulative exposure or an HPEE (OR = 1.65; 95% CI, 1.33-2.05). In analysis of a subgroup without a history of acute poisoning, high cumulative exposure was significantly associated with depression (OR = 1.54; 95% CI, 1.16-2.04).

**Conclusion:** These findings suggest that both acute high-intensity and cumulative pesticide exposure may contribute to depression in pesticide applicators. Our study is unique in reporting that depression is also associated with chronic pesticide exposure in the absence of a physician-diagnosed poisoning.

**Comment:** *Psychiatric disease after pesticide poisoning has been seen after acute pesticide poisoning for decades but a clear association with distinct types of disease has been reported only in the past decade or so. These studies link poisoning and high chronic exposure with depression. The study cohort in the Agricultural Health Study is reported to have a lower incidence of depression than the general population. Nonetheless, poisoning events and high exposure are associated with depression. While family history of depression needs to be recorded and may be of importance due to genetic factors in the disease, preventative measures need to be established for farmers. Physicians treating farmers need to know the likelihood of high pesticide use in their communities and to be sensitive to affect disorders. If affect disorders surface, then exposure history becomes of even greater importance. In addition, at a time where increasing numbers of children are being treated for attention deficit hyperactivity disorders, autism spectrum disorders, depression and anxiety, health care and mental health professionals need to be versed on the relationship of pesticide exposures to such disorders, include environmental exposure history when treating both pediatric and adult patients with psychiatric disorders and educate patients about reducing or eliminating their exposures—especially when pesticide poisoning is suspected.*  
– L.K.G. and R.B.

## PEDIATRICS

### CHILDREN'S ENVIRONMENTAL HEALTH AND THE PRECAUTIONARY PRINCIPLE

Jarosinska D, Gee D.

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*International Journal of Hygiene and Environmental Health*. 2007 Oct; 210(5):541-6. Epub 2007 Sep 21. PMID: 17889608

The concept of precaution has a long history in medicine and public health. The modern precautionary principle (PP), originating from environmental debates in Germany in the 1970s, has been included in many international agreements, such as the Treaty on European Union. PP is a public policy tool that

justifies actions, which protect human health and the environment in the face of uncertain risks. The outcome of the application of PP depends on the level, nature, and distribution of acceptable risks and on the availability of alternatives, and can range from taking no action to banning of substances or the activities of concern. Given the complex nature and uncertainty of environmental risks to children's health, a precautionary approach is warranted. Public health professionals and clinical practitioners could adopt such an approach within the wider context of considering the environment as a source of risks to children's health. Relevant knowledge and skills are needed to enable health care professionals to address these issues. New methodological and scientific approaches are necessary to make use of scattered, but potentially relevant clinical evidence in providing 'early warnings' of health hazards.

**Comment:** The authors describe the precautionary principle and review its more recent development and application in international agreements and treaties. This paper can be recommended for the general reader interested in understanding and applying its principles. – R.L.H.

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## RISK OF CHILDHOOD CANCERS ASSOCIATED WITH RESIDENCE IN AGRICULTURALLY INTENSE AREAS IN THE UNITED STATES

Carozza SE, Li B, Elgethun K, Whitworth R.

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*Environmental Health Perspectives*. 2008 Apr;116(4):559-65. PMID: 18414643

**Background:** The potential for widespread exposure to agricultural pesticides through drift during application raises concerns about possible health effects to exposed children living in areas of high agricultural activity.

**Objectives:** We evaluated whether residence in a county with greater agricultural activity was associated with risk of developing cancer in children < 15 years of age.

**Methods:** Incidence data for U.S. children 0-14 years of age diagnosed with cancer between 1995 and 2001 were provided by member registries of the North American Association of Central Cancer Registries. We determined percent cropland for each county using agricultural census data, and used the overall study distribution to classify agriculturally intense counties. We estimated odds ratios and 95% confidence intervals for all ages and 5-year age groups for total cancers and selected cancer sites using logistic regression.

**Results:** Our study results showed statistically significant increased risk estimates for many types of childhood cancers associated with residence at diagnosis in counties having a moderate to high level of agricultural activity, with a remarkably consistent dose-response effect seen for counties having  $\geq 60\%$  of the total county acreage devoted to farming. Risk for different cancers varied by type of crop.

**Conclusions:** Although interpretation is limited by the ecologic design, in this study we were able to evaluate rarer childhood cancers across a diverse agricultural topography. The findings of this exploratory study support a continued interest in the possible impact of long-term, low-level pesticide exposure in communities located in agriculturally intense areas.

**Comment:** In this study based upon geographic areas having high levels of agricultural activity (more than 60% by area) compared with less or no agricultural activity, children in the high areas had signifi-

cantly increased risk for many types of childhood cancers including rarer types. The authors suggest that “long-term, low-level pesticide exposure” may be a factor that needs to be considered. (And this may be something that we should try to do something about.) – R.L.H.

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## RISK FACTORS FOR ACUTE LEUKEMIA IN CHILDREN: A REVIEW

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*Environmental Health Perspectives*. 2007 Jan; 115(1):138-45. PMID: 17366834

Although overall incidence is rare, leukemia is the most common type of childhood cancer. It accounts for 30% of all cancers diagnosed in children younger than 15 years. Within this population, acute lymphocytic leukemia (ALL) occurs approximately five times more frequently than acute myelogenous leukemia (AML) and accounts for approximately 78% of all childhood leukemia diagnoses.

Epidemiologic studies of acute leukemias in children have examined possible risk factors, including genetic, infectious, and environmental, in an attempt to determine etiology. Only one environmental risk factor (ionizing radiation) has been significantly linked to ALL or AML. Most environmental risk factors have been found to be weakly and inconsistently associated with either form of acute childhood leukemia. Our review focuses on the demographics of childhood leukemia and the risk factors that have been associated with the development of childhood ALL or AML. The environmental risk factors discussed include ionizing radiation, non-ionizing radiation, hydrocarbons, pesticides, alcohol use, cigarette smoking, and illicit drug use. Knowledge of these particular risk factors can be used to support measures to reduce potentially harmful exposures and decrease the risk of disease. We also review genetic and infectious risk factors and other variables, including maternal reproductive history and birth characteristics.

**Comment:** This is a critical review of all factors leading to childhood acute leukemias. While more than pesticide risk is reviewed, it will be of interest to many as a comprehensive look at where we stand in our knowledge today of an important topic, since this is the most common cancer in childhood. As we have noted in other places in this collection of articles and in previous publications, there is a consistent association with pesticides. The studies are not designed such that selection biases are eliminated as noted by these reviewers. However, the persistence of the association is notable. Many will wish to seek to council avoidance on the basis of what we know so far. – L.K.G.

## PESTICIDES AND CHILDHOOD CANCER: AN UPDATE OF ZAHM AND WARD'S 1998 REVIEW

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*Journal of Toxicology and Environmental Health, Part B Critical Reviews*. 2007 Jan-Mar. 10(1-2): 81-99. PMID: 18074305

Children are exposed to pesticides through a number of sources, including residential and agricultural applications. Parental occupational exposure to pesticides is also a concern because exposures occurring during pregnancy and carry-home residues also contribute to children's cumulative burden. A number of epidemiological studies consistently reported increased risks between pesticide exposures and childhood leukemia, brain cancer, neuroblastoma, non-Hodgkin's lymphoma, Wilms' tumor, and Ewing's sarcoma. An extensive review of these studies was published in 1998 (Zahm & Ward, 1998). Fifteen case-control studies, 4 cohort studies, and 2 ecological studies have been published since this review, and 15 of these 21 studies reported statistically significant increased risks between either childhood pesticide exposure or parental occupational exposure and childhood cancer.

Therefore, one can confidently state that there is at least some association between pesticide exposure and childhood cancer. However, an unambiguous mechanistic cause-and-effect relationship between pesticide exposure and childhood cancer was not demonstrated in these studies, and modifying factors such as genetic predisposition, rarely considered in the reviewed studies, likely play an important role. While the time window of exposure may be a crucial determinant for biological effects associated with pesticide exposure on children, studies have not contributed definitive information on the most vulnerable period.

Accurate exposure assessment remains a challenge; future epidemiological studies need to assess gene-environment interactions and use improved exposure measures, including separate parental interviews, specific pesticide exposure questions, and semiquantitative exposure measures that can be used to confirm information obtained through questionnaires.

**Comment:** *This is a review of the literature which provides a useful bibliography. Their conclusions are similar to ones offered in these and previous Journal abstracts. – L.K.G.*

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## HUMAN EXPOSURE TO ENDOCRINE-DISRUPTING CHEMICALS AND PRENATAL RISK FACTORS FOR CRYPTORCHIDISM AND HYPOSPADIAS: A NESTED CASE-CONTROL STUDY

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*Environmental Health Perspectives*. 2007 Dec; 115 Supplement 1:8-14. PMID: 18174944

**Background:** Exposure to xenoestrogens during pregnancy may disturb the development and function of male sexual organs.

**Objective:** In this study we aimed to determine whether the combined effect of environmental estrogens measured as total effective xenoestrogen burden (TEXB) is a risk factor for male urogenital malformations.

**Methods:** In a case-control study, nested in a mother-child cohort (n = 702) established at Granada University Hospital, we compared 50 newborns with diagnosis of cryptorchidism and/or hypospadias with 114 boys without malformations matched by gestational age, date of birth, and parity. Controls did not differ from the total cohort in confounding variables. TEXB and levels of 16 organochlorine pesticides were measured in placenta tissues. Characteristics of parents, pregnancy, and birth were gathered by questionnaire. We used conditional and unconditional regression models to estimate odds ratios (ORs) and 95% confidence intervals (CIs).

**Results:** TEXB from organohalogenated compounds was detectable in 72% and 54% of case and control placentas, respectively. Compared with controls, cases had an OR for detectable versus non-detectable TEXB of 2.82 (95% CI, 1.10-7.24). More pesticides were detected in cases than in controls (9.34 +/- 3.19 vs. 6.97 +/- 3.93). ORs for cases with detectable levels of pesticides, after adjusting for potential confounders in the conditional regression analysis, were o,p'-DDT (OR = 2.25; 95% CI, 1.03-4.89), p,p'-DDT (OR = 2.63; 95% CI, 1.21-5.72), lindane (OR = 3.38; 95% CI, 1.36-8.38), mirex (OR = 2.85; 95% CI, 1.22-6.66), and endosulfan alpha (OR = 2.19; 95% CI, 0.99-4.82). Engagement of mothers in agriculture (OR = 3.47; 95% CI, 1.33-9.03), fathers' occupational exposure to xenoestrogens (OR = 2.98; 95% CI, 1.11-8.01), and history of previous stillbirths (OR = 4.20; 95% CI, 1.11-16.66) were also associated with risk of malformations.

**Conclusions:** We found an increased risk for male urogenital malformations related to the combined effect of environmental estrogens in placenta.

**Comment:** *The cause of the epidemic of hypospadias, seen in the USA and Europe, remains inadequately understood. This article reports a study that logically follows the assumption that endocrine disruptors contribute. The positive findings are from a global study of pesticides. It will take more specific links before we can be fully convinced. However, in the event of parental occupational exposure, it is reasonable to try to limit occupational exposure through per-*

sonal protective devices and in addition, to protect family members through proper handling of clothing from parents working with pesticides to prevent take-home exposure. – L.K.G

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HOUSEHOLD EXPOSURE TO PESTICIDES AND RISK OF CHILDHOOD HEMATOPOIETIC MALIGNANCIES: THE ESCALE STUDY (SFCE)

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*Environmental Health Perspectives*. 2007 Dec; 115 (12):1787-93. PMID: 18087601

**Objectives:** We investigated the role of household exposure to pesticides in the etiology of childhood hematopoietic malignancies.

**Methods:** The national registry-based case-control study ESCALE (Etude sur les cancers de l'enfant) was carried out in France over the period 2003-2004. Population controls were frequency matched with the cases on age and sex. Maternal household use of pesticides during pregnancy and paternal use during pregnancy or childhood were reported by the mothers in a structured telephone questionnaire. Insecticides (used at home, on pets, or for garden crops), herbicides, and fungicides were distinguished. We estimated odds ratios (ORs) using unconditional regression models closely adjusting for age, sex, degree of urbanization, and type of housing (flat or house).

**Results:** We included a total of 764 cases of acute leukemia (AL), 130 of Hodgkin lymphoma (HL), 166 of non-Hodgkin lymphoma (NHL), and 1,681 controls. Insecticide use during pregnancy was significantly associated with childhood AL [OR = 2.1; 95% confidence interval (CI), 1.7-2.5], both lymphoblastic and myeloblastic, NHL (OR = 1.8; 95% CI, 1.3-2.6), mainly for Burkitt lymphoma (OR = 2.7; 95% CI, 1.6-4.5), and mixed-cell HL (OR = 4.1; 95% CI, 1.4-11.8), but not nodular sclerosis HL (OR = 1.1; 95% CI, 0.6-1.9). Paternal household use of pesticides was also related to AL (OR = 1.5; 95% CI, 1.2-1.8) and NHL (OR = 1.7; 95% CI, 1.2-2.6); but for AL the relationships did not remain after adjustment for maternal pesticide use during pregnancy.

**Conclusion:** The study findings strengthen the hypothesis that domestic use of pesticides may play a role in the etiology of childhood hematopoietic malignancies. The consistency of the findings with those of previous studies on AL raises the question of the advisability of preventing pesticide use by pregnant women.

**Comment:** This is another study finding an association between pesticide exposure and childhood leukemia and other cancers. We have reported on several of these studies in past Journal editions. We lack mechanisms for this action. We lack timing of the exposure with regard to risk of disease. Yet, the consistency of the findings is compelling. Further answers are indeed needed. But, individual practitioners must decide when the time has come to take preventative action through counseling against exposure. The authors of this article favor action on the basis of current findings. – L.K.G.

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

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*Environmental Health Perspectives*. 2007 Oct;115(10):1482-9. PMID: 17938740

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

**Objective:** Our goal was 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-birth-weight, term infants as controls. We determined proximity to pesticide applications 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 errors.

**Results:** Of 249 unique hypotheses, four that described organochlorine pesticide applications—specifically those of dicofol and endosulfan—occurring during the period immediately before and concurrent with central nervous system 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 nonzero 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 the 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.

**Comment:** See comment at end of right column.

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## HOUSEHOLD PESTICIDE USE IN RELATION TO AUTISM

Presented at the International Meeting for Autism Research, May 15-17, 2008, London

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*Epidemiology*. Volume 20(1), January 2009, pp 84-90

**Background:** Pesticides affect a number of targets in the CNS, and cross the placenta. One previous report suggests a link between maternal residential proximity to commercial organochlorine pesticide exposure during early prenatal life and the risk of autism. That study did not evaluate individual exposures to household pesticides.

**Objectives:** To examine household pesticide use during the prenatal period or early postnatal period in relation to autism.

**Methods:** Participants were from the CHARGE (Childhood Autism Risks from Genetics and the Environment) study, a large population-based case-control study in California. Autism spectrum disorders were confirmed using the ADI and ADOS. Mothers were extensively interviewed regarding demographics, lifestyle, and prenatal and early postnatal exposures of the child. Questions addressed use of numerous household products, including insecticides for flies and ants, pet shampoos, and weed control products. Interview data were available for 333 ASD cases and 198 confirmed typically developing controls. Logistic regression models were adjusted for family socioeconomic status. An index exposure period was defined as three months prior to conception through the child's first year of life.

**Results:** Mothers of ASD children were twice as likely to report using pet shampoos for fleas or ticks during the index period as compared with control mothers: adjusted Odds Ratio (aOR) = 2.0, 95% Confidence Interval (CI) = [1.2, 3.6]. When examined by trimester, the strongest association was during the second trimester: aOR = 2.6, 95% CI = [1.3, 6.0].

**Conclusions:** The higher prevalence of self-reported use of pet shampoos by CHARGE study mothers of children with ASD

could be due to reporting bias, although many other products did not show differences. Pyrethrins have largely replaced organophosphates for flea control, but early life exposure to pyrethrins has been shown to compromise the blood-brain barrier in rodents, raising concern about prenatal and early postnatal exposures.

**Comment:** See comment below.

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## THE RISE IN AUTISM AND THE ROLE OF AGE IN DIAGNOSIS; EARLY DEVELOPMENT

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*Epidemiology*. 2009 Jan;20(1):84-90. PMID: 19234401

**Background:** Autism prevalence in California, based on individuals eligible for state-funded services, rose throughout the 1990s. The extent to which this trend is explained by changes in age at diagnosis or inclusion of milder cases has not been previously evaluated.

**Methods:** Autism cases were identified from 1990 through 2006 in databases of the California Department of Developmental Services, which coordinates services for individuals with specific developmental disorders. The main outcomes were population incident cases younger than age 10 years for each quarter, cumulative incidence by age and birth year, age-specific incidence rates stratified by birth year, and proportions of diagnoses by age across birth years.

**Results:** Autism incidence in children rose throughout the period. Cumulative incidence to 5 years of age per 10,000 births rose consistently from 6.2 for 1990 births to 42.5 for 2001 births. Age-specific incidence rates increased most steeply for 2- and 3-year olds. The proportion diagnosed by age 5 years increased only slightly, from 54% for 1990 births to 61% for 1996 births. Changing age at diagnosis can explain a 12% increase, and inclusion of milder cases, a 56% increase.

**Conclusions:** Autism incidence in California shows no sign yet of plateauing. Younger ages at diagnosis, differential migration, changes in diagnostic criteria, and inclusion of milder cases do not fully explain the observed increases. Other artifacts have yet to be quantified, and as a result, the extent to which the continued rise represents a true increase in the occurrence of autism remains unclear.

**Comment:** Autistic Spectrum Disorders (ASD) are characterized by substantial impairments in social interaction and communication and the presence of unusual behaviors and interests. According to

the Centers for Disease Control and Prevention (CDC), one of every 150 eight-year old children has an ASD. ASD reached levels of 2.0-7.0 per 1,000 children, greater than a tenfold increase from the prevalence rates identified in the 1980s, 0.1-0.4 per 1,000 children. The prevalence has reached a point where increasing numbers of health care and mental health professionals are questioning whether genetics is the sole link to autism. As the first two studies indicate, we need to further explore the possible link between pesticides and an increasing epidemic of autism spectrum disorders. The study of those living near agricultural fields has a dramatic odds ratio. The affected age of exposure was in the first trimester. In the household exposure study, the target age was the second trimester. We must await further studies for confirmation of the effect, the critical age of exposure, and the agents involved. – R.B.

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### WITHIN- AND BETWEEN-HOME VARIABILITY IN INDOOR-AIR INSECTICIDES LEVELS DURING PREGNANCY AMONG AN INNER-CITY COHORT FROM NEW YORK CITY

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*Environmental Health Perspectives*. 2007 Mar; 115 (3):383-9. Epub 2006 Dec 11. PMID: PMC1849946. PMID: 17431487

**Background:** Residential insecticide use is widespread in the United States, but few data are available on the persistence and variability in levels in the indoor environment.

**Objective:** The study aim was to assess within- and between-home variability in indoor-air insecticides over the final 2 months of pregnancy among a cohort of African-American and Dominican women from New York City.

**Methods:** Women not employed outside the home were enrolled between February 2001 and May 2004 (n = 102); 9 insecticides and an adjuvant were measured in 48-hr personal air samples and 2-week integrated indoor air samples collected sequentially for 7.0 +/- 2.3 weeks (n = 337 air samples).

**Results:** Sixty-one percent of the women reported using pest control during the air samplings. Chlorpyrifos, diazinon, and propoxur were detected in 99-100% of personal and indoor samples (range, 0.4-641 ng/m<sup>3</sup>). Piperonyl butoxide (a pyrethroid adjuvant) was detected in 45.5-68.5% (0.2-608 ng/m<sup>3</sup>). There was little within-home variability and no significant difference in air concentrations within homes over time (p > or = 0.2); between-home variability accounted for 88% of the variance in the indoor air levels of propoxur, 92% in chlorpyrifos, 94% in diazinon, and 62% in piperonyl butoxide (p < 0.001). Indoor and maternal personal air insecticide

levels were highly correlated (r = 0.7-0.9, p < 0.001). Diazinon and chlorpyrifos levels declined 5-fold between 2001 and 2004 but were detected in all homes 1.5 and 2.5 years, respectively, after the U.S. Environmental Protection Agency ban on their residential use.

**Conclusion:** Results showed that the insecticides were persistent in the home with little variability in air concentrations over the 2 months and contributed to chronic maternal inhalation exposures during pregnancy.

**Comment:** This group has been one of the most productive regarding information about pesticides in the homes of children. This analysis has good and bad news. Removing a persistent pesticide from use leads to reductions in pesticides in the air of children's breathing space. However, the reduction is slow with no measurable change over 7 weeks. Past work has shown that pesticide levels correlate infant head and body size with a dose relationship. Between home variability shows that those who use less expose their children less. Pesticides, particularly organophosphates, are a quick fix to a problem but have major implications for the development of children. Pest prevention through exclusion and proper sanitation and maintenance, and non-chemical tools such as traps—staples of what is called integrated pest management—are equally effective and lessen risk to the unborn. Such approaches must become the societal norm. – L.K.G.

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### OCCUPATIONAL EXPOSURE TO PESTICIDES DURING PREGNANCY AND NEUROBEHAVIORAL DEVELOPMENT OF INFANTS AND TODDLERS

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*Epidemiology*. 2008 Sep 20. PMID: 18813021

**Background:** Few studies have examined the effects of in utero exposure to organophosphate and carbamate pesticides on neurobehavioral development in infants and young children. This study considers the potential effects of maternal occupation in the cut-flower industry during pregnancy on neurobehavioral development in Ecuadorian children.

**Methods:** Data were collected during 2003-2004 for 121 children aged 3-23 months and living in the rural highland region of Cayambe, Ecuador. Children were administered the Ages and Stages Questionnaire and were given specific developmental tests including prehension (reach-and-grasp) and visual skills. Information was gathered on maternal health and work characteristics, the home environment, and child health status.

Growth measurements and a hemoglobin finger-prick blood test were obtained. We conducted multiple linear and logistic regression analyses.

**Results:** Children whose mothers worked in the flower industry during pregnancy scored lower on communication (8% decrease in score, 95% confidence interval [CI]: -16% to 0.5%) and fine motor skills (13% decrease, 95% CI: -22% to -5), and had a higher odds of having poor visual acuity (odds ratio = 4.7 [CI =1.1-20]), compared with children whose mothers did not work in the flower industry during pregnancy, after adjusting for potential confounders.

**Comment:** See following item.



## THE EFFECTS OF ORGANOPHOSPHATE PESTICIDE EXPOSURE ON HISPANIC CHILDREN'S COGNITIVE AND BEHAVIORAL FUNCTIONS

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*Journal of Pediatric Psychology*, 2008 Jan.-Feb., 33(1):91-101. Epub 2007 Jun 14. PMID: 17569709

**Objective:** This study investigates the effects of Organophosphate (OP) pesticides exposure on the cognitive and behavioral functioning of Hispanic children living in an agricultural community.

**Methods:** Forty-eight children were administered a battery of cognitive measures, and their parents and teachers completed behavior rating scales. Children provided a urine sample for analysis of OP pesticides metabolites.

**Results:** All children had a detectable level of at least one OP pesticide metabolite. Higher OP pesticide metabolite concentration levels were significantly correlated with poorer performance on some subtests of the Wisconsin Card Sorting Test. However, the significance of this association was dependent upon the inclusion of two samples with noticeable higher OP pesticide metabolite concentration levels.

**Conclusions:** Short-term OP pesticide exposure seems to have deleterious effects on children's speed of attention, sequencing, mental flexibility, visual search, concept formation, and conceptual flexibility. This study is among a relatively small number of studies investigating an extremely complex problem. Limitations and suggestions for future studies are discussed.

**Comment:** This study supports a growing body of research that links pesticides, and in some studies specifically organophosphate pesticides, to impaired cognitive and behavioral functioning in children. A 2006 study (Kofman et.al, *Motor Inhibition and Learning in School-Aged Children Following Exposure to Organophosphate Pesticides in Infancy*, *Pediatric Research*, 2006, July) concluded that children who had been exposed to organophosphate pesticides had a deficit in inhibitory motor control. An earlier landmark study conducted by Elizabeth Guillet, PhD, (*An Anthropological Approach to the Evaluation of Preschool Children Exposed to Pesticides in Mexico*, *Environmental Health Perspectives.*, Vol. 6 #106, 1998) found that children living in a pesticide-intensive agrarian community demonstrated cognitive and behavioral deficiencies. These studies above and others regarding the long-term impacts of pesticides on children's neurological development underscore the need to educate pediatricians doing developmental assessments of this important historical data. Prevention will require that parents, day care centers and schools are aware of these risks and are educated about safer pest management strategies. Farmers should also be educated about the hazards of pesticides and reducing their pesticide use by transitioning to integrated pest management and organic land care. — R.B.

## PULMONARY

### LOW LEVEL OF EXPOSURE TO PESTICIDES LEADS TO LUNG DYSFUNCTION IN OCCUPATIONALLY EXPOSED SUBJECTS

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*Inhalation Toxicology*. 2008 Jul; 20(9):839-49. PMID: 18645724

Pesticides may contribute to adverse respiratory health effects among farmers and have been considered one causal factor for

the rise in asthma prevalence. This cross-sectional study was conducted to evaluate potential respiratory function abnormalities following long-term pesticide exposure by means of a complete pulmonary function testing, including spirometry, lung volumes, and diffusing capacity for carbon monoxide. The study population was comprised by workers from a prominent intensive agriculture area of southern Spain that relied on pesticides for the control of plagues. Eighty-nine pesticide sprayers of plastic greenhouse farming and a control group of 25 non-spraying control farmers from the same area were interviewed by a general practitioner asking about sociodemographic factors, occupational exposure, and clinical symptoms by using a structured questionnaire. Multiple regression analyses showed

a relationship of short-term exposure to pesticides (as indicated by a drop in serum cholinesterase > 25% of baseline levels) with reduced forced expired volume in 1 s, and of long-term exposure (as indicated by a cumulative pesticide exposure index) with reduced forced expiratory flow rate. Exposure to bipyridilium-class herbicides was a determinant of a fall in the diffusing capacity of the lungs, and neonicotinoid insecticides showed a relationship with lower pulmonary volumes (total lung capacity, residual volume, and functional residual capaci-

ty), suggestive of restrictive lung disease, and with an increased risk of reporting irritative symptoms.

**Comment:** *Although the exposure is not well controlled and may be large, this study shows a link between pesticide exposure and diminished lung function. We will look for further studies. However, the newly diagnosed adult with respiratory symptoms clearly needs to have this kind of history taken to discover a possible environmental link. – L.K.G.*

## CANCER

### AGRICULTURAL PESTICIDE USE AND PANCREATIC CANCER RISK IN THE AGRICULTURAL HEALTH STUDY COHORT

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*International Journal of Cancer.* 2009 May 15;124 (10):2495-500. PMID: 19142867

Pancreatic cancer is a rapidly fatal disease that has been linked with pesticide use. Previous studies have reported excess risks of pancreatic cancer with organochlorines such as DDT, however, many other commonly used pesticides have not been examined. To further examine the potential associations between the use of a number of pesticides and pancreatic cancer, we conducted a case-control analysis in the Agricultural Health Study, one of the largest prospective cohorts with over 89,000 participants including pesticide applicators and their spouses in Iowa and North Carolina.

This analysis included 93 incident pancreatic cancer cases (64 applicators, 29 spouses) and 82,503 cancer-free controls that completed an enrollment questionnaire providing detailed pesticide use, demographic and lifestyle information. Ever use of 24 pesticides and intensity-weighted lifetime days [(lifetime exposure days) x (exposure intensity score)] of 13 pesticides was assessed. Risk estimates were calculated using unconditional logistic regression controlling for age, smoking, and diabetes. Among pesticide applicators, 2 herbicides (EPTC and pendimethalin) of the 13 pesticides examined for intensity-weighted lifetime use showed a statistically significant exposure-response association with pancreatic cancer. Applicators in the top half of lifetime pendimethalin use had a 3.0-fold (95% CI 1.3-7.2, p-trend = 0.01) risk compared with never users, and those in the top half of lifetime EPTC use had a 2.56-fold (95% CI = 1.1-5.4, p-trend = 0.01) risk compared with never users. Organochlorines were not associated with an excess risk of pancreatic cancer in this study. These findings suggest that herbicides, particularly pendimethalin and EPTC, may be associated with pancreatic cancer.

**Comment:** *The authors extend previous studies that have linked pancreatic cancer with organochlorine pesticides such as DDT. A case-control study with more than 89,000 participants with exposure to 13 different pesticides and more than 82,000 controls was evaluated. Two herbicides were implicated, EPTC and pendimethalin with OR of 3.0 and 2.56 respectively, when the top half of lifetime use was compared with never users. Interestingly, organochlorines were not implicated in this study. These sorts of studies are very important as they begin to sort out the relationships between specific tumors and individual pesticides. – R.L.H.*

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### HETEROCYCLIC AROMATIC AMINE PESTICIDE USE AND HUMAN CANCER RISK: RESULTS FROM THE U.S. AGRICULTURAL HEALTH STUDY

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*International Journal of Cancer.* 2009 Mar 1;124 (5):1206-12. PMID: 19058219

Imazethapyr, a heterocyclic aromatic amine, is a widely used crop herbicide first registered for use in the United States in 1989. We evaluated cancer incidence among imazethapyr-exposed pesticide applicators enrolled in the Agricultural Health Study (AHS). The AHS is a prospective cohort of 57,311 licensed pesticide applicators in the U.S., enrolled from 1993-1997. Among the 49,398 licensed pesticide applicators eligible for analysis, 20,646 applicators reported use of imazethapyr and 2,907 incident cancers developed through 2004. Imazethapyr exposure was classified by intensity-weighted lifetime exposure days calculated as [years of use x days per year x intensity level]. Poisson regression analysis was used to evaluate the relationship between imazethapyr exposure and cancer incidence. We found significant trends in risk with increasing lifetime exposure for bladder cancer (p for trend 0.01) and colon cancer (p for trend 0.02). Rate ratios (RRs)

were increased by 137% for bladder cancer and 78% for colon cancer when the highest exposed were compared to the non-exposed. The excess risk for colon cancer was limited to proximal cancers, (RR = 2.73, 95% confidence intervals 1.42, 5.25, p for trend 0.001). No association was observed for prostate, lung, rectum, kidney, oral, pancreas, lymphohematopoietic cancers or melanoma.

These findings provide new evidence that exposure to aromatic amine pesticides may be an overlooked exposure in the etiology of bladder and colon cancer. The use of imazethapyr and other imidazolinone compounds should continue to be evaluated for potential risk to humans.

**Comment:** *The heterocyclic aromatic amine herbicide imazethapyr, was evaluated among 49,398 applicators for its relationship to cancer risk. Bladder cancer and proximal colon cancer were shown to be associated with increasing lifetime exposure. No association was shown for prostate, lung, rectum, kidney, oral, pancreas, lymphohematopoietic cancers or melanoma. It would be interesting to link these observations to the method of excretion of this agent and other imidazolinone compounds and their metabolic breakdown products since colon and bladder are organs where toxic compounds might be expected to be concentrated and retained for a time prior to discharge. – R.L.H.*



## AGENT ORANGE EXPOSURE, VIETNAM WAR VETERANS AND THE RISK OF PROSTATE CANCER

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**Background:** It has been demonstrated that Agent Orange exposure increases the risk of developing several soft tissue malignancies. Federally funded studies, now nearly a decade old, indicated that there was only a weak association between exposure and the subsequent development of prostate cancer. Because Vietnam War veterans are now entering their 60s, the authors reexamined this association by measuring the relative risk of prostate cancer among a cohort of men who were stratified as either exposed or unexposed to Agent Orange between the years 1962 and 1971 and who were followed during the interval between 1998 and 2006.

**Methods:** All Vietnam War era veterans who receive their care in the Northern California Veteran Affairs Health System were stratified as either exposed (n=6214) or unexposed (n=6930) to Agent Orange. Strata-specific incidence rates of prostate cancer (International Classification of Diseases, 9th Revision code 185.0) were calculated. Differences in patient and disease characteristics (age, race, smoking history, family history, body

mass index, finasteride exposure, prebiopsy prostate-specific antigen (PSA) level, clinical and pathologic stage, and Gleason score) were assessed with chi-square tests, t tests, a Cox proportional hazards model, and multivariate logistic regression.

**Results:** Twice as many exposed men were identified with prostate cancer (239 vs 124 unexposed men, respectively; odds ratio [OR], 2.19; 95% confidence interval [95% CI], 1.75-2.75). This increased risk also was observed in a Cox proportional hazards model from the time of exposure to diagnosis (hazards ratio [HR], 2.87; 95% CI, 2.31-3.57). The mean time from exposure to diagnosis was 407 months. Agent Orange-exposed men were diagnosed at a younger age (59.7 years; 95% CI, 58.9-60.5 years) compared with unexposed men (62.2 years; 95% CI, 60.8-63.6 years), had a 2-fold increase in the proportion of Gleason scores 8 through 10 (21.8%; 95% CI, 16.5%-27%) compared with unexposed men (10.5%; 95% CI, 5%-15.9%), and were more likely to have metastatic disease at presentation than men who were not exposed (13.4%; 95% CI, 9%-17.7%) than unexposed men (4%; 95% CI, 0.5%-7.5%). In univariate analysis, distribution by race, smoking history, body mass index, finasteride exposure, clinical stage, and mean prebiopsy PSA were not statistically different. In a multivariate logistic regression model, Agent Orange was the most important predictor not only of developing prostate cancer but also of high-grade and metastatic disease on presentation.

**Conclusions:** Individuals who were exposed to Agent Orange had an increased incidence of prostate cancer; developed the disease at a younger age, and had a more aggressive variant than their unexposed counterparts. Consideration should be made to classify this group of individuals as 'high risk,' just like men of African-American heritage and men with a family history of prostate cancer.

**Comment:** *More than 6,000 Vietnam War veterans who were exposed to Agent Orange [a mixture of 2,4-D and 2,4,5-T, both chlorophenoxy herbicides] were compared with a similar number of veterans who were not exposed and a two fold increased risk for prostate cancer was demonstrated. The mean time from exposure to diagnosis was almost 34 years. In addition, the exposed men were diagnosed at a younger age, had a higher Gleason score, and were more likely to have metastases at diagnosis. The authors conclude that this group deserves a "high risk" classification similar to black males, and men with a positive family history. The study is also interesting because it clearly shows that an exposure to a carcinogenic agent many years or decades before the emergence and diagnosis of a cancer can have a prolonged and often unrecognized latency. One wonders about the magnitude of the effects of the use of such pesticides as Agent Orange on the indigenous population who were also exposed but remained in the exposed areas for the rest of their lives and may have been especially vulnerable, such as children. Herbicide defoliation of large areas of Columbia in the "war on drugs" comes to mind. – R.L.H.*



## OCCUPATIONAL EXPOSURE TO PESTICIDES AND LYMPHOID NEOPLASMS AMONG MEN: RESULTS OF A FRENCH CASE-CONTROL STUDY

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**Objectives:** Investigating the relationship between occupational exposure to pesticides and the risk of lymphoid neoplasms (LN) in men.

**Methods:** A hospital-based case-control study was conducted in six centres in France between 2000 and 2004. The cases were incident cases with a diagnosis of lymphoid neoplasm aged 18 to 75 years. During the same period, controls of the same age and gender as the cases were recruited in the same hospital, mainly in the orthopaedic and rheumatological departments. Exposures to pesticides were evaluated through specific interviews and case-by-case expert reviews. Four hundred and ninety-one cases (244 cases of non-Hodgkin's lymphoma (NHL), 87 of Hodgkin's lymphoma (HL), 104 of lymphoproliferative syndromes (LPS) and 56 of multiple myeloma (MM) cases) and 456 controls were included in the analyses. The odds ratios (OR) and 95% confidence intervals (95% CI) were estimated using unconditional logistic regressions.

**Results:** Positive associations between HL and occupational exposure to triazole fungicides and urea herbicides were observed (OR=8.4 [2.2-32.4], 10.8 [2.4-48.1] respectively). Exposure to insecticides, fungicides and herbicides were linked to a three-fold increases in MM risk (OR=2.8 [1.2-6.5], 3.2 [1.4-7.2], 2.9 [1.3-6.5]). For LPS subtypes, associations restricted to hairy-cell leukaemia (HCL) were evidenced for exposure to organochlorine insecticides, phenoxy herbicides and triazine herbicides (OR=4.9 [1.1-21.2], 4.1 [1.1-15.5], 5.1 [1.4-19.3], although based on small numbers. Lastly, despite the increased odds ratios for organochlorine and organophosphate insecticides, carbamate fungicides and triazine herbicides, no significant associations were evidenced for NHL.

**Conclusions:** The results, based on case-by-case expert review of occupation-specific questionnaires, support the hypothesis that occupational pesticide exposures may be involved in HL, MM and HCL and do not rule out a role in NHL. The analyses identified specific pesticides that deserve further investigation and the findings were consistent with those of previous studies.

**Comment:** This study separates the lymphoproliferative malignancies into their major subtypes and correlates these groupings with occupational exposure to pesticides. The study group was confined to men. A more than eight fold increased risk of Hodgkin's lymphoma was seen with occupational exposure to triazole fungicides and urea

herbicides. A three fold increase in multiple myeloma risk was seen with exposure to insecticides, fungicides and herbicides. Although based on small numbers, a four to five fold increased risk was seen in hairy-cell leukemia with exposure to organochlorine insecticides and phenoxy and triazine herbicides. Curiously no significant increased risks were detected for non-Hodgkin's lymphoma although a role could not be ruled out for insecticides, carbamate fungicides and triazine herbicides. The authors conclude that they have identified specific pesticides worthy of further study and that their results are consistent with previous studies. – R.L.H.

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## PESTICIDE EXPOSURE AS A RISK FACTOR FOR NON-HODGKIN LYMPHOMA INCLUDING HISTOPATHOLOGICAL SUBGROUP ANALYSIS

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We report a population based case-control study of exposure to pesticides as risk factor for non-Hodgkin lymphoma (NHL). Male and female subjects aged 18-74 years living in Sweden were included during December 1, 1999, to April 30, 2002. Controls were selected from the national population registry. Exposure to different agents was assessed by questionnaire. In total 910 (91%) cases and 1016 (92%) controls participated. Exposure to herbicides gave odds ratio (OR) 1.72, 95% confidence interval (CI) 1.18-2.51. Regarding phenoxyacetic acids highest risk was calculated for MCPA; OR 2.81, 95% CI 1.27-6.22, all these cases had a latency period >10 years. Exposure to glyphosate gave OR 2.02, 95% CI 1.10-3.71 and with >10 years latency period OR 2.26, 95% CI 1.16-4.40. Insecticides overall gave OR 1.28, 95% CI 0.96-1.72 and impregnating agents OR 1.57, 95% CI 1.07-2.30. Results are also presented for different entities of NHL. In conclusion our study confirmed an association between exposure to phenoxyacetic acids and NHL and the association with glyphosate was considerably strengthened.

**Comment:** This population based case-control study from Sweden follows up on the authors' previous work and again demonstrates a linkage between pesticide exposure and the risk of developing non-Hodgkin lymphoma (NHL). Unique to this study is the incorporation of the histopathological subtypes of NHL according to the WHO classification. There were 910 cases with 1016 controls. An odds ratio of 2.81 was observed for the exposure to 4chloro-2-methyl phenoxyacetic acid herbicide (MCPA) with a latency of more than 10 years. Glyphosate exposure resulted in an OR of 2.02 also with a latency of more than 10 years. [MCPA is chemically similar to 2,4-D but one chlorine is replaced with a methyl group. Glyphosate is sold in the USA as Round-up.]

When analyzed by NHL subtype, lymphocytic lymphoma/B-CLL was associated with herbicides with the highest OR of 3.35 seen with exposure to glyphosate. Diffuse large B-cell lymphoma had an OR of 3.94 for exposure to MCPA. If both phenoxyacetic acids and glyphosate were excluded, exposure to other herbicides resulted in no significant ORs. In recent years the authors comment on the leveling off of the previously seen steady increase in the incidence of NHL. They speculate that this leveling off may be due in part to the regulation of and hence reduction in the usage of the phenoxyacetic herbicides (including MCPA) but they note that the increased use of glyphosate is not without its own risks.

They also mention other factors such as the regulation and decrease of environmental exposure to polychlorinated biphenyls (PCBs) that may be playing a role in this leveling off. Like the abstract by Chamie discussed above, the remarkably long latent period should ring alarm bells about the risks we are taking with future generations and how long a period is required to detect a risk and how hard it is to see a reversal.—R.H.L.

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## OCCUPATIONAL EXPOSURE TO CHEMICALS AND THE RISK OF THYROID CANCER IN SWEDEN

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**Purpose:** To explore thyroid cancer (TC) risk in the Swedish population, associated with occupational exposure to certain chemicals.

**Methods:** National cancer and death registries were used to follow-up (1971-1989) all Swedish workers employed in the 1970 census. Each combination of occupation and industry was linked to a Swedish job-exposure matrix (JEM), with exposure to 13 chemicals classified as “possible exposure”, “probable exposure” or “unexposed”. Relative risks were obtained using Poisson models adjusted for age, period and geographical area. A second analysis was performed, in which adjustment was additionally made for simultaneous exposure to other matrix chemicals and ionizing radiations.

**Results:** Probable exposure to solvents among women displayed an increased risk (RR = 1.91; 95%CI:1.05-3.45), mainly due to a higher risk observed among shoe-cutters, lasters and sewers engaged in shoe-making.

**Conclusions:** Exposure to solvents, used mainly in the shoe and leather industry, seems to be associated with excess TC among women.

**Comment:** This is a very large study involving almost 3 million worker subjects for the years of 1971-1989 who were in the National Cancer and Death Registries of Sweden. Men and women were studied separately. Myeloma was diagnosed in 3,127 men and 1,282 women. Elevated risk for developing myeloma in males occurred in a variety of occupations including agriculture, horticulture, forestry, dental technicians, stone cutters/carvers, etc. Among women excess risk was seen among metal workers, paper/paper-board product workers, etc. Both men and women bakers and pastry cooks had an excess risk of over 40% and accounted for about 60% of the cases. Occasional “although intense” pesticide exposure was also a risk factor for men. The authors note that the high risk found in bakers and pastry cooks has not been previously recognized and they attribute it to exposure to “high molecular weight sensitizing agents” present in this work environment. Clearly this association is a candidate for further study. — R.L.H.

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## RENAL CELL CARCINOMA, OCCUPATIONAL PESTICIDE EXPOSURE AND MODIFICATION BY GLUTATHIONE S-TRANSFERASE POLYMORPHISMS

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This study investigated associations between occupational pesticide exposure and renal cell carcinoma (RCC) risk. To follow-up on a previous report by Buzio et al., we also considered whether this association could be modified by glutathione S-transferase M1 and T1 (GSTM1 and GSTT1) genotypes. About 1097 RCC cases and 1476 controls from Central and Eastern Europe were interviewed to collect data on lifetime occupational histories. Occupational information for jobs held for at least 12 months duration was coded for pesticide exposures and assessed for frequency and intensity of exposure. GSTM1 and GSTT1 gene deletions were analyzed using TaqMan assays. A significant increase in RCC risk was observed among subjects ever exposed to pesticides [odds ratio (OR): 1.60; 95% confidence interval (CI): 1.00-2.55]. After stratification by genotypes, increased risk was observed among exposed subjects with at least one GSTM1 active allele (OR: 4.00; 95% CI: 1.55-10.33) but not among exposed subjects with two GSTM1 inactive alleles compared with unexposed subjects with two inactive alleles (P-interaction: 0.04). Risk was highest among exposed subjects with both GSTM1 and GSTT1 active genotypes (OR: 6.47; 95% CI: 1.82-23.00; P-interaction: 0.02) compared with unexposed subjects with at least one GSTM1 or T1 inactive genotype. In the largest

RCC case-control study with genotype information conducted to date, we observed that risk associated with pesticide exposure was exclusive to individuals with active GSTM1/T1 genotypes. These findings further support the hypothesis that glutathione S-transferase polymorphisms can modify RCC risk associated with occupational pesticide exposure.

**Comment:** *In this case control study 1097 patients with renal cell carcinoma were compared to 1476 controls according to their pesticide exposure and their glutathione S-transferase M1 and T1 genotypes (GSTM1 and GSTT1). When active these genes are thought to activate halogenated alkanes, alkenes and other solvent pesticides in the kidney. For the cases “ever exposed” the OR was 1.6 which rose to 4.0 when they were stratified for having at least one active GSTM1 allele. The OR of 6.47 was seen with both GSTM1 and GSTT1 active genotypes compared with unexposed controls with at least one GSTM1 or –T1 inactive alleles. Overall, in this study the added risk of renal cell carcinoma by pesticide exposure was contributed exclusively by individuals with active GSTM1/T1 genotypes. This interesting study adds to the growing literature on the important yet subtle interplay of environmental exposures and an individual’s genetic makeup. – R.L.H.*



## **POLYMORPHISMS IN METABOLIC GSTP1 AND DNA-REPAIR XRCC1 GENES WITH AN INCREASED RISK IF DNA DAMAGE IN PESTICIDE-EXPOSED FRUIT GROWERS**

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Pesticide exposure is associated with various neoplastic diseases and congenital malformations. Previous studies have indicated that pesticides may be metabolized by cytochrome P450 3A5 or glutathione S-transferases. DNA-repair genes, including X-ray repair cross-complementing group 1 (XRCC1) and xeroderma pigmentosum group D (XPB), may also be implicated in the process of pesticide-related carcinogenesis. Thus, we investigated whether various metabolic and DNA-repair genotypes increase the risk of DNA damage in pesticide-exposed fruit growers. Using the comet assay, the extent of DNA damage was evaluated in the peripheral blood of 135 pesticide-exposed fruit growers and 106 unexposed controls. The metabolic genotypes CYP3A5 (A(-44)G) and GSTP1 (Ile105Val) and DNA-repair genotypes XRCC1 (Arg399Gln, Arg194Trp, T(-77)C) and XPB (Asp312Asn, Lys751Gln) were identified by polymerase chain reaction. Our multiple regression model for DNA tail moment showed that age, high pesticide exposure, low pesticide exposure, GSTP1

Ile-Ile, and XRCC1 399 Arg-Arg genotype were associated with increased DNA tail moment (DNA damage). Further analysis of interaction between GSTP1 and XRCC1 genes that increase susceptibility revealed a significant difference in DNA tail moment for high pesticide-exposed subjects carrying both GSTP1 Ile-Ile with XRCC1 399 Arg-Arg genotypes (2.49+/-0.09 microm/cell; P=0.004), compared to those carrying GSTP1 Ile-Val/Val-Val with XRCC1 399 Arg-Gln/Gln-Gln genotypes (1.98+/-0.15 microm/cell). These results suggest that individuals with susceptible metabolic GSTP1 and DNA-repair XRCC1 genotypes may be at increased risk of DNA damage due to pesticide exposure.

**Comment:** *This complicated study examines a possible mechanism for DNA damage that could explain some of the linkages seen between pesticide exposure and various cancers and congenital malformations. In essence, genes that increase susceptibility to DNA damage when present in a subject who also has the appropriate genes to bioactivate in vivo harmful metabolites of pesticides results in evidence of DNA damage. The subjects were 135 Taiwanese pesticide-exposed fruit growers compared with 106 unexposed controls. For example, high pesticide-exposure subjects with both the glutathione S-transferase gene GSTP1 Ile-Ile gene who also carried the X-ray repair cross-complementing group gene 1 (XRCC1 399 Arg-Arg) had statistically different assays for increased DNA damage (comet assay) when compared to subjects with the normal genes. These types of real world studies dissecting out the susceptible individuals from the resistant individuals will help to further establish the risk of pesticide exposure, perhaps suggest protective measures (don't expose the susceptible) and should surely invoke more active and rigorous application of the precautionary principle. – R.L.H.*



## **DNA DAMAGE IN WORKERS OCCUPATIONALLY EXPOSED TO PESTICIDE MIXTURES**

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Pesticides are used in agriculture to protect crops but represent at the same time a potential risk to farmers and environment. The aim of this work is the evaluation of 54 subjects occupationally exposed to pesticides and 30 subjects as a control group using the quantification of DNA damage level by means of the alkaline Comet assay and the evaluation of repair processes. Damage index Comet assay (DICA) and damage index repair assay (DIRA) were studied in 27 pesticide applicator workers, 27 non-pesticide applicators and controls. Our results show that both exposed groups revealed significant increase in DICA when compared with controls (P < 0.0001), as well as in DIRA (P < 0.0001). However, the spraying group exhibited a marginally

significant difference in DICA ( $P = 0.05$ ) when years of exposure are considered and a significant difference ( $P < 0.05$ ) when the personal protective equipment used by individuals was taken as a comparison factor. The influence of confounding factors on the genotoxic effects of occupational exposure to pesticides was investigated and no significant differences were observed considering age, gender, smoking and alcohol consumption in relation to DICA and DIRA. Since DNA damage is an important step in events leading from carcinogen exposure to cancer disease, our study highlights the potential health risk associated with agrochemical exposure in developing countries with vast cultivated areas, such as Argentina.

**Comment:** *This study from Argentina in some ways is similar to the previous study in that DNA damage was assessed by the use of the alkaline Comet assay. The study group was divided into two, 27 pesticide sprayer and applicator workers and 27 agricultural workers and farmers. The control group was 30 social healthcare workers with no history of occupational pesticide exposure. Both exposed groups showed a significant increase in damage index Comet assay (DICA) as well as damage index repair assay (DIRA) when compared to the control group. There also was a significant difference in DICA when the use of protective equipment was considered which highlights the need for and the necessity of using protective equipment. – R.L.H.*

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## PERSISTENT ORGANOCHLORINE PESTICIDES AND THE RISK OF TESTICULAR GERM CELL TUMORS

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**Background:** Exposure to endocrine-disrupting chemicals, such as persistent organochlorine pesticides, has been suggested to increase the risk of testicular germ cell tumors (TGCTs).

**Methods:** To study the relationship of POP exposure to TGCT risk, prediagnostic serum samples from 754 case subjects and 928 control subjects enrolled in the Servicemen's Testicular Tumor Environmental and Endocrine Determinants Study were analyzed for cis-nonachlor, trans-nonachlor, oxychlordanes, total chlordanes, beta-hexachlorocyclohexane, mirex, p,p'-dichlorodiphenyldichloroethylene (p,p'-DDE), and p,p'-dichlorodiphenyltrichloroethane. Adjusted odds ratios (ORs) and their associated 95% confidence intervals (CIs) for the risk of TGCT overall and for the histological subgroups, seminoma and nonseminoma, were estimated using multivariable logistic regression. All statistical tests were two-sided.

**Results:** TGCT risk was statistically significantly associated with higher plasma levels of p,p'-DDE (for highest quartile [Q4] vs lowest quartile [Q1], OR = 1.71, 95% CI = 1.23 to 2.38, P(trend) = .0002) and of two chlordane components, cis-nonachlor (Q4 vs Q1, OR = 1.56, 95% CI = 1.11 to 2.18, P(trend) = .009) and trans-nonachlor (Q4 vs Q1, OR = 1.46, 95% CI = 1.07 to 2.00, P(trend) = .026). Seminoma risk was statistically significantly associated with p,p'-DDE (Q4 vs Q1, OR = 1.91, 95% CI = 1.22 to 2.99, P(trend) = .0008), cis-nonachlor (Q4 vs Q1, OR = 1.93, 95% CI = 1.27 to 2.93, P(trend) = .0045), trans-nonachlor (Q4 vs Q1, OR = 1.72, 95% CI = 1.11 to 2.67, P(trend) = .033), and a chlordane metabolite, oxychlordanes (Q4 vs Q1, OR = 1.64, 95% CI = 1.04 to 2.60, P(trend) = .048), whereas nonseminoma risk showed a statistically significant association with p,p'-DDE only (Q4 vs Q1, OR = 1.63, 95% CI = 1.10 to 2.42, P(trend) = .0044).

**Conclusions:** Increased exposure to p,p'-DDE may be associated with the risk of both seminomatous and nonseminomatous TGCTs, whereas exposure to chlordane compounds and metabolites may be associated with the risk of seminoma. Because evidence suggests that TGCT is initiated in very early life, it is possible that exposure to these persistent organic pesticides during fetal life or via breast feeding may increase the risk of TGCT in young men.

**Comment:** *Suspected endocrine-disrupting chemicals and their metabolites were assayed in the serum of 754 cases of testicular germ cell tumors (TGCT) and 928 controls. The study showed that increased risk of both seminomatous and nonseminomatous tumors were associated with exposure to p,p'-dichlorodiphenyltrichloroethane (p,p'-DDE) and its metabolites whereas exposure to chlordane compounds and metabolites may be associated with increase of seminoma. Since it is believed that TGCT is initiated in very early life, the authors suspect that exposure to these persistent organic pesticides probably occurs in utero or with breast feeding. This would be another example of the long latent period between a carcinogenic exposure and the development of a cancer making it very difficult to both pinpoint exposures as well as to take preventive measures apart from reducing these agents in our environment. – R.L.H.*

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## ENVIRONMENTAL AND OCCUPATIONAL CAUSES OF CANCER: NEW EVIDENCE 2005-2007

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What do we currently know about the occupational and environmental causes of cancer? As of 2007, the International Agency for Research on Cancer (IARC) identified 415 known or suspected carcinogens. Cancer arises through an extremely

complicated web of multiple causes, and we will likely never know the full range of agents or combinations of agents. We do know that preventing exposure to individual carcinogens prevents the disease. Declines in cancer rates—such as the drop in male lung cancer cases from the reduction in tobacco smoking or the drop in bladder cancer among cohorts of dye workers from the elimination of exposure to specific aromatic amines—provides evidence that preventing cancer is possible when we act on what we know. Although the overall age-adjusted cancer incidence rates in the United States among both men and women have declined in the last decade, the rates of several types of cancers are on the rise, some of which are linked to environmental and occupational exposures. This report chronicles the most recent epidemiologic evidence linking occupational and environmental exposures with cancer.

Peer-reviewed scientific studies published from January 2005 to June 2007 were reviewed, supplementing our state-of-the-evidence report published in September 2005. Despite weaknesses in certain individual studies, we consider the evidence linking the increased risk of several types of cancer with specific exposures somewhat strengthened by recent publications, among them brain cancer from exposure to non-ionizing radiation, particularly radio frequency fields emitted by mobile telephones; breast cancer from exposure to the pesticide dichlorodiphenyltrichloroethane (DDT) before puberty; leukemia from exposure to 1,3-butadiene; lung cancer from exposure to air pollution; non-Hodgkin's lymphoma (NHL) from exposure to pesticides and solvents; and prostate cancer from exposure to pesticides, polyaromatic hydrocarbons (PAHs), and metal working fluids or mineral oils. In addition to NHL and prostate cancer, early findings from the National Institutes of Health Agricultural Health Study suggest that several additional cancers may be linked to a variety of pesticides.

Our report also briefly describes the toxicological evidence related to the carcinogenic effect of specific chemicals and mechanisms that are difficult to study in humans, namely exposures to bis-phenol A and epigenetic, trans-generational effects. To underscore the multi-factorial, multi-stage nature of cancer, we also present a technical description of cancer causation summarizing current knowledge in molecular biology. We argue for a new cancer prevention paradigm, one based on an understanding that cancer is ultimately caused by multiple interacting factors rather than a paradigm based on dubious attributable fractions. This new cancer prevention paradigm demands that we limit exposure to avoidable environmental and occupational carcinogens, in combination with additional important risk factors like diet and lifestyle. The research literature related to environmental and occupational causes of cancer is constantly growing, and future updates will be carried out in light of new biological understanding of the mechanisms and new methods for studying exposures in human populations. The current state of knowledge is sufficient to compel us to act on what we know. We repeat the call of ecologist Sandra Steingraber: "From the right to know and the duty to inquire flows the obligation to act."

**Comment:** *This review of the literature is included in this Journal edition because it represents an extensive and exhaustive overview of the subject that is otherwise unavailable to anyone except a researcher in the field. Emphasized is the concept that the web of interactions is very complicated and that it is very unlikely that we will know all of the factors involved. The authors have taken a broad perspective that should convince even a confirmed skeptic that a serious problem exists and that we should do all that can be done to follow the first rule of the hole. Namely, when you find yourself in one, stop digging. A more formal stating of this would be known as the precautionary principle. For the reader who is serious about coming to grips with this subject, this paper would be a good place to start. – R.L.H.*

## OTHER RESEARCH

### RELATION OF PON1 AND CYP1A1 GENETIC POLYMORPHISMS TO CLINICAL FINDINGS IN A CROSS-SECTIONAL STUDY OF A GREEK RURAL POPULATION PROFESSIONALLY EXPOSED TO PESTICIDES

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*Toxicology Letters*. 2009 Apr 10;186(1):66-72. Epub 2008 Oct 28. PMID: 19022366

Allelic variants of CYP1A1 and PON1 have been extensively studied as susceptibility factors in toxic response, although little is known about the role of these variants as risk factors

for the plethora of diseases appearing in the human population. In this study we investigated the hypothesis of correlation of CYP1A1 and PON1 enzymes with the incidence of various medical examination findings in a Greek rural population professionally exposed to a variety of pesticides. The medical history of 492 individuals, randomly selected for the total population of 42,000, was acquired by interviews and their genotype determined for the CYP1A1\*2A, PON1 M/L and PON1 Q/R polymorphisms. The assessment of exposure to pesticides of the population was verified by analytical methods.

Analysis of the genetic data revealed that the allele frequencies of PON1 R, M and CYP1A1\*2A alleles were 0.243, 0.39 and 0.107 respectively. The CYP1A1\*2A polymorphism was found to have significant association with chronic obstructive pneumonopathy ( $p=0.045$ ), peripheral circulatory problems (trend  $p=0.042$ ), arteritis ( $p=0.022$ ), allergies (trend  $p=0.046$ ), hemorrhoids (trend  $p=0.026$ ), allergic dermatitis ( $p=0.0016$ ) and miscarriages ( $p=0.012$ ). The PON1 Q/R polymorphism

was found to have significant association with hypertension ( $p=0.046$ ) and chronic constipation ( $p=0.028$ ) whereas, the L/M polymorphism, with diabetes ( $p=0.036$ ), arteritis (trend  $p=0.022$ ) and hemorrhoids (trend  $p=0.027$ ). Our results demonstrated an association between the CYP1A1/PON1 polymorphisms and several medical examination findings, thus indicating the possible involvement of the human detoxification system to health effects in a rural population exposed professionally to pesticides.

**Comment:** In 2004, McKeown-Eyssen *et al* reviewed studies indicating that genotypes may control the biotransformation of environmental chemicals. These included CYP and PON variants. This newer Greek study found that in a population that was exposed to pesticides, persons with certain of these variants were significantly more likely to have some medical problems such as chronic obstructive pneumonopathy, peripheral circulatory problems, arteritis, allergies, hemorrhoids, allergic dermatitis, miscarriages, hypertension, and diabetes. This indicates that an individual's genotype can increase his/her risk of developing these illnesses in humans exposed to pesticides professionally. An ability to correlate detoxification genes with clinical symptoms in pesticide-exposed workers would be an important step forward in our effort to make sure that testing of pesticides protects the most genetically susceptible members of the population. – L.A.P.

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### CUMULATIVE EFFECTS OF IN UTERO ADMINISTRATION OF MIXTURES OF ANTIANDROGENS ON MALE RAT REPRODUCTIVE DEVELOPMENT

Rider CV, Wilson VS, Howdeshell KL, Hotchkiss AK, Furr JR, Lambright CR, Gray LE Jr.

*Toxicologic Pathology*. 2009 Jan 15. Epub ahead of print.

**Abstract:** Although risk assessments are typically conducted on a chemical-by-chemical basis, the 1996 Food Quality Protection Act (FQPA) required the Environmental Protection Agency (EPA) to consider cumulative risk of chemicals that act via a common mechanism of toxicity. To this end, we are conducting studies with mixtures to provide a framework for assessing the cumulative effects of "antiandrogenic" chemicals. Rats were dosed during pregnancy with antiandrogens singly or in pairs at dosage levels equivalent to about one half of the ED50 for hypospadias or epididymal agenesis. The pairs include: AR antagonists (vinclozolin plus procymidone), phthalate esters (DBP plus BBP and DEHP plus DBP), a phthalate ester plus an AR antagonist (DBP plus procymidone), and linuron plus BBP. We predicted that each chemical by itself would induce few malformations; however, by mixing any two chemicals together, about 50% of the males would be malformed. All binary combinations produced cumulative, dose-additive effects on the androgen-dependent tissues. We also conducted a mixture study combining seven "antiandrogens" together. These chemicals elicit antiandrogenic effects at

two different sites in the androgen signaling pathway (i.e., AR antagonist or inhibition of androgen synthesis). In this study, the complex mixture behaved in a dose additive manner. Our results indicate that compounds that act by disparate mechanisms of toxicity display cumulative, dose-additive effects when present in combination.

**Comment:** This study represents a relatively new approach in toxicological research. The EPA has called for studies of compounds in combination. There is little that gives us much insight into the problem of chemicals in combination. Of interest in this paper is the finding of additive effects when compounds hit different receptors. This situation might be thought of as a set up for multiplied effects. But, we will have to wait for generalizations and they may be different for each system under study. There is much to be learned but clinical medicine will surely be informed and the data may not be easy to incorporate into clinical decision making. Stay tuned. – L.K.G.

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### GLYPHOSATE FORMULATIONS INDUCE APOPTOSIS AND NECROSIS IN HUMAN UMBILICAL, EMBRYONIC, AND PLACENTAL CELLS.

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*Chemical Research in Toxicology*. 2009 Jan;22(1):97-105. PMID: 19105591

We have evaluated the toxicity of four glyphosate (G)-based herbicides in Roundup formulations, from 10(5) times dilutions, on three different human cell types. This dilution level is far below agricultural recommendations and corresponds to low levels of residues in food or feed. The formulations have been compared to G alone and with its main metabolite AMPA or with one known adjuvant of R formulations, POEA. HUVEC primary neonate umbilical cord vein cells have been tested with 293 embryonic kidney and JEG3 placental cell lines. All R formulations cause total cell death within 24 h, through an inhibition of the mitochondrial succinate dehydrogenase activity, and necrosis, by release of cytosolic adenylate kinase measuring membrane damage. They also induce apoptosis via activation of enzymatic caspases 3/7 activity.

This is confirmed by characteristic DNA fragmentation, nuclear shrinkage (pyknosis), and nuclear fragmentation (karyorrhexis), which is demonstrated by DAPI in apoptotic round cells. G provokes only apoptosis, and HUVEC are 100 times more sensitive overall at this level. The deleterious effects are not proportional to G concentrations but rather depend on the nature of the adjuvants. AMPA and POEA separately and synergistically damage cell membranes like R but at different concentrations. Their mixtures are generally even more harmful with G. In conclusion, the R adjuvants like POEA change human cell permeability and amplify toxicity induced already

by G, through apoptosis and necrosis. The real threshold of G toxicity must take into account the presence of adjuvants but also G metabolism and time-amplified effects or bioaccumulation. This should be discussed when analyzing the in vivo toxic actions of R. This work clearly confirms that the adjuvants in Roundup formulations are not inert. Moreover, the proprietary mixtures available on the market could cause cell damage and even death around residual levels to be expected, especially in food and feed derived from R formulation-treated crops.

**Comment:** For several years, abstracts of these authors and others that have been cited in this Journal have documented in both humans and cell cultures that glyphosate with adjuvants in some Roundup formulations are toxic at doses that actually occur in food and feed. This paper elucidates the toxic mechanisms of these mixtures and confirms that the mixture of chemicals in Roundup is more toxic than its so-called active ingredient, glyphosate. – L.A.P.

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## HUMAN SEMEN QUALITY AND SPERM DNA DAMAGE IN RELATION TO URINARY METABOLITES OF PYRETHROID INSECTICIDES

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*Human Reproduction*. 2008 Aug; 23(8):1932-40. Epub 2008 Jun 25.

**Background:** Exposure to synthetic pyrethroid insecticides is widespread, and is expected to increase among the general population due to the need to replace other common insecticides following regulatory use restrictions. On the basis of limited studies, there is animal and human evidence for altered reproductive or endocrine function following pyrethroid exposure.

**Methods:** The present study measured urinary pyrethroid metabolites [3-phenoxybenzoic acid (3PBA) and cis- and trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid (CDCCA and TDCCA)], semen quality, sperm motion parameters and sperm DNA damage with the neutral comet assay in 207 men recruited from an infertility clinic.

**Results:** In multivariate analysis, the highest 3PBA quartile was associated with a suggestive 20.2 million sperm/ml reduction (95% confidence interval -37.1 to + 2.6) in sperm concentration compared with men below the 3PBA median. There were significant inverse associations between TDCCA and sperm motility and sperm motion parameters when adjusting for CDCCA and other covariates. The highest TDCCA quartile was associated with a 15.5% decline (95% confidence interval -26.2 to -4.8) in sperm motility compared with men below the median. In multiple logistic analyses, there were dose-depen-

dent increased odds for below reference sperm concentration, motility and morphology in relation to TDCCA. Among the comet assay measures, 3PBA and CDCCA were associated with increased sperm DNA damage, measured as percent DNA in the comet tail.

**Conclusions:** We found evidence for reduced semen quality and increased sperm DNA damage in relation to urinary metabolites of pyrethroid insecticides. These findings may be of concern due to increased pyrethroid use and prevalent human exposure.

**Comment:** The problems of diminishing sperm quality and count are throughout the developed world. These authors add pyrethroids as possible contributors to this decline. Using measures of pyrethroid metabolites in the urine, they found diminished sperm concentration and motility. These findings are made more important because of the widespread use of these compounds. – L.K.G.

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## CHRONIC EXPOSURE TO PYRETHROID-BASED ALLETHRIN AND PRALLETHRIN MOSQUITO REPELLANTS ALTERS PLASMA BIOCHEMICAL PROFILE

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*Chemosphere*. 2008 Sep; 73(3):360-4. Epub 2008 Jul 26. PMID: 18657844

Continuous exposure of humans to pyrethroid-based mosquito repellents for longer durations may lead to adverse health effects. No information is available on long-term use of these mosquito repellents pertaining to the biochemical changes in human subjects. Therefore, the present study is an attempt to evaluate the status of health in human volunteers exposed to two commercially available mosquito repellent pyrethroids, allethrin and prallethrin, in terms of changes in plasma biochemical profile. Results of this study showed less but significant increase in the levels of plasma glucose, phospholipids, nitrite and nitrate, lipidperoxides with a decrease in plasma cholesterol. No significant changes were observed in the contents of total protein, albumin, globulin, HDL-C and LDL-C. However, SGPT activity increased significantly in persons exposed to only allethrin. Though the present investigation involving a limited number of human subjects indicates the onset of both protective changes as well as derangement in metabolism, a detailed and rigorous study is greatly warranted to arrive at a definite conclusion about the effects of pyrethroid mosquito repellents.

**Comments:** This study follows the 8 hr/day inhalation exposure effects in adults. They were exposed to commercial single-pesticide

products daily. Comparisons were made between groups of 12 using one of two non-cyanogroup-pyrethrins and 12 adults who used no pesticide. The changes in glucose, NO and lipids were statistically different but not out of the range of normal. While the importance of

theses changes is unclear, the fact that these changes are being produced by the pesticides will surely lead to further studies and new concepts of monitoring. – L.K.G.

## PREVENTION

### WHAT PHYSICIANS CAN DO TO REDUCE OCCUPATIONAL AND INCIDENTAL PESTICIDE EXPOSURE: A GUIDE TO BEST PRACTICES

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Minnesota Medicine. 2008 Sep; 91(9):31-5. PMID: 18990915

Residents of rural areas trust their physicians to provide them with accurate, unbiased information about pesticides and the effect they can have on health. Educating patients about using pesticides safely and avoiding contact with them need not be difficult or time-consuming and can be based on universal precautions that are already being practiced in the health care industry. This article discusses the prevalence of pesticide use in the United States, the ways people can be exposed, and sev-

eral best practices for helping patients reduce their chance of exposure to pesticides that can cause illness.

**Comment:** *These authors liken best practices in pesticide use to universal precautions in infectious disease. There are steps to be taken which do not require specific information on the pesticide in use. They offer the following 7 steps to best practice: 1) Read and follow labels; 2) Wear protective clothing; 3) Be prepared for the unexpected; (they suggest being sure equipment is calibrated properly and that the work area is clear of other people particularly children); 4) Avoid all routes of ingestion by avoiding having food, drink, or cigarettes in the area; 5) Use proper clean-up; 6) Control dispersion and avoid exposing pregnant women; and 7) Don't bend the rules. These are solid advices for a physician to make to those engaged in pesticide application. While the guidance seems straightforward in content, it has been a repeated surprise in my practice how many workers 'bend the rules.'* – L.K.G.

## PESTICIDES IN THE NEWS

From *The Washington Post*, April 16, 2009

### EPA TO MANDATE PESTICIDE CHEMICALS TESTS TO GAUGE ENDOCRINE SYSTEM DISRUPTIONS

By Juliet Eilperin

The Environmental Protection Agency for the first time will require pesticide manufacturers to test 67 chemicals contained in their products to determine whether they disrupt the endocrine system, which regulates animals' and humans' growth, metabolism and reproduction, the agency said yesterday.

Researchers have raised concerns that chemicals released into the environment interfere with animals' hormone systems, citing problems such as male fish in the Potomac River that are bearing eggs. Known as endocrine disruptors, the chemicals may affect the hormones that humans and animals produce or secrete.

"Endocrine disruptors can cause lifelong health problems, especially for children," EPA Administrator Lisa P. Jackson said in a statement. "Gathering this information will help us work with communities and industry to protect Americans from harmful exposure."

Testing will begin this summer and will focus on whether these chemicals affect estrogen, androgen and thyroid systems. The tests eventually will encompass all pesticide chemicals.

Pesticide industry officials said they had anticipated the move, which was set into motion in 1996 by the passage of the Food Quality Protection Act, and they planned to cooperate on the matter.

"It's been a long time coming," said Jay Vroom, president and chief executive of CropLife America, a major trade association. "For pesticides, we think the likelihood is extremely low we'll have any concerns come to the surface."

Just this month, the EPA rejected a petition from CropLife America that would have changed aspects of the agency's Endocrine Disruptor Screening Program in an effort to reduce the costs and time requirements associated with the new testing. But Vroom said the EPA indicated in its April 3 letter that it would take into account several industry concerns, including leaving open the possibility of sometimes using computer modeling rather than relying exclusively on laboratory animal testing.

"That's an encouraging sign," he said, adding that it appeared the agency would be willing to lower the number of lab animals required for testing.

Linda Birnbaum, who directs the National Institute of Environmental Health Sciences and the National Toxicology Program, said the program represents "a more organized way to look at" how human exposure to pesticide chemicals could affect such things as bone growth and brain development.

“This is a good beginning,” Birnbaum said, adding that scientists need to examine how different hormone disruptors might interact or accumulate in the human body. “It’s very important to know: Can certain chemicals, especially chemicals that are out there that people are exposed to, impact our hormone system?”

Although researchers have observed the most visible effects of these chemicals in animals, Birnbaum said it is likely that some humans, depending on their particular sensitivity, could experience similar problems.

“I think it’s unrealistic that humans are going to be immune,” she said, adding that the studies need to determine dosage, “how much of these chemicals do you need for cause and effect?”

Linda Phillips, who manages the Endocrine Disruptor Screening Program, said it will take about two years to obtain data from the two-tier program, and that it then could take the agency another year to make a final determination about the chemicals’ effect on hormone disruption.

Vroom said pesticide manufacturers are “very confident our products will come through with flying colors.” He added: “If we do learn something about our products that raises a cause for concern, our industry will be at the table, ready and willing to step forward and take action to mitigate risk.”



Excerpted from *The Baltimore Sun*, Oct. 28, 2008

## MD HOSPITALS, CARE FACILITIES WORK TO CUT TOXIC PESTICIDES USAGE

By Kelly Brewington

Johns Hopkins Hospital, the University of Maryland Medical Center and nearly a dozen other health care and retirement facilities are working to eliminate toxic pesticides from their pest control efforts, a move that environmental advocates say is the first like it in the country.

The Maryland Pesticide Network (MPN) launched the effort in 2005 after conducting a survey of pest-control products and practices in state health care facilities statewide. While the chemicals are legal and approved by the U.S. Environmental Protection Agency, advocates point to studies showing that 25 of the most commonly used pesticides are harmful to animals and marine life or have links to cancer, birth defects and neurological problems.

The MPN and a national group, Beyond Pesticides, released a report yesterday describing the most commonly used pesticides and how hospitals are working to avoid them. For instance, ant-killing baits that contain boric acid and rodent-fighting powder with diphacinone both have been found to be toxic to birds, fish and humans, the report said.

Instead of using such baits and sprays, advocates recommend sealing wall cracks and repairing window screens at the first sign of rodents or bugs. If a more rigorous approach is needed, powders, soils and sprays made with organic materials should be tried. Pesticides should be used as a last resort, they say.

Johns Hopkins Hospital first employed the seven-step strategy, known as integrated pest management, about 18 months ago and has since seen a 60 percent decrease in pest sightings, said Chris Seale, the hospital’s environmental services director. Seale said the new plan helps him do the two essential parts of his job: manage the pest population and keep hospital patients, staff and visitors safe. “The cost is slightly higher but completely reasonable, especially considering the outcome,” he said. Seale worked with MPN to devise a pest-fighting plan and then challenged five vendors to meet his needs at the best price.

Key to reducing reliance on pesticides is educating hospitals and vendors, said Ruth Berlin, MPN executive director. “We found that a lot of the health care facilities didn’t know what they were using,” she said. Most hospitals contract their pest-fighting activities to vendors, who are not always aware of the latest science on pesticides, Berlin said. As more health facilities demand “green” techniques, she hopes vendors will provide more nontoxic options.

MPN began confronting the use of pesticides more than a decade ago and pushed in 1999 to get a state law passed limiting the use of pesticides in and around Maryland public schools. “We started our work with the most vulnerable populations,” Berlin said. “And hospitals fit with that.”

Other facilities taking part include Erickson Retirement Communities, Sheppard and Enoch Pratt Hospital, Springfield Hospital Center, Johns Hopkins Bayview Medical Center, Broadmead Retirement Community, Copper Ridge, Harbor Hospital, the Forbush School, Levindale Hebrew Geriatric Center and Hospital, Mercy Medical Center and Sinai Hospital



Excerpted from *The Washington Post*, April 19, 2009

## THE NEW POLLUTERS OF THE POTOMAC

By H. Hedrick Belin

After more than a quarter of a century of Clean Water Act legislation and enforcement, the Washington area’s river and bay waters are nowhere near as healthy as they should be.

The main sources of the impairments are no mystery: sedimentation, agricultural runoff, rainwater running off paved surfaces. But recently, it has come to light that there is more going on in the Potomac River than meets the eye. While we have long tracked traditional pollutants, “Poisoned Waters,” the documentary that will run on PBS’s “Frontline” on Tuesday, highlights a new face in the lineup: chemical

compounds that interact with and possibly interfere with the workings of the endocrine system. The endocrine system controls growth, metabolism and reproduction in humans and animals.

This class of pollutants is called “endocrine disruptors.” These compounds are the primary suspect in the mystery of intersex fish that have been found in the Potomac and Shenandoah rivers. To date, we know that these compounds disrupt the development of many aquatic species, most notably male smallmouth bass that have developed eggs. This condition has been documented in the Potomac River watershed and beyond. It is becoming a global phenomenon.

Washington area residents get almost 90 percent of their drinking water from the river. Endocrine disruptors may enter our water in many different ways. Chemical-laden runoff from our lawns and roads flows into the river through the storm sewer system. Pharmaceuticals and personal-care products go down our toilets and drains and through the wastewater treatment plant, which does not remove them. Agricultural chemicals wash out of fields and chicken houses and into nearby streams. Drinking-water treatment plants do not treat for these chemicals before the water is delivered to our tap. In short, every place where water and chemicals combine becomes a potential source of endocrine disruptors in our drinking water.

Intersex fish in our rivers are an ominous sign of things to come. We know little about what causes this condition, and we need to know more. The Potomac Conservancy believes that it is time to answer the question of whether and how these compounds affect animal and human health, in particular, the development of our children. We call on the new administration to find—and fund—solutions for this important problem.

EPA Administrator Lisa Jackson spoke recently on this issue and promised a hard look at solutions. Last week, the agency announced its plan to test more than 67 chemicals contained in pesticides for possible involvement in endocrine processes. That is a promising start, but the compounds that will be studied represent only a fraction of the hundreds of thousands of chemicals in our water that could act as endocrine disruptors. These include a variety of products we all use in our daily lives, including shampoos, hand sanitizers, pharmaceuticals and lawn products.

The new pollutants don't set our rivers on fire, wash up on our shores or taint our air. As such, they are easy to overlook. We think it's high time to take a closer look at what is in our river water and our drinking water.

*The writer is president of the Potomac Conservancy.*



Excerpted from *Beyond Pesticides Daily News*, Sept. 16, 2008

## **IPM EFFORT IMPROVES BOSTON PUBLIC HOUSING PEST CONTROL**

Responding to grassroots pressure highlighting the impact of pests and pesticides on public health, the Boston Public Housing Authority (BHA) is promoting integrated pest management (IPM) through its Healthy Pest Free Housing Initiative Project (HPFHI) in the city's public housing facilities. The program was launched after the Committee for Boston Public Housing, a tenant rights group, began looking into the connection between respiratory health, asthma and housing conditions.

“The project's goal is to provide intensive in-home and community-based education designed to change individual and community practices regarding pest control and the use of pesticides,” explained John Kane, IPM coordinator and planner for the Boston Housing Authority (BHA). Kane said that there has been up to a 75 percent reduction in work orders dealing with pests and a huge increase in the quality of life for the residents.

Over 1,000 BHA households in eight developments have received in-home and community-based support and education to encourage integrated pest management practices that focus on prevention and use “least toxic” pesticides only as a last resort. BHA hopes to make the project sustainable and expand their efforts into additional developments. “People are beginning to see they no longer have to live with their pest problems. They feel empowered by being able to take control of their pest problems and their health,” said Kane.

The HPFHI project has moved the standard pest management practice from routinely spraying pesticides in an entire complex to inspections and an integrated management plan. Prevention is emphasized, and tactics such as sealing up cracks and crevices, cutting off water supply, and removing habitat are all steps that are taken once unit is vacated and during yearly unit inspections. Insecticide gels are used as a last resort.

According to BHA, at the beginning of the project every home tested showed evidence of at least one pesticide that has either been banned or restricted to non-residential use. Nearly 50 percent had cockroach allergen levels in excess of asthma sensitivity exposure.

Teams of IPM health advocates are providing outreach and in-home education in eight BHA developments involved in the project. “Our team trains the residents in IPM, and we also utilize a train-the-trainer approach in which people are trained to provide education about IPM to newly arriving residents during their orientation,” said Kane. The Boston Public Health Commission has also developed informational brochures and posters in multiple languages that can be used in public housing situations and beyond.

To enhance their educational efforts, a “pesticide buyback” occurs twice a year and gives residents an opportunity to trade

unused pesticides for safer products and provides another opportunity for health advocates to connect with residents. “Buybacks are scheduled to coincide with Boston’s biannual residential hazardous waste collection. So far, this project has collected a wide array of pesticides including over the counter sprays and bombs, as well as restricted use pesticides that by law can only be applied by a licensed professional,” Kane explained.



Excerpted from *United Press International*, June 5, 2008

## LONG-TERM PESTICIDE USE MAY UP DIABETES

BETHESDA, Md., June 5 (UPI). Licensed pesticide applicators who used chlorinated pesticides on more than 100 days in their lifetime were at greater risk of diabetes, U.S. researchers say.

Scientists with the National Institutes of Health National Institute of Environmental Health Sciences and the National Cancer Institute say the associations between specific pesticides and incident diabetes ranged from a 20 percent to a 200 percent increase in risk.

“The results suggest that pesticides may be a contributing factor for diabetes along with known risk factors such as obesity, lack of exercise and having a family history of diabetes,” study co-author Dale Sandler of the NIEHS said in a statement. “Although the amount of diabetes explained by pesticides is small, these new findings may extend beyond the pesticide applicators in the study.”

The study, published in the *American Journal of Epidemiology*, found pesticide applicators in the highest category of lifetime days of use of any pesticide had an increase in risk for diabetes of 17 percent compared with those in the lowest pesticide use category of zero to 64 lifetime days.

The researchers analyzed data from 31,787 licensed pesticide applicators in North Carolina and Iowa. The study found that 1,171 reported a diagnosis of diabetes in the five-year follow-up interview.



Excerpted from *Environmental Health Perspective*, April 2008

## HAZARDOUS PESTICIDES FOUND IN CHILDREN WHO EAT CHEMICALLY-TREATED FOODS

A new study finds that children who eat a conventional diet of food produced with chemical-intensive practices carry residues of organophosphate pesticides that are reduced or eliminated when they switch to an organic diet. The study is entitled “Dietary Intake and Its Contribution to Longitudinal Organophosphorus Pesticide Exposure in Urban/Suburban

Children” (Chensheng Lu, Dana B. Barr, Melanie A. Pearson, and Lance A. Waller) and includes authors from Rollins School of Public Health, Emory University, and the National Center for Environmental Health, Centers for Disease Control and Prevention.

According to the authors, “The objective of this article is to present the data of assessing young urban/suburban children’s longitudinal exposure to OP [organophosphate] pesticides in a group [of] young children participating in the Children Pesticide Exposure Study (CPES).

The results from this study identify not only the predominant source of OP pesticide exposure but also the profile of exposures in children that are vital in formulating the strategies, both from the regulatory policy and personal behavior change perspectives, in reducing children’s exposures to OP pesticides.”

The study design included 23 children, male and female, from the Seattle area, ages 3-11 years who only consumed conventional diets and were recruited for a one-year study conducted in 2003-2004. Of the 23, 19 completed the study. Children switched to organic diets for five consecutive days in the summer and fall sampling seasons. The authors measured specific urinary metabolites for malathion, chlorpyrifos and other OP pesticides in urine samples collected twice daily for a period of 7, 12, or 15 consecutive days during each of the four seasons. According to the authors, “By substituting organic fresh fruits and vegetables for corresponding conventional food items, the median urinary metabolite concentrations were reduced to non-detected or close to non-detected levels for malathion and chlorpyrifos at the end of 5-day organic diet intervention period in both summer and fall seasons. We also observed a seasonal effect on the OP urinary metabolite concentrations, and this seasonality is correspondent to the consumption of fresh produce throughout the year.” And, “Considering the lack of residential use of OP pesticides among the families of CPES-WA children, consumption of conventional diets is likely to be the sole contributing factor to the seasonality effect of pesticide exposures.”

The authors point out that few studies evaluate the longitudinal exposure to pesticides that all children experience. According to the authors, “Most of the studies published in the literature have either targeted children living in agricultural environments or have used a cross-sectional design with spot sample collection.”

The authors raise concerns about inadequate attention being given by regulators to chronic low-level exposures to pesticides, such as those found in their study. They point out that, “Using spot biomarkers [one-time measurement of urinary metabolites] of OP pesticide exposure to examine the link between adverse health outcomes and cumulative OP pesticide exposure is obviously an inadequate approach.”



Excerpted from *Beyond Pesticides Daily News*, March 18, 2009

## **EPA RELEASES DATABASE ON ENVIRONMENTAL CHEMICALS, EXPOSES DATA GAPS**

The U.S. Environmental Protection Agency (EPA) has released a new online database that collects information on more than 500,000 synthetic chemicals from over 200 public sources. The Aggregated Computational Toxicology Resource (ACToR) database provides access to hundreds of data sources in one place, enabling easy access for environmental researchers, scientific journalists and the public. However, more than half of these chemicals do not have any detailed testing data.

ACToR, which is actually a collection of databases, was developed to support the ToxCast program of the EPA National Center for Computational Toxicology (NCCT). ToxCast was designed to develop faster methods to evaluate the potential toxicity for thousands of chemicals using computer modeling and advanced molecular biology techniques. More than 200 sources of publicly available data on environmental chemicals have been brought together on ACToR and made searchable by chemical name and other identifiers, and by chemical structure. Data includes chemical structure, physico-chemical values, *in vitro* assay data and *in vivo* toxicology data.

Chemicals include, but are not limited to, high and medium production volume industrial chemicals, pesticides (active and inert ingredients), and potential ground and drinking water contaminants. Sources of information include EPA, U.S. Food and Drug Administration, U.S. National Institutes of Health, U.S. Centers for Disease Control and other federal agencies; state databases, Health and Environment Canada, the European Union, the World Health Organization and other international groups; and non-governmental organizations, private companies and universities.

ACToR was used to analyze toxicity information on almost 10,000 chemicals regulated by EPA and identify data gaps to be addressed by ToxCast, to help EPA prioritize future testing of chemicals. While acute toxicity data is available for 59 percent of the surveyed chemicals, detailed testing information is much more limited. Only 26 percent of the 10,000 chemicals have carcinogenicity testing data, 29 percent have developmental toxicity testing data, and 11 percent have complete reproductive toxicity test results.

The lack of toxicological data on more than half of the 10,000 chemicals overseen by the EPA means that there are numerous data gaps and thus, a lack of adequate safety tests which continues to undermine the integrity of EPA's risk assessment process. With little to no data on chemicals that are allowed to enter the consumer market place, the agency is failing to protect human and environmental health. A recent GAO report found that the EPA does not have sufficient chemical assessment information to determine whether it should establish controls to limit public exposure to many chemicals that may pose substantial health risks. The report went on to state that

EPA has not responded to recommendations made to reduce agency shortcomings and has "not sufficiently improved the scientific information available to support critical decisions regarding whether and how to protect human health from toxic chemicals."

Source: *EPA News Release*



Excerpted from *National Environmental Law Center news release*, January 7, 2009

## **CONSERVATIONISTS WIN DECISION PROTECTING LOCAL WATER SUPPLIES, FISHERIES & WILDLIFE; BUSH EXEMPTION VACATED**

Cincinnati, Ohio - In a stinging defeat for the Bush Environmental Protection Agency, the 6th Circuit Court of Appeals today issued a clear rebuke against the administration's 2006 rule which exempted certain commercial pesticide applications from the oversight provided by Congress under the Clean Water Act. The Court held that pesticide residuals and biological pesticides constitute pollutants under federal law and therefore must be regulated under the Clean Water Act to minimize the impact to human health and the environment.

Several manufacturers and industry associations had joined the case in an attempt to broaden the Environmental Protection Agency's 2006 exemption. The Court told them in no uncertain terms that their products are harmful to human health and the environment, and therefore EPA must regulate aquatic pesticide applications under the Clean Water Act.

With this decision, virtually all commercial pesticide applications to, over and around waterways will now require National Pollutant Discharge Elimination System (NPDES) permits. The NPDES permits will allow for local citizen input, and provide for accountability and oversight. The permits will also require the regulatory agencies to evaluate effects on fish and wildlife from individual applications, to monitor exactly how much of a pesticide application goes into our nation's waters, and to evaluate the cumulative impact this residual effect has on aquatic organisms.

"The decision today is a victory for clean water and for fish and wildlife" declared Charlie Tebbutt, Western Environmental Law Center attorney and lead counsel for the environmental organizations and organic farms that challenged the rule. "Furthermore, this decision is another in a long line of rebukes to the Bush administration policies that overstepped their statutory authority and to the chemical manufacturers who peddle their poisons without concern to the effect on human health and the environment. We look forward to working with the new EPA to protect the environment rather than the chemical industry."

“This decision will help ensure, in communities across the country, that aquatic pests are addressed in ways that protect both water quality and the public health,” noted Chuck Caldart of the National Environmental Law Center, one of the attorneys litigating the case on behalf of those challenging the exemption.

“We’re thrilled by the court’s decision—particularly in providing clarity on the aerial applications of pesticides over navigable waters for mosquito control,” said Peconic Baykeeper Kevin McAllister. “It’s well recognized that many pesticides can pose a significant threat to aquatic life. Ensuring that the required discharge permits have been obtained provides for greater protection of our water resources.”

“This is an important victory for clean water and, the people who rely on our nation’s aquatic resources for their livelihood,” declared Long Island Soundkeeper Terry Backer. “With today’s ruling, it’s becoming abundantly clear that our courts are now looking at EPA’s rulemaking with increasing and deserved skepticism.”

“Time and again during these past eight years EPA has walked into federal courts and tried to defend absolutely indefensible rules like the one vacated today,” said Waterkeeper Alliance Legal Director Scott Edwards. “And time and again they’ve been sent back to the drawing board to rewrite these unlawful rules. Hopefully, EPA’s days of pandering to industry and other polluters and wasting taxpayers’ dollars in illegal rulemaking are drawing to a close.”

“This is a significant victory for our nation’s waters. More than 8 million pounds of pesticides are applied each year in the Bay Area alone,” said Sejal Choksi, Program Director for San Francisco Baykeeper. “These toxic chemicals enter our creeks harming numerous species of fish, frogs and other aquatic life and will now be regulated under the Clean Water Act.”

“Pesticides have been documented as the most pervasive group of toxic pollutants in our waterways. This decision is a significant step forward in protecting and restoring our seriously degraded fisheries,” said Bill Jennings, Chairman and Executive Director of the California Sportfishing Protection Alliance.

“When it comes to toxic pesticides and their effects on our rivers and salmon, we need to be certain that good science is being used and those resources are protected. This ruling is a victory for clean water and fish, and a victory for Americans who care about healthy rivers and streams,” added Steve Pedery, Oregon Wild Conservation Director.

The organizations bringing the case included Baykeeper, National Center for Conservation Science and Policy, Oregon Wild, Saint John’s Organic Farm, Californians for Alternatives to Toxics, California Sportfishing Protection Alliance, Waterkeeper Alliance, Environment Maine, Toxics Action Center, Peconic Baykeeper and Soundkeeper.

The organizations were represented by the Western Environmental Law Center, the National Environmental Law Center, the Pace Environmental Litigation Clinic, the Columbia Environmental Law Clinic and Waterkeeper Alliance.



Excerpted from *Beyond Pesticides Daily News*, April 1, 2009

## **BIRTH DEFECTS LINKED TO PESTICIDE EXPOSURE AT TIME OF CONCEPTION**

A study published in the April 2009 issue of the medical journal *Acta Paediatrica* reports that the highest rates of birth defects for U.S. babies arise when conception occurs during the spring and summer months, when pesticide use increases and high concentrations of pesticides are found in surface waters.

The study entitled, “Agrichemicals in surface water and birth defects in the United States” is the first study to link increased seasonal concentration of pesticides in surface water with the peak in birth defects in infants conceived in the same months. Researchers analyzed all 30.1 million births in the U.S. between 1996 and 2002. A strong association between higher rates of birth defects among women whose last menstrual period was in April, May, June or July and elevated levels of nitrates, atrazine and other pesticides in surface water during those same months was found.

The correlation between the month of last menstrual period and higher rates of birth defects is statistically significant for half of the 22 categories of birth defects reported in the Centers for Disease Control database from 1996 to 2002, including spina bifida, cleft lip, clubfoot and Down’s syndrome.

“Elevated concentrations of pesticides and other agrochemicals in surface water during April through July coincided with significantly higher risk of birth defects in live births conceived by women whose last menstrual period began in the same months. While our study didn’t prove a cause and effect link, the fact that birth defects and pesticides in surface water peak during the same four months makes us suspect that the two are related,” said Paul Winchester, M.D., Indiana University School of Medicine professor of clinical pediatrics, the first author of the study.

The study relies on findings by the U.S. Geological Survey, the U.S. Environmental Protection Agency and other agencies on the seasonal variations in nitrates, atrazine and other pesticides in the surface water. Pesticides, such as atrazine, even at low levels, have been associated with reproductive and developmental effects as well as endocrine disruption. Atrazine is the second most commonly used agricultural pesticide in the U.S. and the most commonly detected pesticide in rivers, streams and wells. An estimated 76.4 million pounds of atrazine are applied in the U.S. annually. Atrazine has a tendency to persist in soils and move with water, making it a common water contaminant.

Birth defects are known to be associated with risk factors such as alcohol, smoking, diabetes or advanced age. However, the researchers found that even mothers who didn't report these risk factors had higher overall birth defect rates for babies conceived from April to July. "Birth defects, which affect about 3 out of 100 newborns in the U.S., are one of the leading causes of infant death. What we are most excited about is that if our suspicions are right and pesticides are contributing to birth defect risk, we can reverse or modify the factors that are causing these lifelong and often very serious medical problems," said Dr. Winchester.

This is not the first documentation of birth defects resulting from pesticide exposure during pregnancy. In 2004, three female farmworkers gave birth to babies with severe birth defects after being exposed to pesticides. One baby was born without arms or legs and with spinal and lung deformities.

Source: *U.S. News and World Report*



Excerpted from *Beyond Pesticides Daily News*, March 31, 2009

## **USGS SURVEY FINDS PESTICIDES, FERTILIZERS IN WELL WATER**

More than 20 percent of private domestic wells sampled nationwide contain at least one contaminant at levels of potential health concern, according to a study by the U.S. Geological Survey (USGS).

About 43 million people—or 15 percent of the Nation's population—use drinking water from private wells, which are not regulated by the federal Safe Drinking Water Act.

USGS scientists sampled about 2,100 private wells in 48 states and found that the contaminants most frequently measured at concentrations of potential health concern were inorganic contaminants, including radon and arsenic. These contaminants are mostly derived from the natural geologic materials that make up the aquifers from which well water is drawn.

Nitrate was the most common inorganic contaminant derived from man-made sources—such as from fertilizer applications and septic-tanks—that was found at concentrations greater than the federal drinking-water standard for public-water supplies (10 parts per million). Nitrate was greater than the standard in about four percent of sampled wells. Other contaminants found in the private wells were man-made organics, including herbicides, insecticides, solvents, disinfection by-products, and gasoline chemicals.

The study shows that the occurrence of selected contaminants varies across the country, often following distinct geographic patterns related to geology, geochemical conditions, and land use. For example, elevated concentrations of nitrate were largely associated with intensively farmed land, such as in parts of the Midwest corn belt and the Central Valley of California.

Radon was found at relatively high concentrations in crystalline-rock aquifers in the Northeast, in the central and southern Appalachians, and in central Colorado.

"The results of this study are important because they show that a large number of people may be unknowingly affected," said Matt Larsen, USGS Associate Director for Water. "Greater attention to the quality of drinking water from private wells and continued public education are important steps toward the goal of protecting public health."

USGS sampled private wells from 1991 to 2004 in 30 of the nation's principal aquifers used for water supply. As many as 219 properties and contaminants, including pH, major ions, nutrients, radionuclides, trace elements, pesticides, volatile organic compounds, and microbial contaminants, were measured. Sampled water was taken from private wells before any home treatment.

Few organic contaminants (7 out of 168) exceeded health benchmarks, and were found above health benchmarks in less than one percent of sampled wells. Organic contaminants were detected at lower concentrations in more than half (60 percent) of sampled wells, indicating that a variety of contaminant sources—including agricultural, residential, and industrial—can affect the quality of water from private wells. The study measured organic chemicals at very low concentrations—often well below human-health benchmarks—in order to assess occurrence and sources. Pesticides can, however, be dangerous at low levels; view "Facing Scientific Realities: Debunking the 'Dose Makes the Poison' Myth" for more information.

Contaminants found in private wells usually co-occurred with other contaminants as mixtures rather than alone, which can be a concern because the total combined toxicity of contaminant mixtures can be greater than that of any single contaminant. Mixtures of contaminants at relatively low concentrations were found in the majority of wells, but mixtures with multiple contaminants above health benchmarks were uncommon (about four percent). The USGS report identifies the need for continued research because relatively little is known about the potential health effects of most mixtures of contaminants, and the additive or synergistic effects on human health of mixtures of man-made chemicals at low levels are not well understood.

Bacteria, including total coliform bacteria and *Escherichia coli*, were found in as many as one third of a subset of 400 wells. These bacteria are typically not harmful but can be an indicator of fecal contamination. About half of the 2,100 sampled wells had at least one property or contaminant outside recommended ranges for cosmetic or aesthetic purposes, such as total dissolved solids, pH, iron, and manganese.

Human-health benchmarks used in the study include drinking-water standards for contaminants regulated under the federal Safe Drinking Water Act and non-enforceable USGS Health-Based Screening Levels (HBSLs) for unregulated contaminants, developed by USGS in collaboration with the U.S.

Environmental Protection Agency. About half of the wells deemed to have potential health concerns had concentrations greater than Maximum Contaminant Levels specified by the Safe Drinking Water Act for public-water supplies. In relating measured concentrations to health benchmarks, this study offers a preliminary assessment of potential health concerns that identifies conditions that may require further investigation. The research is not a substitute for comprehensive risk and toxicity assessments.

Private well owners, who generally are responsible for testing the quality of their well water and treating, if necessary, can contact local and state health agencies for guidance and information about well maintenance and siting, water quality and testing options, and in-home water treatment devices. Last fall, a similar USGS survey found low-level pesticides and fertilizers in drinking water around the country.



Excerpted from *Milwaukee Journal Sentinel*, January 24, 2009

## **EPA A FAILURE ON CHEMICALS. AUDIT FINDS ASSESSMENT OF TOXIC RISKS INADEQUATE, SAYS NEW CHIEF**

By Meg Kissinger

The Environmental Protection Agency's ability to assess toxic chemicals is as broken as the nation's financial markets and needs a total overhaul, a congressional audit has found.

The Government Accountability Office has released a report saying the EPA lacks even basic information to say whether chemicals pose substantial health risks to the public. It says actions are needed to streamline and increase the transparency of the EPA's registry of chemicals. And it calls for measures to enhance the agency's ability to obtain health and safety information from the chemical industry.

Lisa Jackson, the EPA's new administrator, promised to take the report under consideration. "It is clear that we are not doing an adequate job of assessing and managing the risks of chemicals in consumer products, the workplace and the environment," Jackson said in a prepared statement Friday. "It is now time to revise and strengthen EPA's chemicals management and risk assessment programs."

The Journal Sentinel has chronicled the failure of the EPA to disclose information about toxic chemicals in its series, "Chemical Fallout," which began in 2007. Last month, the newspaper reported that the agency routinely allows companies to keep new information about their chemicals secret, including compounds that have been shown to cause cancer and respiratory problems.

Earlier in 2008, the Journal Sentinel revealed that the EPA's Voluntary Children's Chemical Evaluation Program, which

relies on companies to provide information about the dangers of the chemicals they produce, is all but dead. And it disclosed that the agency's program to screen chemicals that damage the endocrine system had failed to screen a single chemical more than 10 years after the program was launched.

Health and environmental advocates pounced on the GAO's findings as proof that the EPA has been shirking its responsibilities for years.

"This just shows that the EPA is not any better able to protect Americans from risky chemicals than FEMA was to save New Orleans or the SEC was to cope with the financial collapse," said John Peterson Myers, a scientist and author who has been writing about chemical risks to human health for more than three decades.

For the EPA to be compared to the collapsed financial markets dramatically underscores the need for a complete overhaul of the regulation of toxic chemicals, said Richard Wiles, executive director of Environmental Working Group, a health watchdog organization based in Washington, D.C.

"The EPA joins the hall of shame of failed government programs," Wiles said.

The EPA is at high risk for waste, fraud, abuse and mismanagement and needs a broad-based transformation, the auditors found. "The EPA lacks adequate scientific information on the toxicity of many chemicals that may be found in the environment—as well as on tens of thousands of chemicals used commercially in the United States," the GAO report said. "EPA's inadequate progress in assessing toxic chemicals significantly limits the agency's ability to fulfill its mission of protecting human health and the environment."

The EPA's ability to protect public health and the environment depends on credible and timely assessments of the risks posed by toxic chemicals, the GAO found. Its Integrated Risk Information System, which contains assessments of more than 500 toxic chemicals, "is at serious risk of becoming obsolete because the EPA has been unable to keep its existing assessments current or to complete assessments of important chemicals of concern."

The EPA urgently needs to streamline and increase the transparency of this assessment process, the report says. "Overall, the EPA has finished only nine assessments in the past three years," the report found. "At the end of 2007, most of the 70 ongoing assessments had been under way for more than five years."

The EPA needs additional authority to that provided in the Toxic Substances Control Act to obtain health and safety information from the chemical industry, the GAO auditors found. "They need to shift more of the burden to chemical companies to demonstrate the safety of their products," the report found.

Strengthening the EPA is one of the GAO's three most urgent priorities for the Obama administration. The GAO also called for overhauling the nation's financial regulatory system, whose inattention helped trigger the global financial crisis, and improving the Food and Drug Administration's ability to protect the public from unsafe or ineffective drugs and other medical products.

The list is updated every two years and released at the start of each new Congress to help in setting oversight agendas. Recent Congresses and administrations have been particularly alert to GAO's High-Risk List and have used its findings to help tailor agency-specific solutions as well as broader initiatives across government.



Excerpted from *The Independent (UK)*, January 19, 2009

## RIVER POLLUTANTS LINKED TO MALE INFERTILITY

By Steve Connor, Science Editor

The rise in male infertility and the decline in human sperm counts could be linked with chemicals in the environment known as anti-androgens which block the action of the male sex-hormone testosterone, a study has found.

Scientists have identified a group of river pollutants that are able to stop testosterone from working. These anti-androgens have been linked with the feminisation of fish in British rivers and could be affecting the development of male reproductive organs in humans, it found.

The study has established a link between anti-androgens released into rivers from sewage outflows and abnormalities in wild fish where males develop female reproductive organs. It is the first time that anti-androgens and hermaphrodite fish have been linked in this way.

Until now it was thought another class of chemicals, which mimic the effect of the female sex-hormone oestrogen, were responsible for sex-changed fish. However the latest study indicates that the cause may be the result of a rather more complicated interaction taking place between different pollutants.

Dr Susan Jobling of Brunel University, is one of the authors of the study carried out with colleagues from Exeter and Reading universities and the Centre of Ecology and Hydrology. She said: "We have identified a new group of chemicals in our study on fish, but we do not know where they are coming from or what they are. We've only been able to measure their testosterone-blocking potential."

For the study, published in the journal *Environmental Health Perspectives*, the scientists analysed anti-androgenic activity in samples of river water taken near 30 sewage outflows. They

were able to demonstrate statistically that this activity could be linked with hermaphrodite fish found in the same rivers.

Dr Jobling said that there are several chemicals in widely-used pharmaceuticals and pesticides that are known to have anti-androgenic activity. They included flutamide and cyproterone, used to treat prostate cancer, and several compounds found in agricultural pesticides.

The scientists detected relatively high levels of anti-androgenic chemicals near sewage outflows – suggesting they came from domestic sources. One possibility is that drugs excreted from the body may end up in rivers. However the scientists have not discounted the idea that anti-androgens may also be seeping into rivers as run-off from agricultural land.

Scientists first detected sex-change fish in British rivers more than 20 years ago. During the same period, medical researchers found that human sperm counts have been falling in several countries over a period of 30 years or more. This has been matched by a corresponding rise in other male reproductive problems, such as the congenital condition testicular dysgenesis, which can affect fertility.



Excerpted from *Beyond Pesticides Daily News*, May. 8, 2009

## INTERNATIONAL AGENCIES TO REDUCE DDT USE IN MALARIA CONTROL

The United Nations Environment Programme (UNEP) and the World Health Organization (WHO), in partnership with the Global Environment Facility, have announced a renewed international effort to combat malaria with an incremental reduction of reliance on the synthetic pesticide DDT, *Environmental News Service* reported.

As recently as two years ago, WHO was criticized for promoting DDT as the answer for malaria control in Africa, leading activists to call for increased use of alternatives. DDT has been recognized as a significant human and environmental health risk, including increased risk of breast cancer a wealth of other health concerns, and have built up in waterways and, in particular, the arctic.

Now, ten projects, all part of the global program "Demonstrating and Scaling-up of sustainable Alternatives to DDT in Vector Management," involving some 40 countries in Africa, the Eastern Mediterranean and Central Asia, are set to test non-chemical methods ranging from eliminating potential mosquito breeding sites and securing homes with mesh screens to deploying mosquito-repellent trees and fish that eat mosquito larvae.

The new projects follow a successful demonstration of alternatives to DDT in Mexico and Central America. There, pesticide-

free techniques and management regimes have helped cut cases of malaria by over 60 percent.

The success of the five year-long pilot indicates that sustainable alternatives to DDT are emerging as cost effective solutions that may be applicable regionally and globally. The Integrated Vector Management (IVM) strategy promoted by the World Health Organization provides the framework to include these measures in combinations of interventions adapted to differing local circumstances. The initiatives come amid long-standing and growing concern over the use of DDT and evidence that in many countries there is increasing mosquito resistance to the pesticide.

However, concern over DDT is matched by concern over the global malaria burden in which close to 250 million cases a year result in over 880,000 deaths. Thus any reduction in the use of DDT or other residual pesticides must ensure the level of transmission interruption is, at least, maintained.

The international community has, under the Stockholm Convention, agreed to ban a 'dirty dozen' of persistent organic pollutants including, ultimately, DDT on environmental and health grounds. However, a specific and limited exemption was made for the use of DDT to control malaria, because it was recognized that in some situations adequate alternative control methods were not currently available.

The aim of the new projects, a major initiative of the Global Environment Facility with close to \$40 million funding, being spearheaded by WHO and the UNEP, is to achieve a 30% cut in the application of DDT worldwide by 2014 and its total phase-out by the early 2020s, if not sooner, while staying on track to meet the malaria targets set by WHO.

Achim Steiner, UN Under-Secretary General and UNEP Executive Director which hosts the secretariat of the Stockholm Convention, said, "The new projects underline the determination of the international community to combat malaria while realizing a low, indeed zero DDT world."

"Today we are calling time on a chemical rooted in the scientific knowledge and simplistic options of a previous age. In doing so, innovative solutions are being catalyzed and sustainable choices brought forward that meet the genuine health and environmental aspirations of a 21st century society".

"WHO faces a double challenge—a commitment to the goal of drastically and sustainably reducing the burden of vector-borne diseases, in particular malaria, and at the same time a commitment to the goal of reducing reliance on DDT in disease vector control", said Dr. Margaret Chan, WHO Director-General.

WHO sees these projects in the context of IVM which it promotes as the approach of choice to control transmission of malaria and other vector-borne diseases. A key element of IVM is a solid evidence base for the effectiveness of combinations of locally-adapted, cost-effective and sustainable vector-control methods. This approach will facilitate sustainable transition away from DDT.

Monique Barbut, Chief Executive Officer and Chairperson of the Global Environment Facility (GEF), the financial arm of the convention and which is funding over half of the initiative, said, "The GEF is investing in these projects to take decisive action toward ridding the world of dangerous chemicals now and forever. The dividends from these investments will mean a cleaner, safer and sustainable environment for future generations."



## 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.dhmh.md.gov/eh](http://www.dhmh.md.gov/eh) then click on Report an Exposure**

### 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](mailto: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 organochlorines, 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](mailto:millertuck@dhmh.state.md.us).

### DIAGNOSING PESTICIDE INJURY

For information on taking a pesticide exposure history go to: [www.mdpestnet.org/history.pdf](http://www.mdpestnet.org/history.pdf).

For a brief overview of diagnosing and treating pesticide injuries go to: [www.mdpestnet.org/diagnostreatmnt.pdf](http://www.mdpestnet.org/diagnostreatmnt.pdf), and [www.mdpestnet.org/diagnostreatchart.pdf](http://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](http://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](http://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: "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 Water Action-MD, Environment Maryland, Federated Garden Clubs of MD, Leukemia and Lymphoma Society-MD Chapter, MaryPIRG, MD Organic Food and Farmers Association, MCS Referral and Resources, MD Nurses Association, MD Association of School Health Nurses, MD Interfaith Coalition for the Environment, MD League of Women Voters, MD League of Conservation Voters, MD State Teachers Association, MD PTA, Beyond Pesticides, Sierra Club-MD Chapter.



## MPN HEALTH CARE PROVIDER COMMITTEE MEMBERS

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

**Ruth Berlin, L.C.S.W.-C**, has been a practicing psychotherapist and a teacher in the field for the past 37 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 47 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.



*“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**  
MARYLAND PESTICIDE NETWORK

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## MARYLAND PESTICIDE NETWORK PUBLICATIONS FOR HEALTHCARE PROVIDERS

SEE INSERT ORDER FORM

### **Pesticide-Related Illness: Identifying the Threat, Treating the Problem DVD Course for Health Care Providers**

This course was originally a one-day symposium co-sponsored by MedChi, the Maryland State Medical Society and MPN and held at the Johns Hopkins Bloomberg School of Public Health in April 2006. It 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.

The symposium 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.

### **Pesticides and Public Health: A Kit for Health Care Providers**

This user-friendly publication includes eight inserts that address diagnosing, treating, reporting and preventing acute pesticide injuries. The kit also provides information on pesticides and respiratory disease, neurological, behavioral, reproductive and behavioral effects, cancer and the immune system.

### **Pesticides and Public Health: Critical Literature on Human Health Issue #1 (2005), Issue #2 (2007), Issue #3 (2009)**

The Journal reviews peer-reviewed epidemiological studies relevant to health care providers and public health professionals. It also includes news items on pesticides and health helpful to practitioners, including information on the DHMH regulations mandating reporting of pesticide injury.