Pesticide Exposures and Risk Bibliography

(214 References, 82 pages)

Adgate,J.L., D.B.Barr, C.A.Clayton, L.E.Eberly, N.C.Freeman, P.J.Lioy, L.L.Needham, E.D.Pellizzari, J.J.Quackenboss, A.Roy, and K.Sexton. 2001. "Measurement of children's exposure to pesticides: analysis of urinary metabolite levels in a probability-based sample." Environ.Health Perspect. 109:583-590.
Abstract: The Minnesota Children's Pesticide Exposure Study is a probability-based sample of 102 children 3-13 years old who were monitored for commonly used pesticides. During the summer of 1997, first-morning-void urine samples (1-3 per child) were obtained for 88% of study children and analyzed for metabolites of insecticides and herbicides: carbamates and related compounds (1-NAP), atrazine (AM), malathion (MDA), and chlorpyrifos and related compounds (TCPy). TCPy was present in 93% of the samples, whereas 1-NAP, MDA, and AM were detected in 45%, 37%, and 2% of samples, respectively. Measured intrachild means ranged from 1.4 microg/L for MDA to 9.2 microg/L for TCPy, and there was considerable intrachild variability. For children providing three urine samples, geometric mean TCPy levels were greater than the detection limit in 98% of the samples, and nearly half the children had geometric mean 1-NAP and MDA levels greater than the detection limit. Interchild variability was significantly greater than intrachild variability for 1-NAP ($p = 0.0037$) and TCPy ($p < 0.0001$). The four metabolites measured were not correlated within urine samples, and children's metabolite levels did not vary systematically by sex, age, race, household income, or putative household pesticide use. On a log scale, mean TCPy levels were significantly higher in urban than in nonurban children (7.2 vs. 4.7 microg/L; $p = 0.036$). Weighted population mean concentrations were 3.9 [standard error (SE) = 0.7; 95% confidence interval (CI), 2.5, 5.3] microg/L for 1-NAP, 1.7 (SE = 0.3; 95% CI, 1.1, 2.3) microg/L for MDA, and 9.6 (SE = 0.9; 95% CI, 7.8, 11) microg/L for TCPy. The weighted population results estimate the overall mean and variability of metabolite levels for more than 84,000 children in the census tracts sampled. Levels of 1-NAP were lower than reported adult reference range concentrations, whereas TCPy concentrations were substantially higher. Concentrations of MDA were detected more frequently and found at higher levels in children than in a recent nonprobability-based sample of adults. Overall, Minnesota children's TCPy and MDA levels were higher than in recent population-based studies of adults in the United States, but the relative magnitude of intraindividual variability was similar for adults and children

Agricultural Market Service. Pesticide Data Program Annual Summary Calendar Year 2000. 2002. United States Department of Agriculture, Washington, D.C.
Ref Type: Report

Agricultural Market Service. Pesticide Data Program Annual Summary Calendar Year 2001. 2003. Washington, D.C., U.S. Department of Agriculture.
Ref Type: Generic

Agricultural Market Service. Pesticide Data Program Annual Summary Calendar Year 2002. 2004. Washington, D.C., U.S. Department of Agriculture.
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Alavanja,M.C., D.P.Sandler, S.B.McMaster, S.H.Zahm, C.J.McDonnell, C.F.Lynch, M.Pennybacker, N.Rothman, M.Dosemeci, A.E.Bond, and A.Blair. 1996. "The Agricultural Health Study." Environ.Health Perspect. 104:362-369.
Abstract: The Agricultural Health Study, a large prospective cohort study has been initiated in North Carolina and Iowa. The objectives of this study are to: 1) identify and quantify cancer risks among men, women, whites, and minorities associated with direct exposure to pesticides and other agricultural agents; 2) evaluate noncancer health risks including neurotoxicity reproductive effects, immunologic effects, nonmalignant respiratory disease, kidney disease, and growth and development among children; 3) evaluate disease risks among spouses and children of farmers that may arise from direct contact with pesticides and agricultural chemicals used in the home lawns and gardens, and from indirect contact, such as spray drift, laundering work clothes, or contaminated food or water; 4) assess current and past occupational and nonoccupational agricultural exposures using periodic interviews and environmental and biologic monitoring; 5) study the relationship between agricultural exposures, biomarkers of exposure, biologic effect, and genetic susceptibility factors relevant to carcinogenesis; and 6) identify and quantify cancer and other disease risks associated with lifestyle factors such as diet, cooking practices, physical activity, smoking and alcohol consumption, and hair dye use. In the first year of a 3-year enrollment period, 26,235 people have been enrolled in the study, including 19,776 registered pesticide applicators and 6,459 spouses of registered farmer applicators. It is estimated that when the total cohort is assembled in 1997 it will include approximately 75,000 adult study subjects. Farmers, the largest group of registered pesticide applicators comprise 77% of the target population enrolled in the study. This experience compares favorably with enrollment rates of previous prospective studies

Allan,B.B., R.Brant, J.E.Seidel, and J.F.Jarrell. 1997. "Declining sex ratios in Canada." Canadian Medical Association Journal. 156:37-41.
Abstract: OBJECTIVE: To examine the trends in the proportion of annual live births that were male in Canada and to compare the trends with those in the United States. DESIGN: Analysis of census data. SETTING: Canada as a whole and 4 main regions (West, Ontario, Quebec and Atlantic). SUBJECTS: All live births from 1930 to 1990. OUTCOME MEASURES: Sex ratio (expressed as the proportion of total live births that were male [male proportion]) overall and by region. RESULTS: The male proportion in Canada decreased significantly after 1970 ($p < 0.001$); this represented a cumulative loss of 2.2 male births per 1000 live births from 1970 to 1990. Although a decrease was observed in all four regions studied, only that in the Atlantic region was significant ($p < 0.001$), representing a cumulative loss of 5.6 male births per 1000 live births from 1970 to 1990. A significant decrease in the male proportion was also observed in the United

States from 1970 to 1990 ($p < 0.001$), although to a lesser degree than that observed in Canada, and represented a cumulative loss of 1.0 male births per 1000 live births. CONCLUSIONS: The decreased sex ratio in Canada adds to the growing debate over changes in biological markers and their potential causes. In addition, the study illustrates the potential use of the sex ratio as a widely available, unambiguous measure of the reproductive health of large populations.

Amr,M.M., Z.S.Halim, and S.S.Moussa. 1997. "Psychiatric disorders among Egyptian pesticide applicators and formulators." Environ.Res. 73:193-199.
Abstract: Two hundred eight pesticide formulators, 172 pesticide applicators, and 223 control subjects (72 from an urban region matching the pesticide formulators and 151 from a rural area matching the pesticide applicators) underwent psychiatric assessment. The study aimed to screen for psychiatric morbidity using a standardized screening tool, the General Health Questionnaire, and a widely recognized system of diagnosis and classification, the revised third edition of the Diagnostic and Statistical Manual of Psychiatric Disorders (DSM-III-R). Significantly higher frequencies of psychiatric disorders were found in the exposed groups. The predominant diagnosis was depressive neurosis; the most frequent symptoms were irritability and erectile dysfunction. Theoretical and practical implications of these findings are discussed

Anway,M.D., A.S.Cupp, M.Uzumcu, and M.K.Skinner. 2005. "Epigenetic transgenerational actions of endocrine disruptors and male fertility." Science. 308:1466-1469.
Abstract: Transgenerational effects of environmental toxins require either a chromosomal or epigenetic alteration in the germ line. Transient exposure of a gestating female rat during the period of gonadal sex determination to the endocrine disruptors vinclozolin (an antiandrogenic compound) or methoxychlor (an estrogenic compound) induced an adult phenotype in the F1 generation of decreased spermatogenic capacity (cell number and viability) and increased incidence of male infertility. These effects were transferred through the male germ line to nearly all males of all subsequent generations examined (that is, F1 to F4). The effects on reproduction correlate with altered DNA methylation patterns in the germ line. The ability of an environmental factor (for example, endocrine disruptor) to reprogram the germ line and to promote a transgenerational disease state has significant implications for evolutionary biology and disease etiology

Arbuckle,T.E. and L.E.Sever. 1998. "Pesticide exposures and fetal death: a review of the epidemiologic literature." Crit Rev Toxicol. 28:229-270.
Abstract: Despite considerable concern regarding the effects on reproductive outcome of exposures to pesticides, convincing evidence for the developmental toxicity of occupational and environmental pesticide exposure in humans is lacking. In this comprehensive review of the English language epidemiologic literature, we summarize studies that have examined potential associations between fetal deaths (both spontaneous abortions and stillbirths) and specific pesticides, as well as maternal and paternal employment in occupations with potential for exposure. While many of the epidemiologic studies to date suffer from methodologic problems, the data are suggestive of increased risks of fetal deaths associated with pesticides in general and maternal

employment in the agricultural industry. There is a clear need for epidemiologic research that focuses on specific pesticide products or chemical families, with improved exposure assessment. The potential role of solvents in developmental toxicity associated with pesticide use by both males and females should also be considered

Arbuckle,T.E., S.M.Schrader, D.Cole, J.C.Hall, C.M.Bancej, L.A.Turner, and P.Claman. 1999. "2,4-Dichlorophenoxyacetic acid residues in semen of Ontario farmers." Reproductive Toxicology. 13:421-429.
Abstract: Although paternal exposures to environmental toxicants probably play a role in adverse pregnancy outcomes, few data are available on the extent of this exposure. One semen and two 24-h urine samples were collected from 97 Ontario farmers who had recently used the phenoxy herbicides 2,4-D (2.4-dichlorophenoxyacetic acid) and/or MCPA ([4- chloro-2-methylphenoxyl acetic acid). Both samples were analyzed for 2,4-D using an immunoassay-based technique. Approximately 50% of the semen samples had detectable levels of 2, 4-D (> or =5.0 pph (ng/mL)). Semen levels of 2.4-D were correlated more closely with the second of the two urine samples. Although several studies have measured 2.4-D in the urine of applicators, this study is the first to attempt to measure 2,4-D levels in semen. As these pesticides can be excreted in the semen, they could be toxic to sperm cells and be transported to the woman and developing embryo/fetus. Further research is needed to understand how pesticide handling practices can affect semen pesticide residues and the relationship between the levels observed and reproductive health.

Arbuckle,T.E., Z.Lin, and L.S.Mery. 2001. "An exploratory analysis of the effect of pesticide exposure on the risk of spontaneous abortion in an Ontario farm population." Environ.Health Perspect. 109:851-857.
Abstract: The toxicity of pesticides on human reproduction is largely unknown--particularly how mixtures of pesticide products might affect fetal toxicity. The Ontario Farm Family Health Study collected data by questionnaire on the identity and timing of pesticide use on the farm, lifestyle factors, and a complete reproductive history from the farm operator and eligible couples living on the farm. A total of 2,110 women provided information on 3,936 pregnancies, including 395 spontaneous abortions. To explore critical windows of exposure and target sites for toxicity, we examined exposures separately for preconception (3 months before and up to month of conception) and postconception (first trimester) windows and for early (< 12 weeks) and late (12-19 weeks) spontaneous abortions. We observed moderate increases in risk of early abortions for preconception exposures to phenoxy acetic acid herbicides [odds ratio (OR) = 1.5; 95% confidence interval (CI), 1.1-2.1], triazines (OR = 1.4; 95% CI, 1.0-2.0), and any herbicide (OR = 1.4; 95% CI, 1.1-1.9). For late abortions, preconception exposure to glyphosate (OR = 1.7; 95% CI, 1.0-2.9), thiocarbamates (OR = 1.8; 95% CI, 1.1-3.0), and the miscellaneous class of pesticides (OR = 1.5; 95% CI, 1.0-2.4) was associated with elevated risks. Postconception exposures were generally associated with late spontaneous abortions. Older maternal age (> 34 years of age) was the strongest risk factor for spontaneous abortions, and we observed several interactions between pesticides in the older age group using Classification and Regression Tree analysis. This study shows that

timing of exposure and restricting analyses to more homogeneous endpoints are important in characterizing the reproductive toxicity of pesticides

Baatrup,E. and M.Junge. 2001. "Antiandrogenic pesticides disrupt sexual characteristics in the adult male guppy Poecilia reticulata." Environ.Health Perspect. 109:1063-1070.
Abstract: Environmental contaminants have been identified as endocrine disruptors through their antiandrogenic activity. Thus, as androgen receptor antagonists, the fungicide vinclozolin and the principal DDT metabolite p,p'-DDE have been demonstrated to induce demasculinization in rats. Whether this is also the case in fish remains to be demonstrated. For a period of 30 days, groups of adult male guppies were exposed to vinclozolin, p,p'-DDE, or the therapeutic antiandrogen flutamide (used as positive control) applied to the fodder at concentrations between 0.1 and 100 microg/g fodder. Subsequently, sexual characteristics of relevance to the male reproductive capacity were measured and compared with untreated control fish. All three chemicals caused profound alterations at increasing levels of biological organization, even in these fully matured males. At the cellular level, the three compounds induced a significant reduction in the number of ejaculated sperm cells. At the organ level, the sexually attractive orange-yellow coloration was reduced in area and discolored, and treated fish also had smaller testes. Further, at the organismal level, computer-aided behavior analyses demonstrated a severe disruption in male courtship behavior. We conclude that this demasculinization is consistent with an antiandrogenic action of vinclozolin and p,p'-DDE and is likely to compromise reproductive capability in this fish

Baker,B.P., C.M.Benbrook, E.Groth, III, and K.L.Benbrook. 2002. "Pesticide residues in conventional, integrated pest management (IPM)-grown and organic foods: insights from three US data sets." Food Addit.Contam. 19:427-446.
Abstract: An analysis of pesticide residue data was performed to describe and quantify differences between organically grown and non-organic fresh fruits and vegetables. Data on residues in foods from three different market categories (conventionally grown, integrated pest management (IPM)-grown/no detectable residues (NDR), and organically grown) were compared using data from three test programmes: The Pesticide Data Program of the US Department of Agriculture; the Marketplace Surveillance Program of the California Department of Pesticide Regulation; and private tests by the Consumers Union, an independent testing organization. Organically grown foods consistently had about one-third as many residues as conventionally grown foods, and about one-half as many residues as found in IPM/NDR samples. Conventionally grown and IPM/NDR samples were also far more likely to contain multiple pesticide residues than were organically grown samples. Comparison of specific residues on specific crops found that residue concentrations in organic samples were consistently lower than in the other two categories, across all three data sets. The IPM/NDR category, based on data from two of the test programmes, had residues higher than those in organic samples but lower than those in conventionally grown foods

Baldi,I., L.Filleul, B.Mohammed-Brahim, C.Fabrigoule, J.F.Dartigues, S.Schwall, J.P.Drevet, R.Salamon, and P.Brochard. 2001. "Neuropsychologic effects of long-term

exposure to pesticides: results from the French Phytoner study." Environ.Health Perspect. 109:839-844.
Abstract: The Phytoner study investigated a possible association between neuropsychologic performances and long-term exposure to pesticides in Bordeaux vineyard workers, most of whom use fungicides. Among the 917 subjects interviewed from February 1997 to August 1998, 528 were directly exposed to pesticides through mixing and/or spraying (mean exposure duration: 22 years), 173 were indirectly exposed through contact with treated plants, and 216 were never exposed. All subjects performed neuropsychologic tests administered at home by trained psychologists. The risk of scoring a low performance on the tests was constantly higher in exposed subjects. When taking into account educational level, age, sex, alcohol consumption, smoking, environmental exposures, and depressive symptoms and when restricting analysis to subgroups, results remained significant for most tests, with odds ratios (OR) exceeding 2. These results point to long-term cognitive effects of low-level exposure to pesticides in occupational conditions. Given the frequency of pesticide use and the potential disabilities resulting from cognitive impairments, further toxicologic and epidemiologic research is needed to confirm these results and assess the impact on public health

Baskin,L.S., K.Himes, and T.Colborn. 2001. "Hypospadias and endocrine disruption: Is there a connection?" Environmental Health Perspectives. 109:1175-1183.
Abstract: Hypospadias is one of the most common congenital anomalies in the United States, occurring in approximately 1 in 250 newborns or roughly 1 in 125 live male births. It is the result of arrested development of the urethra, foreskin, and ventral surface of the penis where the urethral opening may be anywhere along the shaft, within the scrotum, or in the perineum. The only treatment is surgery. Thus, prevention is imperative. To accomplish this, it is necessary to determine the etiology of hypospadias, the majority of which have been classified as idiopathic. In this paper we briefly describe the normal development of the male external genitalia and review the prevalence, etiology, risk factors, and epidemiology of hypospadias. The majority of hypospadias are believed to have a multifactorial etiology, although a small percentage do result from single gene mutations. Recent findings suggest that some hypospadias could be the result of disrupted gene expression. Discoveries about the antiandrogenic mechanisms of action of some contemporary-use chemicals have provided new knowledge about the organization and development of the urogenital system and may provide additional insight into the etiology of hypospadias and direction for prevention. Key words: antiandrogens, differentiation, external genitalia, gene expression, urogenital development.

Bell,E.M., I.Hertz-Picciotto, and J.J.Beaumont. 2001. "Case-cohort analysis of agricultural pesticide applications near maternal residence and selected causes of fetal death." American Journal of Epidemiology. 154:702-710.
Abstract: The potential association between fetal death and residential proximity to agricultural pesticide applications was examined in 10 California counties for 1984. A case-cohort analysis utilized 319 cases of selected causes of fetal death other than congenital anomalies and 611 non-cases. A statewide database of all applications of restricted pesticides was linked to maternal address; residential proximity within 1 mile

(1.6 km) provided a surrogate for daily exposure. Pesticides were grouped by chemical class and mechanism of acetylcholinesterase inhibition. Multivariate proportional hazards models using time- dependent exposure variables were fit for each pesticide grouping. Overall, pesticides showed no strong association with fetal death. Slightly elevated risks were observed for women who resided near applications of halogenated hydrocarbons, carbamates, estrogenic pesticides, and carbamate acetylcholinesterase inhibitors during the second trimester, with hazard ratios of 1.3 (95% confidence interval (CI): 1.0, 1.8), 1.3 (95% CI: 1.0, 1.8), 1.4 (95% CI: 0.8, 2.5), and 1.3 (95% CI: 1.0, 1.8), respectively. In a month-by-month analysis, elevated risks were observed when exposure occurred during gestational months 3 and 4 for carbamates and carbamate inhibitors and during months 4 and 5 for halogenated hydrocarbons. Since previous studies have relied on personal recall of exposure, major strengths of this study were the objective source for environmental pesticide exposure assessment and the use of data on the timing of exposure.

Bell,E.M., I.Hertz-Picciotto, and J.J.Beaumont. 2001. "A case-control study of pesticides and fetal death due to congenital anomalies." Epidemiology. 12:148-156.
Abstract: We examined the association between late fetal death due to congenital anomalies (73 cases, 611 controls) and maternal residential proximity to pesticide applications in ten California counties. A statewide database of all applications of restricted pesticides was linked to maternal address to determine daily exposure status. We examined five pesticide chemical classes. The odds ratios from logistic regression models, adjusted for maternal age and county, showed a consistent pattern with respect to timing of exposure; the largest risks for fetal death due to congenital anomalies were from pesticide exposure during the 3rd-8th weeks of pregnancy. For exposure either in the square mile of the maternal residence or in one of the adjacent 8 square miles, odds ratios ranged from 1.4 (95% confidence interval = 0.8-2.4) for phosphates, carbamates, and endocrine disruptors to 2.2 (95% confidence interval = 1.3-3.9) for halogenated hydrocarbons. Similar odds ratios were observed when a more restrictive definition of nonexposure (not exposed to any of the five pesticide classes during the 3rd-8th weeks of pregnancy) was used. The odds ratios for all pesticide classes increased when exposure occurred within the same square mile of maternal residence.

Benbrook,C., E.Groth, J.M.Halloran, M.K.Hansen, and S.Marquardt. Pest Management at the Crossroads. 1-272. 1996. Yonkers, New York, Consumers Union.
Ref Type: Generic

Benbrook,C. The Effectiveness of Farm and Private Sector Initiatives to Reduce Children's Pesticide Exposures. Presented at the 2006 annual meeting of the AAAS . 2006. The Organic Center.
Ref Type: Generic

Benbrook,C.M. Impacts of Genetically Engineered Crops on Pesticide Use in the United States: The First Eight Years. 3 A.D.
Ref Type: Report

Benbrook,C.M. Performance criteria for IPM: measuring IPM results. henk, M. Kogan M. IPM in Oregon: Achievements and Future Directions, Special Report 1020 , 19-27. 2000. Corvallis: Integrated Plant Protection Center, Oregon State University Extension Service.
Ref Type: Statute

Benbrook,C.M. Developing a pesticide risk assessment tool to monitor progress in reducing reliance on high-risk pesticides. Sexson, D. L., Wyman, J. A., Stevenson, W. R., Wallendal, J., Lynch, S., Diercks, S., Van Haren, R., and Granadino, C. A. American Journal of Potato Research 79, 183-199. 2000.
Ref Type: Generic

Benbrook,C.M. 2002. "Organochlorine residues pose surprisingly high dietary risks." J Epidemiol Community Health. 56:822-823.
Abstract: All US government pesticide residue datasets show that persistent organochlorine (OC) insecticide residues are surprisingly common in certain foods despite being off the market for over 20 years. Residues of dieldrin, in particular, pose substantial risks in certain root crops. About 60% of the samples of organic vegetables found to contain pesticides are contaminated with OCs. Government regulators, organic certifiers, and the food industry will face growing pressure to develop methods to identify OC contaminated fields and avoid production of crops prone to assimilating OC residues in harvested foodstuffs

Benbrook,C.M., D.L.Sexson, J.A.Wyman, W.R.Stevenson, S.Lynch, J.Wallendal, S.Dierks, R.Van Haren, and C.A.Granadino. 2002. "Developing a pesticide risk assessment tool to monitor progress in reducing reliance on high-risk pesticides." American Journal of Potato Research. 79:183-199.

Benbrook,C.M. Genetically Engineered Crops and Pesticide Use in the United States: The First Nine Years. Technical Paper Number 7. 2005. Ag BioTech InfoNet.
Ref Type: Generic

Benbrook,C.M. Tracking the Impacts of the FQPA on Pesticide Dietary Risks -- A Preliminary Assessment. 2005. Consultant Report to the EPA Office of Inspector General.
Ref Type: Generic

Benbrook,C.M. Minimizing Pesticide Dietary Exposure Through the Consumption of Organic Food. State of Science Review . 2006. Foster, Rhode Island, The Organic Center.
Ref Type: Generic

Birnbaum,L.S. and S.E.Fenton. 2003. "Cancer and developmental exposure to endocrine disruptors." Environ.Health Perspect. 111:389-394.
Abstract: Developing organisms have increased susceptibility to cancer if they are exposed to environmental toxicants during rapid growth and differentiation. Human

studies have demonstrated clear increases in cancer after prenatal exposure to ionizing radiation, and there is suggestive evidence that brain tumors and leukemia are associated with parental exposures to chemicals. Animal experiments have demonstrated increased tumor formation induced by prenatal or neonatal exposure to a variety of chemicals, including direct-acting carcinogens and drugs. Recently, natural estrogens have been classified as known human carcinogens. Prenatal exposure to natural and synthetic estrogens is associated with increases in breast and vaginal tumors in humans as well as uterine tumors in animals. Synthetic halogenated chemicals increase liver tumors after early life-stage exposure. Recently, a prototypical endocrine-disrupting compound, 2,3,7,8-tetrachlorodibenzo-p-dioxin, has been shown to be a developmental toxicant of the mammary gland in rodents. Dioxin alters multiple endocrine systems, and its effects on the developing breast involve delayed proliferation and differentiation of the mammary gland, as well as an elongation of the window of sensitivity to potential carcinogens. Implications of these new findings suggest that causes of endocrine-related cancers or susceptibility to cancer may be a result of developmental exposures rather than exposures existing at or near the time of tumor detection

Blatter,B.M., N.Roeleveld, G.A.Zielhuis, F.J.M.Gabreels, and A.L.M.Verbeek. 1996. "Maternal occupational exposure during pregnancy and the risk of spina bifida." Occupational & Environmental Medicine. 53:80-86.
Abstract: Objectives-A carried between exposure of the mother. Methods-The cases were children with spina bifida aperta born between 1980 and 1992 from nine hospitals in the Netherlands. The controls were children born healthy in the same period as the cases, from hospitals and from the general population. Data collection was carried out in two steps. Firstly, postal questionnaires were sent to all the parents of cases and controls to gather information on occupations and potential confounders. In the second phase of the study, information on specific exposures was collected by means of job and task specific personal interviews. Interviews were performed with 55 case mothers and 66 control mothers who had occupations with a potential for chemical or physical exposure. Those exposures were assumed to be negligible for-for example, teachers and secretaries, so personal interviews were not indicated for these women. Information was collected on specific tasks in the period just after conception, and on the associated use of chemical or physical agents, frequency of exposure, and use of protective equipment. Results-The analyses showed an increased working in agricultural occupations (OR = 3 . 4, CI:1 . 3-9 . 0), and, although less distinct, for cleaning women (OR = 1 . 7, CI:0 . 9-3 . 4). Only a few women seemed to be occupationally exposed to chemical or physical agents. No differences in occurrence of specific exposures could be detected between cases and controls. Besides, no differences were seen in pesticide or disinfectant exposure among case and control mothers in agricultural occupations. Conclusions-Occupational exposures of the mother during pregnancy were infrequent and did not seem to play an important part in the aetiology of spina bifida in this study. The association found between spina bifida and maternal agricultural occupations could not be explained by the use of pesticides by the mother or by any other occupational exposure.

Bonde,J.P., T.Kold Jensen, S.Brixen Larsen, A.Abell, T.Scheike, N.H.Hjollund, H.A.Kolstad, E.Ernst, A.Giwercman, N.E.Skakkebaek, N.Keiding, and J.Olsen. 1998.

"Year of birth and sperm count in 10 Danish occupational studies." Scandinavian Journal of Work & Environmental Health. 24:407-13.
Abstract: OBJECTIVES: Several reports indicate a secular decline of human sperm counts. It is still not known if these findings are artifacts related to shortcomings in the data and applied methodologies. Even less is known about possible mechanisms, but it has been proposed that potential changes may be related to disruption of the hormonal regulation of testicular development in prenatal life. The objective of this study was to examine whether sperm count was related to year of birth. METHODS: An analysis was made of the sperm count of 1196 men participating in 10 cross-sectional occupational sperm studies in 3 regions of Denmark from 1986 through 1995. RESULTS: The median sperm concentration was 63 million per milliliter for men born in 1937-1949 and 52 million per milliliter for men born in 1970 or later, and the median total sperm was 206 million and 117 million, respectively. The inverse relationship between sperm concentration and year of birth was statistically significant even after adjustment for duration of sexual abstinence, season of the year, and study population. However, bias because of differential participation related to age and fertility or lack of comparability across the populations cannot be ruled out. CONCLUSIONS: The apparent decline of sperm count with increasing year of birth is compatible with the hypothesis of a common risk factor for male reproductive health operating in prenatal life or early childhood, but the evidence is circumstantial. Age-related selection bias is an alternative and perhaps not a less likely explanation.

Bordeleau,G., I.Myers-Smith, M.Midak, and A.Szeremeta. Food Quality: A comparison of organic and conventioanl fruits and vegetables. 2002.
Ref Type: Video Recording

Bradman,A., D.B.Barr, B.G.Claus Henn, T.Drumheller, C.Curry, and B.Eskenazi. 2003. "Measurement of pesticides and other toxicants in amniotic fluid as a potential biomarker of prenatal exposure: a validation study." Environ.Health Perspect. 111:1779-1782.

Abstract: Prenatal pesticide exposures may adversely affect children's health. However, exposure and health research is hampered by the lack of reliable fetal exposure data. No studies have been published that report measurements of commonly used nonpersistent pesticides in human amniotic fluid, although recent studies of pesticides in urine from pregnant women and in meconium indicate that fetuses are exposed to these chemicals. Amniotic fluid collected during amniocentesis is the only medium available to characterize direct fetal exposures early in pregnancy (approximately 18 weeks of gestation). As a first step in validating this exposure biomarker, we collected 100 amniotic fluid samples slated for disposal and evaluated analytical methods to measure organophosphate and carbamate pesticides and metabolites, synthetic pyrethroid metabolites, herbicides, and chlorinated phenolic compounds. The following six phenols were detected (detection frequency): 1- and 2-naphthol (70%), 2,5-dichlorophenol (55%), carbofuranphenol (5%), ortho-phenylphenol (30%), and pentachlorophenol (15%), with geometric mean concentrations of 0.72, 0.39, 0.12, 0.13, and 0.23 microg/L, respectively, for positive values. The organophosphate metabolites diethylphosphate and dimethylphosphate were detected in two (10%) samples, and dimethylthiophosphate was

detected in one (5%) sample, with geometric mean concentrations of 0.31, 0.32, and 0.43 microg/L, respectively, for positive values. These levels are low compared with levels reported in urine, blood, and meconium in other studies, but indicate direct exposures to the young fetus, possibly during critical periods of development. Results of this pilot study suggest that amniotic fluid offers a unique opportunity to investigate fetal exposures and health risks

Brien,S.E., J.P.Heaton, W.J.Racz, and M.A.Adams. 2000. "Effects of an environmental anti-androgen on erectile function in an animal penile erection model." J.Urol. 163:1315-1321.
Abstract: PURPOSE: Erectile function is testosterone dependent. For example, interference with either the levels or receptor binding of this steroid hormone may induce erectile dysfunction. Several environmental contaminants can interfere with the actions of endogenous hormones and have been termed 'endocrine disrupters.' p,p-DDE, a prominent and persistent metabolite of the insecticide DDT, has been shown to be an androgen receptor antagonist. The objective was to determine whether endocrine disrupters, as exemplified by p,p-DDE, are factors in the etiology of erectile dysfunction. MATERIALS AND METHODS: Using the established rat model of apomorphine-induced (80 microg./kg, s.c.) erections we assessed the dose-response effects of p,p-DDE in comparison to the known androgen receptor antagonist flutamide in acute (0.5 to 12 hours) and short-term (up to 8 weeks) experiments in both intact (Study 1) and castrated (Study 2) rats. As a follow up (Study 3), castrated rats treated with p,p-DDE were given increasing doses of testosterone (0.48 to 2.4 mg./kg., i.p.), eight weeks after p,p-DDE administration, to assess reversibility of p,p-DDE effect. RESULTS: A single dose of flutamide (50 mg./kg., i.p.) was found to significantly decrease apomorphine-induced erections to less than 50% over 12 hours following flutamide administration with recovery of erectile response within 48 hours. In comparison, a single dose of p,p-DDE (500 mg./kg., i.p.) decreased apomorphine-induced erections for at least two weeks (1.15+/-0.3 versus 2.5+/-1.1). Castration significantly decreased apomorphine-induced erections to approximately 0.5 erections/30 minutes. Flutamide (50 mg./kg.; i.p.) or p,p-DDE (50 mg./kg.; i.p.) did not further suppress the apomorphine erections in castrated rats. Testosterone supplementation (480 microg./kg; s.c.) in vehicle treated castrated rats recovered erectile response to pre-castrated levels, whereas p,p-DDE treated castrated rats required 4 times the dose of testosterone (2 mg./kg.; s.c.) given to vehicle treated rats to recover erections. CONCLUSIONS: The endocrine disrupter p,p-DDE can markedly interfere with erectile function and demonstrates persistence after a single dose. This supports our novel concept that environmental hormones may cause erectile dysfunction

Brien,S.E., C.Smallegange, W.T.Gofton, J.P.Heaton, and M.A.Adams. 2002. "Development of a rat model of sexual performance anxiety: effect of behavioural and pharmacological hyperadrenergic stimulation on APO-induced erections." Int.J.Impot.Res. 14:107-115.
Abstract: As part of the multifactorial nature of erectile dysfunction, anxiety associated with sexual performance (SPA) remains a major contributing factor to its progression. In fact, the heightened sympathetic activity associated with sexual performance anxiety may be a key early component of this disruption of normal erectile responses. We are not

aware that any animal models have been developed to assess this phenomenon. Using apomorphine (APO, 80 microg/kg s.c.)-induced erections in rats we characterised the effects of behavioural or pharmacological hyperadrenergic stimulation (that is, anxiety) on erections and hemodynamics. We developed an experimental SPA paradigm by exposing male rats to the stress of being observed by a larger, older male rat placed in close proximity to test rats during APO testing. In a separate group, adrenergic stress was simulated using a sympathomimetic, methoxamine (MXA) given prior to APO testing. In a third group, the changes in circulatory parameters (mean arterial pressure, heart rate) were determined following instrumentation with radiotelemetric transducers for each scenario. APO-induced erections were significantly lower in both the behavioural (1.25+/-0.8) and pharmacological (0.33+/-0.5) stressor paradigms compared to controls (2.81+/-0.9). Further, erections in MXA-treated rats were significantly lower than in the observed scenario. Despite the differences in erections hemodynamic assessments showed no differences in MAP or HR changes between the different experimental conditions. Thus, both the behavioural and pharmacological paradigms of SPA decreased erections, but did not affect the circulation. This suggests that the level of hyperadrenergic input required to induce erectile dysfunction can be subtle, and target only erectogenic pathways

Brock,J.W., L.J.Melnyk, S.P.Caudill, L.L.Needham, and A.E.Bond. 1998. "Serum levels of several organochlorine pesticides in farmers correspond with dietary exposure and local use history." Toxicology & Industrial Health. 14:275-289.
Abstract: In response to reported increased cancer risks among farmers, the Agricultural Health Study (AHS) was designed to examine health outcomes and environmental exposures among farm families in the United States. In the pilot phase of the AHS, food, beverage, air, dermal, dust, surface wipe, and biological specimens (blood and urine) were collected and analyzed for six farm families in two states (IA and NC). In addition, questionnaires were administered to examine previous pesticide use. This paper reports the organochlorine pesticide results of the serum and dietary analyses as well as questionnaire results from the pilot exposure study of farmers and their families. Note, no organochlorine pesticides were reported as currently being applied to the study farms. In all human serum samples examined, typical U.S. population levels were found for the majority of the pesticides. In addition, human serum levels of organochlorine pesticides showed no significant daily or seasonal variation. However, serum trans-nonachlor levels were found to be higher in people living on the two farms in North Carolina than in people living on the four farms in Iowa ($p < 0.05$). Further, unusually high dieldrin levels were found in serum samples from a farmer and spouse living on an Iowa farm, and these levels were significantly higher than those of people living on the other farms ($p < 0.05$). Dieldrin was persistent in the foods consumed on the same Iowa farm where family members showed elevated serum levels. In addition, dietary samples from the North Carolina farms exhibited high levels of chlordane. No organochlorine pesticides were found in any of the drinking water samples. Dietary dieldrin levels on the same Iowa farm exceeded the oral reference dose (RfD) eight- to eleven-fold (50 ng/kg-day). No other pesticide exceeded the RfD. However, dietary chlordane levels at a North Carolina farm reached 17% of the RfD. Previous use of aldrin on an Iowa farm corresponded to dieldrin found in the diet and in the serum of the farmer and spouse. Previous reported

use of chlordane on the North Carolina farms corresponded with measurable dietary levels of chlordance and higher serum trans-nonachlor levels than the levels in Iowa farm families.

Buckley,J.D., A.T.Meadows, M.E.Kadin, M.M.Le Beau, S.Siegel, and L.L.Robison. 2000. "Pesticide exposures in children with non-Hodgkin lymphoma." Cancer. 89:2315-2321.
Abstract: BACKGROUND: The association between pesticide exposure and non-Hodgkin lymphoma (NHL) in adults has been the subject of numerous case-control and cohort studies. However, to the authors' knowledge, data regarding pesticide exposures in children diagnosed with NHL have been lacking. METHODS: The Children's Cancer Group conducted a study comparing 268 children who developed NHL or leukemia with bulk disease with a group of matched, randomly selected regional population controls. The telephone interviews of both the case and control mothers included selected questions regarding occupational and home exposures to pesticides around the time of the index pregnancy and exposure of the child. RESULTS: A significant association was found between risk of NHL and increased frequency of reported pesticide use in the home (odds ratio [OR] = 7.3 for use most days; trend P = 0.05), professional exterminations within the home (OR = 3.0; P = 0.002), and postnatal exposure (OR = 2.4; P = 0.001). Elevated risks were found for T-cell and B-cell lymphomas; for lymphoblastic, large cell, and Burkitt morphologies; and in both young (age < 6 years) and older children. There was an increased risk of NHL with occupational exposure to pesticides (OR = 1.7) that was not significant overall, but that was significant for Burkitt lymphoma (OR = 9.6; P < 0.05). CONCLUSIONS: The results of the current study provide further evidence linking pesticide exposure to the risk of NHL, but the authors were unable to implicate any specific agent

Bujan,L., A.Mansat, F.Pontonnier, and R.Mieusset. 1996. "Time series analysis of sperm concentration in fertile men in Toulouse, France between 1977 and 1992." British Medical Journal. 312:471-472.
Abstract: Objectives-To investigate whether sperm production has changed during the past 16 years in the Toulouse area of France. Design-Time series analysis of sperm donors' specimens between 1977 and 1992. Setting-Sperm bank of university hospital in Toulouse, France. Subjects-302 healthy fertile men candidate sperm donors more than 20 and up to 45 years old and without any infertile brothers. Main outcome measure-Spermatozoa concentration. Results-Donors' mean age at time of donation was 34.05 (SD 5.13), but this increased significantly (P<0.001) during the study, from 32.4 in 1977 to 36 in 1992. Mean sperm count of samples was 83.12 x 10(6)/ml (SD 68.42 x 10(6)/ml). Sperm concentration was positively linked to the year of donation (Pearson's coefficient r = 0.12, P < 0.05), but this correlation disappeared after adjustment for age of donors (r = 0.09, P > 0.05). Conclusion-Sperm concentration has not changed with time in the Toulouse area.

Calderon,R.L., E.Hudgens, X.C.Le, D.Schreinemachers, and D.J.Thomas. 1999. "Excretion of arsenic in urine as a function of exposure to arsenic in drinking water." Environ.Health Perspect. 107:663-667.

Abstract: Urinary arsenic (As) concentrations were evaluated as a biomarker of exposure in a U.S. population chronically exposed to inorganic As (InAs) in their drinking water. Ninety-six individuals who consumed drinking water with As concentrations of 8-620 microg/L provided first morning urine voids for up to 5 consecutive days. The study population was 56% male, and 44% was younger than 18 years of age. On one day of the study period, all voided urines were collected over a 24-hr period. Arsenic intake from drinking water was estimated from daily food diaries. Comparison between the concentration of As in individual urine voids with that in the 24-hr urine collection indicated that the concentration of As in urine was stable throughout the day. Comparison of the concentration of As in each first morning urine void over the 5-day study period indicated that there was little day-to-day variation in the concentration of As in urine. The concentration of As in drinking water was a better predictor of the concentration of As in urine than was the estimated intake of As from drinking water. The concentration of As in urine did not vary by gender. An age-dependent difference in the concentration of As in urine may be attributed to the higher As dosage rate per unit body weight in children than in adults. These findings suggest that the analysis of a small number of urine samples may be adequate to estimate an individual's exposure to InAs from drinking water and that the determination of the concentration of InAs in a drinking water supply may be a useful surrogate for estimating exposure to this metalloid

Castorina,R., A.Bradman, T.E.McKone, D.B.Barr, M.E.Harnly, and B.Eskenazi. 2003. "Cumulative organophosphate pesticide exposure and risk assessment among pregnant women living in an agricultural community: a case study from the CHAMACOS cohort." Environ.Health Perspect. 111:1640-1648.
Abstract: Approximately 230,000 kg of organophosphate (OP) pesticides are applied annually in California's Salinas Valley. These activities have raised concerns about exposures to area residents. We collected three spot urine samples from pregnant women (between 1999 and 2001) enrolled in CHAMACOS (Center for the Health Assessment of Mothers and Children of Salinas), a longitudinal birth cohort study, and analyzed them for six dialkyl phosphate metabolites. We used urine from 446 pregnant women to estimate OP pesticide doses with two deterministic steady-state modeling methods: method 1, which assumed the metabolites were attributable entirely to a single diethyl or dimethyl OP pesticide; and method 2, which adapted U.S. Environmental Protection Agency (U.S. EPA) draft guidelines for cumulative risk assessment to estimate dose from a mixture of OP pesticides that share a common mechanism of toxicity. We used pesticide use reporting data for the Salinas Valley to approximate the mixture to which the women were exposed. Based on average OP pesticide dose estimates that assumed exposure to a single OP pesticide (method 1), between 0% and 36.1% of study participants' doses failed to attain a margin of exposure (MOE) of 100 relative to the U.S. EPA oral benchmark dose(10) (BMD(10)), depending on the assumption made about the parent compound. These BMD(10) values are doses expected to produce a 10% reduction in brain cholinesterase activity compared with background response in rats. Given the participants' average cumulative OP pesticide dose estimates (method 2) and regardless of the index chemical selected, we found that 14.8% of the doses failed to attain an MOE of 100 relative to the BMD(10) of the selected index. An uncertainty analysis of the pesticide mixture parameter, which is extrapolated from pesticide application data for the

study area and not directly quantified for each individual, suggests that this point estimate could range from 1 to 34%. In future analyses, we will use pesticide-specific urinary metabolites, when available, to evaluate cumulative OP pesticide exposures

Centers for Disease Control and Prevention. National Report on Human Exposure to Environmental Chemicals. 2001. Atlanta, Georgia.
Ref Type: Report

Chapin,R.E., W.A.Robbins, L.A.Schieve, A.M.Sweeney, S.A.Tabacova, and K.M.Tomashek. 2004. "Off to a good start: the influence of pre- and periconceptional exposures, parental fertility, and nutrition on children's health." Environ.Health Perspect. 112:69-78.
Abstract: The scientific community is developing a compelling body of evidence that shows the importance of the in utero environment (including chemical and hormonal levels) to the ultimate health of the child and even of the aging adult. This article summarizes the evidence that shows this impact begins with conception. Only a full life-cycle evaluation will help us understand these impacts, and only such an understanding will produce logically prioritized mitigation strategies to address the greatest threats first. Clearly, the time for analysis begins when the next generation is but a twinkle in the eye

Charnley,G. 2003. "Pesticide exposures and children's risk tradeoffs." Environ.Health Perspect. 111:A689-A691.

Chen,Z., P.A.Stewart, S.Davies, R.Giller, M.Krailo, M.Davis, L.Robison, and X.O.Shu. 2005. "Parental occupational exposure to pesticides and childhood germ-cell tumors." American Journal of Epidemiology. 162:858-867.
Abstract: In a recently completed US case-control study (Children's Oncology Group, 1993-2001) with 253 cases and 394 controls, the authors investigated the association between parental occupational exposure to pesticides and risk of childhood germ-cell tumors. Information on occupational pesticide exposure was collected using job-specific module questionnaires and assessed by an experienced industrial hygienist. Odds ratios for childhood germ-cell tumors associated with maternal exposures before pregnancy, during pregnancy, and after the birth of the index child were 1.0 (95% confidence interval (CI): 0.8, 1.4), 1.1 (95% CI: 0.7, 1.6), and 1.3 (95% CI: 0.9, 1.8), respectively. Paternal exposures before pregnancy, during pregnancy, and after the birth of the index child were not related to germ-cell tumors (odds ratios (ORs) were 0.9 (95% CI: 0.7, 1.2), 0.8 (95% CI: 0.5, 1.2), and 0.8 (95% CI: 0.5, 1.3), respectively). When both parents had ever been occupationally exposed to pesticides before the index pregnancy, the odds ratio was 0.8 (95% CI: 0.4, 1.3). Subgroup analyses showed a positive association between maternal exposure to herbicides during the postnatal period and risk of germ-cell tumors in girls (OR = 2.3, 95% CI: 1.0, 5.2) and an inverse association between paternal exposure to pesticides during the index pregnancy and germ-cell tumors in boys (OR = 0.2, 95% CI: 0.1, 1.0). This study did not provide strong evidence supporting a relation between parental pesticide exposure in the workplace and risk of germ-cell tumors among offspring

Cohn,B.A., P.M.Cirillo, M.S.Wolff, P.J.Schwingl, R.D.Cohen, R.I.Sholtz, A.Ferrara, R.E.Christianson, B.J.van den Berg, and P.K.Siiteri. 2003. "DDT and DDE exposure in mothers and time to pregnancy in daughters." Lancet. 361:2205-2206.
Abstract: Reproductive-tract anomalies after administration of the potent oestrogen, diethylstilboestrol, in pregnant women raised concerns about the reproductive effects of exposure to weakly oestrogenic environmental contaminants such as bis[4-chlorophenyl]-1,1,1-trichloroethane (p,p'-DDT) or its metabolites, such as bis[4-chlorophenyl]-1,1-dichloroethene (p,p'-DDE). We measured p,p'-DDT and p,p'-DDE in preserved maternal serum samples drawn 1-3 days after delivery between 1960 and 1963. We recorded time to pregnancy in 289 eldest daughters 28-31 years later. Daughters' probability of pregnancy fell by 32% per 10 microg/L p,p'-DDT in maternal serum (95% CI 11-48). By contrast, the probability of pregnancy increased 16% per 10 microg/L p,p'-DDE (6-27). The decreased fecundability associated with prenatal p,p'-DDT remains unexplained. We speculate that the antiandrogenic activity of p,p'-DDE may mitigate harmful androgen effects on the ovary during gestation or early life

Collier,R.H., S.Finch, and G.Davies. 2001. "Pest insect control in organically-produced crops of field vegetables." Meded.Rijksuniv.Gent Fak.Landbouwkd.Toegep.Biol.Wet. 66:259-267.
Abstract: In the UK, the demand for organic vegetable and salad crops is increasing, mainly as a result of the requirements of the multiple retailers. However, approximately 85% of the organic fruit and vegetable produce sold in the UK is imported. A major constraint to growing field vegetable crops, and particularly organically-produced crops, is the reduction in crop yield and quality caused by pest insects. This paper will consider the control techniques currently available to organic growers and other techniques that may become available in the future. Growing plant varieties with complete or even partial resistance to pest insects can be an effective way of reducing crop damage. There are already varieties of carrot, with resistance to carrot fly, and lettuce, with resistance to certain pest aphid species, which are available commercially. Cultural techniques to exclude, deter or avoid pest insects are also being used by some organic growers. Although isolating new crops from sources of infestation can be a highly effective control strategy, many organic growers cannot use it, as the land converted for organic production is still limited. Various crop covers can be used to prevent pest insects from damaging field crops, but to be effective such covers have to be in place before the pests enter the crop. Several researchers have tried to develop techniques to prevent pest insects from finding their host-plants. No technique involving semiochemicals has been sufficiently successful to be used in field vegetable production in the UK. Other studies have shown that the numbers of pest insects found on crop plants are reduced considerably when the crop is allowed to become weedy, is intercropped with another plant species, or is undersown with a living mulch. Hence, work is now needed to select background plant species that will both reduce pest insect numbers and cause the least reduction in yield to the harvested crop plants. There is also a need to obtain a better understanding of "companion planting", a practice used frequently by organic growers. To date, microbial control is the only biological technique that has been used successfully in field vegetable crops in the UK. However, only the toxicant produced by one microbial agent, the bacterium Bacillus thuringiensis, has so far been registered for use. The use of

bacteria, fungi and viruses to control pests of field vegetable crops certainly has possibilities. However, in many cases there are still problems to be overcome to select pathogens that are compatible with, or can still be effective in, the wide fluctuations in temperature, humidity and soil moisture that occur under field conditions. Attempts are now being made to use entomopathogenic nematodes and predatory arthropods to control one major pest insect, the cabbage root fly. Techniques developed to improve the timing of application of various crop protection procedures in systems of conventional vegetable production apply equally well to organic production, despite the choice of control options being more limited. In particular, models to forecast the timing of pest insect attacks could be used to great effect, to indicate the best times to plant, protect and harvest a specific crop to minimise pest insect damage

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Ref Type: Report

Consumers Union of the United States. Organic foods: Safer? Tastier? More Nutrition? 1998. Consumer Reports Online.
Ref Type: Audiovisual Material

Cooper,R.L., J.M.Goldman, and T.E.Stoker. 1999. "Neuroendocrine and reproductive effects of contemporary-use pesticides." Toxicol.Ind.Health. 15:26-36.
Abstract: Work in our laboratory has focused on the hypothesis that certain environmental contaminants will interfere with reproductive function because they disrupt the neuroendocrine regulation of gonadal function. In this article, we review the evidence that certain classes of contemporary-use pesticides alter gonadotropin secretion through a disruption of hypothalamic mechanisms. Specifically, we discuss the effect of formamidine and dithiocarbamate pesticides on the noradrenergic control of pituitary hormone secretion, ovarian function, and pregnancy in the rat. This is followed by a review of studies evaluating the effect of a chlorotriazine herbicide, atrazine, on the hormonal control of ovulation and lactation. We also discuss the physiological consequences of these endocrine alterations in the female, how toxicant-induced endocrine alterations may differ in physiological outcome in the male and female, and the fact that the reproductive risk assessment of some pesticides that act on the central nervous system (CNS) may be influenced by the development of tolerance

Coronado,G.D., B.Thompson, L.Strong, W.C.Griffith, and I.Islas. 2004. "Agricultural task and exposure to organophosphate pesticides among farmworkers." Environmental Health Perspectives. 112:142-147.
Abstract: Little is known about pesticide exposure among farmworkers, and even less is known about the exposure associated with performing specific farm tasks. Using a random sample of 213 farmworkers in 24 communities and labor camps in eastern

Washington State, we examined the association between occupational task and organophosphate (OP) pesticide residues in dust and OP metabolite concentrations in urine samples of adult farmworkers and their children. The data are from a larger study that sought to test a culturally appropriate intervention to break the take-home pathway of pesticide exposure. Commonly reported farm tasks were harvesting or picking (79.2%), thinning (64.2%), loading plants or produce (42.2%), planting or transplanting (37.6%), and pruning (37.2%). Mixing, loading, or applying pesticide formulations was reported by 20% of our sample. Workers who thinned were more likely than those who did not to have detectable levels of azinphos-methyl in their house dust (92.1% vs. 72.7%; p = 0.001) and vehicle dust (92.6% vs. 76.5%; p = 0.002). Thinning was associated with higher urinary pesticide metabolite concentrations in children (91.9% detectable vs. 81.3%; p = 0.02) but not in adults. Contrary to expectation, workers who reported mixing, loading, or applying pesticide formulations had lower detectable levels of pesticide residues in their house or vehicle dust, compared with those who did not perform these job tasks, though the differences were not significant. Future research should evaluate workplace protective practices of fieldworkers and the adequacy of reentry intervals for pesticides used during thinning.

Cressey,P.J. and R.W.Vannoort. 2003. "Pesticide content of infant formulae and weaning foods available in New Zealand." Food Addit.Contam. 20:57-64.
Abstract: A survey of the pesticide content of 25 commercially available infant formulae and 30 weaning foods available in New Zealand was undertaken in 1996. It included a representative mixture of imported and New Zealand manufactured infant foods. Three different pesticide screening techniques were used: a high-sensitivity organochlorine screen was carried out on all infant formulae, while a multiresidue screen (organochlorine and organophosphorus pesticides, synthetic pyrethroids, carbamate pesticides, fungicides and herbicides), and a specific screen for dithiocarbamate fungicides were both carried out on all weaning foods and on soy-based infant formulae. All results are expressed on a ready-to-feed basis. Extremely low levels of residues of three organochlorine compounds (p,p'-DDE, p,p'-DDT and dieldrin) were detected in infant formulae samples. Residues of p,p'-DDE were found in seven of 20 milk-based infant formulae at concentrations ranging from 0.03 to 0.5 microgram kg(-1). Residues of p,p'-DDT were found in one imported milk-based infant formula at 0.7 microgram kg(-1), and dieldrin residues were detected in four of five soy-based infant formulae at concentrations ranging from 0.05 to 0.08 microgram kg(-1). The multiresidue pesticide screen detected low levels of residues of two organophosphorus pesticides; azinphos-methyl in one soy-based infant formula at a level of 22 microgram kg(-1) and pirimiphos-methyl in two cereal-based weaning foods at concentrations of 5 and 14 microgram kg(-1). None of the other approximately 140 pesticides (including fungicides and herbicides) included in the multiresidue screen were detected in any weaning foods or soy-based infant formulae, at a detection limit of 10 microgram kg(-1). No residues of dithiocarbamate fungicides were detected in any product analysed, at a detection limit of 100 microgram kg(-1)

Curl,C.L., R.A.Fenske, J.C.Kissel, J.H.Shirai, T.F.Moate, W.Griffith, G.Coronado, and B.Thompson. 2002. "Evaluation of take-home organophosphorus pesticide exposure

among agricultural workers and their children." Environ.Health Perspect. 110:A787-A792.
Abstract: We analyzed organophosphorus pesticide exposure in 218 farm worker households in agricultural communities in Washington State to investigate the take-home pathway of pesticide exposure and to establish baseline exposure levels for a community intervention project. House dust samples (n = 156) were collected from within the homes, and vehicle dust samples (n = 190) were collected from the vehicles used by the farm workers to commute to and from work. Urine samples were obtained from a farm worker (n = 213) and a young child (n = 211) in each household. Dust samples were analyzed for six pesticides, and urine samples were analyzed for five dialkylphosphate (DAP) metabolites. Azinphosmethyl was detected in higher concentrations ($p < 0.0001$) than the other pesticides: geometric mean concentrations of azinphosmethyl were 0.53 micro g/g in house dust and 0.75 micro g/g in vehicle dust. Dimethyl DAP metabolite concentrations were higher than diethyl DAP metabolite concentrations in both child and adult urine ($p < 0.0001$). Geometric mean dimethyl DAP concentrations were 0.13 micro mol/L in adult urine and 0.09 micro mol/L in child urine. Creatinine-adjusted geometric mean dimethyl DAP concentrations were 0.09 micro mol/g in adult urine and 0.14 micro mol/g in child urine. Azinphosmethyl concentrations in house dust and vehicle dust from the same household were significantly associated ($r2 = 0.41$, $p < 0.0001$). Dimethyl DAP levels in child and adult urine from the same household were also significantly associated ($r2 = 0.18$, $p < 0.0001$), and this association remained when the values were creatinine adjusted. The results of this work support the hypothesis that the take-home exposure pathway contributes to residential pesticide contamination in agricultural homes where young children are present

Curl,C.L., R.A.Fenske, and K.Elgethun. 2003. "Organophosphorus pesticide exposure of urban and suburban preschool children with organic and conventional diets." Environ.Health Perspect. 111:377-382.
Abstract: We assessed organophosphorus (OP) pesticide exposure from diet by biological monitoring among Seattle, Washington, preschool children. Parents kept food diaries for 3 days before urine collection, and they distinguished organic and conventional foods based on label information. Children were then classified as having consumed either organic or conventional diets based on analysis of the diary data. Residential pesticide use was also recorded for each home. We collected 24-hr urine samples from 18 children with organic diets and 21 children with conventional diets and analyzed them for five OP pesticide metabolites. We found significantly higher median concentrations of total dimethyl alkylphosphate metabolites than total diethyl alkylphosphate metabolites (0.06 and 0.02 micro mol/L, respectively; $p = 0.0001$). The median total dimethyl metabolite concentration was approximately six times higher for children with conventional diets than for children with organic diets (0.17 and 0.03 micro mol/L; $p = 0.0003$); mean concentrations differed by a factor of nine (0.34 and 0.04 micro mol/L). We calculated dose estimates from urinary dimethyl metabolites and from agricultural pesticide use data, assuming that all exposure came from a single pesticide. The dose estimates suggest that consumption of organic fruits, vegetables, and juice can reduce children's exposure levels from above to below the U.S. Environmental Protection Agency's current guidelines, thereby shifting exposures from a range of uncertain risk to a range of

negligible risk. Consumption of organic produce appears to provide a relatively simple way for parents to reduce their children's exposure to OP pesticides

Davis,D.L., M.B.Gottlieb, and J.R.Stampnitzky. 1998. "Reduced ratio of male to female births in several industrial countries - a sentinel health indicator." Journal of the American Medical Association. 279:1018-1023.
Abstract: Context.-The sex ratio of 1.06:1, the ratio of male to female births, has declined over the past decades. Recent reports from a number of industrialized countries indicate that the proportion of males born has significantly decreased, while some male reproductive tract disorders have increased. Objectives.-To examine the evidence for declines in the male proportion at birth and suspected causes for this decline, and to determine whether altered sex ratio can be considered a sentinel health event. Data Sources.-Birth records were analyzed from national statistical agencies. Study Selection.-Published analyses of trends in ratio of males to females at birth and studies of sex determinants evaluating epidemiological and endocrinological factors. Data Extraction.-Proportion of males born, 1950-1994 in Denmark; 1950-1994 in the Netherlands; 1970-1990 in Canada; and 1970-1990 in the United States, Data Synthesis.-Since 1950, significant declines in the proportion of males born have been reported in Denmark and the Netherlands. Similar declines have been reported for Canada and the United States since 1970 and parallel declines also have occurred in Sweden, Germany, Norway, and Finland. In Denmark, the proportion of males declined from 0.515 in 1950 to 0.513 in 1994. In the Netherlands, the proportion of males declined from 0.516 in 1950 to 0.513 in 1994, Similar declines in the proportion of males born in Canada and the United States are equivalent to a shift from male to female births of 8600 and 38 000 births, respectively. Known and hypothesized risk factors for reduced sex ratio at birth cannot fully account for recent trends. Conclusion.-Patterns of reduced sex ratio need to be carefully assessed to determine whether they are occurring more generally, whether temporal or spatial variations are evident, and whether they constitute a sentinel health event.

De Roos,A.J., S.H.Zahm, K.P.Cantor, D.D.Weisenburger, F.F.Holmes, L.F.Burmeister, and A.Blair. 2003. "Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men." Occup.Environ.Med. 60:E11.
Abstract: BACKGROUND: An increased rate of non-Hodgkin's lymphoma (NHL) has been repeatedly observed among farmers, but identification of specific exposures that explain this observation has proven difficult. METHODS: During the 1980s, the National Cancer Institute conducted three case-control studies of NHL in the midwestern United States. These pooled data were used to examine pesticide exposures in farming as risk factors for NHL in men. The large sample size (n = 3417) allowed analysis of 47 pesticides simultaneously, controlling for potential confounding by other pesticides in the model, and adjusting the estimates based on a prespecified variance to make them more stable. RESULTS: Reported use of several individual pesticides was associated with increased NHL incidence, including organophosphate insecticides coumaphos, diazinon, and fonofos, insecticides chlordane, dieldrin, and copper acetoarsenite, and herbicides atrazine, glyphosate, and sodium chlorate. A subanalysis of these "potentially carcinogenic" pesticides suggested a positive trend of risk with exposure to increasing

numbers. CONCLUSION: Consideration of multiple exposures is important in accurately estimating specific effects and in evaluating realistic exposure scenarios

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Ref Type: Art Work

Eskenazi,B., A.Bradman, and R.Castorina. 1999. "Exposures of children to organophosphate pesticides and their potential adverse health effects." Environ.Health Perspect. 107 Suppl 3:409-419.
Abstract: Recent studies show that young children can be exposed to pesticides during normal oral exploration of their environment and their level of dermal contact with floors and other surfaces. Children living in agricultural areas may be exposed to higher pesticide levels than other children because of pesticides tracked into their homes by household members, by pesticide drift, by breast milk from their farmworker mother, or by playing in nearby fields. Nevertheless, few studies have assessed the extent of children's pesticide exposure, and no studies have examined whether there are adverse health effects of chronic exposure. There is substantial toxicologic evidence that repeated low-level exposure to organophosphate (OP) pesticides may affect neurodevelopment and growth in developing animals. For example, animal studies have reported neurobehavorial effects such as impairment on maze performance, locomotion, and balance in neonates exposed (italic)in utero(/italic) and during early postnatal life. Possible mechanisms for these effects include inhibition of brain acetylcholinesterase, downregulation of muscarinic receptors, decreased brain DNA synthesis, and reduced brain weight in offspring. Research findings also suggest that it is biologically plausible that OP exposure may be related to respiratory disease in children through dysregulation of the autonomic nervous system. The University of California Berkeley Center for Children's Environmental Health Research is working to build a community-university partnership to study the environmental health of rural children. This Center for the Health Assessment of Mothers and Children of Salinas, or CHAMACOS in Monterey County, California, will assess (italic)in utero(/italic) and postnatal OP pesticide exposure and the relationship of exposure to neurodevelopment, growth, and symptoms of respiratory illness in children. The ultimate goal of the center is to translate research findings into a reduction of children's exposure to pesticides and other environmental agents, and thereby reduce the incidence of environmentally related disease

Eskenazi,B., E.A.Gladstone, G.S.Berkowitz, C.H.Drew, E.M.Faustman, N.T.Holland, B.Lanphear, S.J.Meisel, F.P.Perera, V.A.Rauh, A.Sweeney, R.M.Whyatt, and K.Yolton.

2005. "Methodologic and logistic issues in conducting longitudinal birth cohort studies: lessons learned from the Centers for Children's Environmental Health and Disease Prevention Research." Environ.Health Perspect. 113:1419-1429.
Abstract: In anticipation of the National Children's Study, lessons can be learned from the smaller birth cohort studies conducted by five Centers for Children's Environmental Health and Disease Prevention Research funded by the National Institute of Environmental Health Sciences and the U.S. Environmental Protection Agency. The populations studied are diverse in ethnicity and social class and reside in urban and rural environments. Although almost all of the centers chose to enroll participants through medical care facilities, they had to develop independent staffs and structures because of the overburdened medical care system. Some of the lessons learned by the centers include the importance of continuous funding, building community partnerships to conduct culturally appropriate research, hiring bilingual and bicultural staff from the community, prioritizing research goals, developing biorepositories to ensure future utility of samples, instituting quality control procedures for all aspects of specimen and data collection, maintaining frequent contact with study participants, ensuring ethical conduct of the research in a changing medical-legal climate, and communicating results in a timely and appropriate manner to participants and the wider community. All centers underestimated the necessary start-up time, staff, and costs in conducting these birth cohort studies. Despite the logistical complexity and added expenses, all centers emphasize the importance of studying the impact of environmental exposures on those children most at risk, those living in minority and low-income communities. These centers present barriers encountered, solutions found, and considerations for future research, with the hope that the lessons learned can help inform the planning and conduct of the National Children's Study

Fattore,E., R.Fanelli, and C.La Vecchia. 2002. "Persistent organic pollutants in food: public health implications." J Epidemiol Community Health. 56:831-832.
Abstract: Persistent organic pollutants are a heterogeneous group of chemicals sharing a number a common properties, including long term persistence and diffusion in the environment, and bioaccumulation through the food chain. Animal experiments and epidemiological studies suggest that the most sensitive adverse effects, such as disturbances on metabolism, development, and reproductive system, may occur in the range of current human exposure. Although the potential cancer risk of persistent organic pollutants remains undefined, the implementation of actions to reduce the exposure to these substances, which mainly occurs through the diet, is important

Fausto,A.M., P.Morera, R.Margarit, and A.R.Taddei. 2001. "Sperm quality and reproductive traits in male offspring of female rabbits exposed to lindane (g-HCH) during pregnancy and lactation." Reproduction, Nutrition, Development. 41:217-225.
Abstract: Fifteen Grimaud female hybrid rabbits, 135 days old and weighting an average of 3.74+/-0.01 kg each, were administered an oral dose of 1 mg x kg(-1) body weight of Lindane during gestation and lactation period. Fertility rate, libido, volume of ejaculate, concentration and morphology of spermatozoa were investigated to test the effects of the treatment on reproductive traits of first generation male rabbits. Ultrastructure of abnormal spermatozoa was described by Transmission Electron Microscopy and the

different abnormalities were quantified. The results obtained indicate that low dose exposure of Lindane has effects on spermatozoa ultrastructure that proved to be susceptible to the treatment with the pesticide (cytoplasmic droplets: 5.3% in control group and 10.3% in Lindane group, P < or = 0.05; coiled tails: 1.3% in control group and 4.3% in Lindane group, P < or = 0.05) and could be utilised as a good marker of toxicity.

Fenske,R.A., J.C.Kissel, C.Lu, D.A.Kalman, N.J.Simcox, E.H.Allen, and M.C.Keifer. 2000. "Biologically based pesticide dose estimates for children in an agricultural community." Environ.Health Perspect. 108:515-520.
Abstract: Current pesticide health risk assessments in the United States require the characterization of aggregate exposure and cumulative risk in the setting of food tolerances. Biologic monitoring can aggregate exposures from all sources and routes, and can integrate exposures for chemicals with a common mechanism of action. Its value was demonstrated in a recent study of organophosphorus (OP) pesticide exposure among 109 children in an agricultural community in Washington State; 91 of the children had parents working in agriculture. We estimated individual OP pesticide doses from urinary metabolite concentrations with a deterministic steady state model, and compared them to toxicologic reference values. We evaluated doses by assuming that metabolites were attributable entirely to either azinphos-methyl or phosmet, the two OP pesticides used most frequently in the region. Creatinine-adjusted average dose estimates during the 6- to 8-week spraying season ranged from 0 to 36 microg/kg/day. For children whose parents worked in agriculture as either orchard applicators or as fieldworkers, 56% of the doses estimated for the spray season exceeded the U.S. Environmental Protection Agency (EPA) chronic dietary reference dose, and 19% exceeded the World Health Organization acceptable daily intake values for azinphos-methyl. The corresponding values for children whose parents did not work in agriculture were 44 and 22%, respectively. The percentage of children exceeding the relevant reference values for phosmet was substantially lower (< 10%). Single-day dose estimates ranged from 0 to 72 microg/kg/day, and 26% of these exceeded the EPA acute reference dose for azinphos-methyl. We also generated dose estimates by adjustment for total daily urine volume, and these estimates were consistently higher than the creatinine-adjusted estimates. None of the dose estimates exceeded the empirically derived no-observable-adverse-effect levels for these compounds. The study took place in an agricultural region during a period of active spraying, so the dose estimates for this population should not be considered representative of exposures in the general population. The findings indicate that children living in agricultural regions represent an important subpopulation for public health evaluation, and that their exposures fall within a range of regulatory concern. They also demonstrate that biologically based exposure measures can provide data for health risk evaluations in such populations

Fenske,R.A., G.Kedan, C.Lu, J.A.Fisker-Andersen, and C.L.Curl. 2002. "Assessment of organophosphorous pesticide exposures in the diets of preschool children in Washington State." J Expo.Anal.Environ.Epidemiol. 12:21-28.
Abstract: Twenty-four hour duplicate diet sampling was employed to investigate dietary pesticide exposures of children aged 2 to 5 years. Duplicate diets were collected from seven children living in the Seattle metropolitan area and six children living in Chelan

and Douglas counties in Central Washington. Diet samples were collected from each child in the summer and again in the fall, and total daily diets were divided into four food categories: fresh fruits and vegetables, beverages, processed foods, and dairy products. A total of 88 individual food category samples were collected and analyzed for 15 organophosphorous (OP) pesticides. Three of the 13 children had no detectable OP pesticides in either of their diet samples, and 14 of the 26 duplicate diets did not contain detectable levels of OP pesticides. Sixteen individual food category samples contained detectable levels of at least one OP pesticide and two of these samples contained detectable levels of two OP pesticides. Of the 15 targeted pesticides, 6 were detected: azinphosmethyl, chlorpyrifos, malathion, methidathion, methyl parathion, and phosmet. Azinphosmethyl was detected most frequently (10% of all samples), particularly in samples containing apples or apple juice. The fresh fruits and vegetable category had the most frequent pesticide determinations, followed by beverages. OP pesticides were not present at detectable levels in any of the dairy samples. Malathion was the only OP pesticide detected in processed food samples, appearing in 4 of the 26 samples (15%). No detections were above the legal tolerances for residues on produce, however the acute population-adjusted reference dose (aPAD) for chlorpyrifos exposure of 1.7 microg/kg/day was exceeded by one subject during one sampling event. This subject's cumulative daily dose of chlorpyrifos equivalents was estimated to be 2.5 microg/kg/day

Fenske,R.A., C.Lu, D.Barr, and L.Needham. 2002. "Children's exposure to chlorpyrifos and parathion in an agricultural community in central Washington State." Environ.Health Perspect. 110:549-553.

Abstract: We measured two diethyl organophosphorus (OP) pesticides--chlorpyrifos and parathion--in residences, and their metabolic by-products, in the urine of children 6 years old or younger in a central Washington State agricultural community. Exposures to two dimethyl OP pesticides (azinphos-methyl and phosmet) in this same population have been reported previously. We categorized children by parental occupation and by household proximity to pesticide-treated farmland. Median chlorpyrifos house dust concentrations were highest for the 49 applicator homes (0.4 microg/g), followed by the 12 farm-worker homes (0.3 microg/g) and the 14 nonagricultural reference homes (0.1 microg/g), and were statistically different ($p < 0.001$); we observed a similar pattern for parathion in house dust. Chlorpyrifos was measurable in the house dust of all homes, whereas we found parathion in only 41% of the homes. Twenty-four percent of the urine samples from study children had measurable 3,5,6-trichloro-2-pyridinol (TCPy) concentrations [limits of quantitation (LOQ) = 8 microg/L], and 7% had measurable 4-nitrophenol concentrations (LOQ = 9 microg/L). Child urinary metabolite concentrations did not differ across parental occupational classifications. Homes in close proximity (200 ft/60 m) to pesticide-treated farmland had higher chlorpyrifos ($p = 0.01$) and parathion ($p = 0.014$) house dust concentrations than did homes farther away, but this effect was not reflected in the urinary metabolite data. Use of OP pesticides in the garden was associated with an increase in TCPy concentrations in children's urine. Parathion concentrations in house dust decreased 10-fold from 1992 to 1995, consistent with the discontinued use of this product in the region in the early 1990s

Fenske,R.A., G.Kedan, C.Lu, J.A.Fisker-Andersen, and C.L.Curl. 2002. "Assessment of organophosphorous pesticide exposures in the diets of preschool children in Washington State." J.Expo.Anal.Environ.Epidemiol. 12:21-28.
Abstract: Twenty-four hour duplicate diet sampling was employed to investigate dietary pesticide exposures of children aged 2 to 5 years. Duplicate diets were collected from seven children living in the Seattle metropolitan area and six children living in Chelan and Douglas counties in Central Washington. Diet samples were collected from each child in the summer and again in the fall, and total daily diets were divided into four food categories: fresh fruits and vegetables, beverages, processed foods, and dairy products. A total of 88 individual food category samples were collected and analyzed for 15 organophosphorous (OP) pesticides. Three of the 13 children had no detectable OP pesticides in either of their diet samples, and 14 of the 26 duplicate diets did not contain detectable levels of OP pesticides. Sixteen individual food category samples contained detectable levels of at least one OP pesticide and two of these samples contained detectable levels of two OP pesticides. Of the 15 targeted pesticides, 6 were detected: azinphosmethyl, chlorpyrifos, malathion, methidathion, methyl parathion, and phosmet. Azinphosmethyl was detected most frequently (10% of all samples), particularly in samples containing apples or apple juice. The fresh fruits and vegetable category had the most frequent pesticide determinations, followed by beverages. OP pesticides were not present at detectable levels in any of the dairy samples. Malathion was the only OP pesticide detected in processed food samples, appearing in 4 of the 26 samples (15%). No detections were above the legal tolerances for residues on produce, however the acute population-adjusted reference dose (aPAD) for chlorpyrifos exposure of 1.7 microg/kg/day was exceeded by one subject during one sampling event. This subject's cumulative daily dose of chlorpyrifos equivalents was estimated to be 2.5 microg/kg/day

Fenske,R.A., C.L.Curl, and J.C.Kissel. 2003. "The effect of the 14-day agricultural restricted entry interval on azinphosmethyl exposures in a group of apple thinners in Washington state." Regul.Toxicol.Pharmacol. 38:91-97.
Abstract: We examined the effect of the 14-day agricultural restricted entry period on absorbed pesticide doses in a group of twenty experienced apple thinners. Thinners entered orchards 1-49 days following azinphosmethyl applications. Urine samples (n=296) collected throughout the thinning season were analyzed for the three dialkylphosphate metabolites of azinphosmethyl to estimate absorbed daily doses. Separate dose distributions were created for samples collected when the interval was <14 days, or 14 days or more; geometric mean doses for these two categories differed by a factor of two (42 and 19 microg/kg/day, respectively; $p<0.0001$). Dose estimates were compared to US Environmental Protection Agency and California EPA regulatory guidance values for occupational azinphosmethyl risk. None of the doses exceeded the U.S. EPA NOAEL (560 microg/kg/day), but nearly all had a margin of exposure of less than 100. Addition of a 10-fold uncertainty factor to California EPAs NOAEL produced a guidance value of 75 microg/kg/day. Only 2.4% of the doses exceeded this value for re-entry intervals 14 days or more, while 27% exceeded the value for re-entry intervals <14 days. We conclude that the 14-day restricted entry interval provides an appropriate level of worker health protection under the field conditions studied

Flower,K.B., J.A.Hoppin, C.F.Lynch, A.Blair, C.Knott, D.L.Shore, and D.P.Sandler. 2004. "Cancer risk and parental pesticide application in children of Agricultural Health Study participants." Environ.Health Perspect. 112:631-635.
Abstract: Parental exposure to pesticides may contribute to childhood cancer risk. Through the Agricultural Health Study, a prospective study of pesticide applicators in Iowa and North Carolina, we examined childhood cancer risk and associations with parental pesticide application. Identifying information for 17,357 children of Iowa pesticide applicators was provided by parents via questionnaires (1993-1997) and matched against the Iowa Cancer Registry. Fifty incident childhood cancers were identified (1975-1998). Risk of all childhood cancers combined was increased [standardized incidence ratio (SIR) = 1.36; 95% confidence interval (CI), 1.03-1.79]. Risk of all lymphomas combined was also increased (SIR = 2.18; 95% CI, 1.13-4.19), as was risk of Hodgkin's lymphoma (SIR = 2.56; 95% CI, 1.06-6.14). We used logistic regression to explore associations between self-reported parental pesticide application practices and childhood cancer risk. No association was detected between frequency of parental pesticide application and childhood cancer risk. An increased risk of cancer was detected among children whose fathers did not use chemically resistant gloves [odds ratio (OR) = 1.98; 95% CI, 1.05-3.76] compared with children whose fathers used gloves. Of 16 specific pesticides used by fathers prenatally, ORs were increased for aldrin (OR = 2.66), dichlorvos (OR = 2.06), and ethyl dipropylthiocarbamate (OR = 1.91). However, these results were based on small numbers and not supported by prior biologic evidence. Identification of excess lymphoma risk suggests that farm exposures including pesticides may play a role in the etiology of childhood lymphoma

Garry,V.F., D.Schreinemachers, M.E.Harkins, and J.Griffith. 1996. "Pesticide appliers, biocides, and birth defects in rural Minnesota." Environ.Health Perspect. 104:394-399.
Abstract: Earlier studies by our group suggested the possibility that offspring of pesticide appliers might have increased risks of birth anomalies. To evaluate this hypothesis, 935 births to 34,772 state-licensed, private pesticide appliers in Minnesota occurring between 1989 and 1992 were linked to the Minnesota state birth registry containing 210,723 live births in this timeframe. The birth defect rate for all birth anomalies was significantly increased in children born to private appliers. Specific birth defect categories, circulatory/respiratory, urogenital, and musculoskeletal/integumental, showed significant increases. For the general population and for appliers, the birth anomaly rate differed by corp-growing region. Western Minnesota, a major wheat, sugar beet, and potato growing region, showed the highest rate of birth anomalies per/1000 live births: 30.0 for private appliers versus 26.9 for the general population of the same region. The lowest rates, 23.7/1000 for private appliers versus 18.3/1000 for the general population, occurred in noncorp regions. The highest frequency of use of chlorophenoxy herbicides and fungicides also occurred in western Minnesota. Births in the general population of western Minnesota showed a significant increase in birth anomalies in the same three birth anomaly categories as appliers and for central nervous system anomalies. This increase was most pronounced for infants conceived in the spring. The seasonal effect did not occur in other regions. The male/female sex ratio for the four birth anomaly categories of interest in areas of high phenoxy herbicide/fungicide use is 2.8 for appliers versus 1.5 for the general population of the same region ($p = 0.05$). In minimal use

regions, this ratio is 2.1 for appliers versus 1.7 for the general population. The pattern of excess frequency of birth anomalies by pesticide use, season, and alteration of sex ratio suggests exposure-related effects in appliers and the general population of the crop-growing region of western Minnesota

Garry,V.F., D.Schreinemachers, M.E.Harkins, and J.Griffith. 1996. "Pesticide appliers, biocides, and birth defects in rural Minnesota." Environmental Health Perspectives. 104:394-399.
Abstract: Earlier studies by our group suggested the possibility that offspring of pesticide appliers might have increased risks of birth anomalies. To evaluate this hypothesis, 4,935 births to 34,772 state-licensed, private pesticide appliers in Minnesota occurring between 1989 and 1992 were linked to the Minnesota state birth registry containing 210,723 live births in this timeframe. The birth defect rate for all birth anomalies was significantly increased in children horn to private appliers. Specific birth defect categories, circulatory/respiratory, urogenital, and musculoskeletal/integumental, showed significant increases. For the general population and for appliers, the birth anomaly rate differed by crop-growing region. Western Minnesota, a major wheat, sugar beet, and potato growing region, showed the highest rate of birth anomalies per/1000 live births: 30.0 for private appliers versus 26.9 for the general population of the same region. The lowest rates, 23.7/1000 for private appliers versus 18.3/1000 for the general population, occurred in noncrop regions. The highest frequency of use of chlorophenoxy herbicides and fungicides also occurred in western Minnesota. Births in the general population of western Minnesota showed a significant increase in birth anomalies in the same three birth anomaly categories as appliers and for central nervous system anomalies. This increase was most pronounced For infants conceived in the spring. The seasonal effect did not occur in other regions. The male/female sex ratio for the four birth anomaly categories of interest in areas of high phenoxy herbicide/fungicide use is 2.8 for appliers versus 1.5 for the general population of the same region ($p = 0.05$). in minimal use regions, this ratio is 2.1 for appliers versus 1.7 for the general population. The pattern of excess frequency of birth anomalies by pesticide use, season, and alteration of sex ratio suggests exposure-related effects in appliers and the general population of the crop-growing region of western Minnesota.

Garry,V.F., B.Burroughs, R.Tarone, and J.S.Kesner. 1999. "Herbicides and adjuvants: an evolving view." Toxicology & Industrial Health. 15:159-167.
Abstract: The present report examines the in vitro genotoxicity (micronucleus assay) of herbicides and adjuvants and reports on an in vivo human study on potential endocrine effects of pesticides, including herbicides. Adjuvants are used in conjunction with 2,4-dichlorophenoxy acetic acid (2,4-D) and other herbicides. Earlier pesticide applier survey results ($n = 709$) show that 59% of the applicators used adjuvants, and the majority of this group used paraffinic oils and/or surfactant mixtures. As a beginning effort to explore the role of adjuvants and herbicides in hormonally based reproductive effects, a prospective, controlled study was performed to analyze blood specimens from three different exposure groups (applicators using herbicides only; applicators using both herbicides and insecticides; and applicators using fumigants in addition to herbicides and insecticides; and a control group composed of other agricultural workers including organic farmers).

The applicators and controls were age- and smoking- matched. Study subjects (n = 78) were tested before, during, and after completion of pesticide application season for the effects of pesticide products on hormone levels in the bloodstream. Of the applicator exposure groups examined, only the herbicide group showed significant endocrinologic differences from controls. Free testosterone levels were significantly elevated in post-season measurements ($p = 0.032$), and follicle-stimulating hormone (FSH) was significantly decreased at the height of the season ($p = 0.016$) and in the post-season ($p = 0.010$) as compared to controls. These endocrinologic findings are discussed in terms of their possible relationship to potential endocrine effects of herbicides, herbicide contaminants, and adjuvants. In vitro genotoxicity examination compared four different commercially available surfactant mixtures with 12 different commercial herbicide products, including six different chlorophenoxy herbicides. Only one herbicide yielded a significant dose-response curve. All four adjuvants showed positive dose-response effects. These preliminary data suggest that adjuvants are not inert but are toxicologically active components added to herbicide mixtures. Whether adjuvant toxicant effects are additive or are independent of herbicide effects is poorly understood.

Garry,V.F., R.E.Tarone, H.R.Kirsch, J.M.Abdallah, D.P.Lombardi, L.K.Long, B.L.Burroughs, D.B.Barr, and J.S.Kesner. 2001. "Biomarker correlations of urinary 2,4-D levels in foresters: Genomic instability and endocrine disruption." Environmental Health Perspectives. 109:1-6.
Abstract: Forest pesticide applicators constitute a unique pesticide use group. Aerial, mechanical-ground, and focal weed control by application of herbicides, in particular chlorophenoxy herbicides, yield diverse exposure scenarios. In the present work, we analyzed aberrations in G-banded chromosomes, reproductive hormone levels, and polymerase chain reaction-based V(D)J rearrangement frequences in applicators whose exposures were mostly limited to chlorophenoxy herbicides. Data from appliers where chlorophenoxy use was less frequent were also examined. The biomarker outcome data were compared to urinary levels of 2,4-dichlorophenoxyacetic acid (2,4-D) obtained at the time of maximum 2,4-D use. Further comparisons of outcome data were made to the total volume of herbicides applied during the entire pesticide-use season. Twenty-four applicators and 15 minimally exposed foresters (control) subjects were studied. Categorized by applicator methods, men who used a hand-held, backpack sprayer in their applications showed the highest average level (453.6 ppb) of 2,4-D in urine. Serum leutinizing hormone (LH) values were correlated with urinary 2,4-D levels, but follicle-stimulating hormone and free and total testosterone were not. At the height of the application series; 6/7 backpack sprayers, 3/4 applicators who use mutlinozzle mechanical (boom) sprayers, 4/8 aerial applicators, and 2/5 skidder-radiarc (closed cab) appliers had two or more V(D)J region rearrangements per microgram of DNA. Only 5 of 15 minimally exposed (control) foresters had two or more rearrangements, and 3 of these 5 subjects demonstrated detectable levels of 2,4-D in the urine. Only 8/24 DNA samples obtained from the exposed group 10 months or more after their last chlorophenoxy use had two rearrangements per microgram of DNA, suggesting that the exposure-related effects observed were reversible and temporary. Although urinary 2,4-D levels were not correlated with chromosome aberration frequency, chromosome aberration frequencies were correlated with total volume of herbicides applied, inlcuding

products other than 2,4-D. In summary, herbicide applicators with high urinary levels of 2,4-D (backpack and boom spray applications) exhibited elevated LH levels. They also exhibited altered genomic stability as measured by V(D)J rearrangement frequency, which appears reversible months after peak exposure. Though highly detailed, the limited sample size warrants cautious interpretations of the data.

Garry,V.F., M.E.Harkins, L.L.Erickson, L.K.Long-Simpson, S.E.Holland, and B.L.Burroughs. 2002. "Birth defects, season of conception, and sex of children born to pesticide applicators living in the Red River Valley of Minnesota, USA." Environmental Health Perspectives. 110 (suppl. 3):441-449.
Abstract: We previously demonstrated that the frequency of birth defects among children of residents of the Red River Valley (RRV), Minnesota, USA, was significantly higher than in other major agricultural regions of the state during the years 1989-1991, with children born to male pesticide applicators having the highest risk. The present, smaller cross-sectional study of 695 families and 1,532 children, conducted during 1997-1998, provides a more detailed examination of reproductive health outcomes in farm families ascertained from parent-reported birth defects. In the present study, in the first year of life, the birth defect rate was 31.3 births per 1,000, with 83% of the total reported birth defects confirmed by medical records. Inclusion of children identified with birth or developmental disorders within the first 3 years of life and later led to a rate of 47.0 per 1,000 (72 children from 1,532 live births). Conceptions in spring resulted in significantly more children with birth defects than found in any other season (7.6 vs. 3.7%). Twelve families had more than one child with a birth defect (n = 28 children). Forty-two percent of the children from families with recurrent birth defects were conceived in spring, a significantly higher rate than that for any other season. Three families in the kinships defined contributed a first-degree relative other than a sibling with the same or similar birth defect, consistent with a Mendelian inheritance pattern. The remaining nine families did not follow a Mendelian inheritance pattern. The sex ratio of children with birth defects born to applicator families shows a male predominance (1.75 to 1) across specific pesticide class use and exposure categories exclusive of fungicides. In the fungicide exposure category, normal female births significantly exceed male births (1.25 to 1). Similarly, the proportion of male to female children with birth defects is significantly lower (0.57 to 1; p = 0.02). Adverse neurologic and neurobehavioral developmental effects clustered among the children born to applicators of the fumigant phosphine (odds ratio [OR] = 2.48; confidence interval [CI], 1.2-5.1). Use of the herbicide glyphosate yielded an OR of 3.6 (CI, 1.3-9.6) in the neurobehavioral category. Finally, these studies point out that a) herbicides applied in the spring may be a factor in the birth defects observed and b) fungicides can be a significant factor in the determination of sex of the children of the families of the RRV. Thus, two distinct classes of pesticides seem to have adverse effects on different reproductive outcomes. Biologically based confirmatory studies are needed.

Garry,V.F., M.E.Harkins, A.Lyubimov, L.Erickson, and L.Long. 2002. "Reproductive outcomes in the women of the Red River Valley of the north. I. The spouses of pesticide applicators: pregnancy loss, age at menarche, and exposures to pesticides." Journal of Toxicology & Environmental Health - Part A. 65:769-786.

Abstract: In the current study, there was a modest but significant increase in risk (1.6- to 2-fold) for miscarriages and/or fetal loss occurring throughout the year in the spouses of applicators who use fungicides. There is a surprisingly significant deficit in the number of male children born to the spouses of fungicide applicators. First-trimester miscarriages occur most frequently in the spring, during the time when herbicides are applied. Use of sulfonylurea (odds ratio OR = 2.1), imidizolinone (OR = 2.6) containing herbicides, and the herbicide combination Cheyenne (OR = 2.9) by male applicators was statistically associated with increased miscarriage risk in the spring. Limited survey data from women who are the spouses of applicators did not show major alterations of long-term endocrinologic status (menarche, menopause, endometriosis). With regard to personal pesticide exposures, only women who engaged in pesticide application where there is direct exposure to these products are at demonstrable risk (OR = 1.8) for miscarriage. It was hypothesized that the overall reproductive toxicity observed in this population is, for the greater part, a male-mediated event. Clarification of exposure events leading to reproductive toxicity through direct measurements of exposure in both men and women is needed to resolve this issue.

George,J.D., P.A.Fail, T.B.Grizzle, R.S.H.Yan, and J.J.Heindel. 1993. "Reproductive toxicity evaluation of a pesticide/fertilizer mixture administered in the drinking water to mice." Toxicologist. 13:77.
Abstract: need abstract

Gonzalez,M., K.S.Miglioranza, J.E.Aizpun de Moreno, and V.J.Moreno. 2003. "Occurrence and distribution of organochlorine pesticides (OCPs) in tomato (Lycopersicon esculentum) crops from organic production." J.Agric.Food Chem. 51:1353-1359.
Abstract: Organochlorine pesticides (OCPs) were quantified by GC-ECD in tomato (Lycopersicon esculentum) during a vegetation period. Plants were harvested at 15, 60, and 151 days after seed germination. Leaves, stem, roots, and fruit (peel and flesh) were analyzed separately. The results showed that tomato plants were able to accumulate OCPs from soils, and a trend to reach the equilibrium among tissues at mature stages was also observed. Endosulfans comprised the main OCP group, probably due to its spray during summer months in the surrounding areas. Banned pesticides such as DDTs, heptachlor, and dieldrin were found. OCPs levels in the fruit were below the maximum residues limits (MRL) considered by the Codex Alimentarius. DDE/DDT and alpha-/gamma-HCH ratios of <1 would indicate recent inputs of DDT and lindane in the environment. The occurrence of OCPs in the study farm, where agrochemicals have never been used, is a result of atmospheric deposition of those pesticides

Graham,S. 1993. "Toward a dietary prevention of cancer." Epidemiol Rev. 5:38-50.
Abstract: I have attempted to address in brief fashion the question as to whether we can recommend a dietary prevention of cancer. This same question was explored in hundreds of pages recently by the large number of advisors assembled by the National Academy of Sciences to assess the animal, cell culture, and human data with regard to diet and cancer (52). My brief assessment has resulted in recommendations to the scientific community not unlike those of the National Academy, but without their clear-cut recommendation

against dietary fat. It is obvious that we need a great deal more research on the factors evaluated here, that is, fiber, ascorbic acid, retinoids, the cruciferae, nitrates, alcohol, coffee, saccharine, alpha-tocopherol, aflatoxins, selenium, and saturated and polyunsaturated fats. These factors need assessment not only as they might affect the incidence of any single cancer, but also in relationship to at least the incidence of the cancers that frequently occur in humans. The human epidemiologic inquires have barely begun. We have a few studies of cancer of the colon and of cancer of the lung, and only one or two studies of such important sites as cancer of the larynx, oropharynx, stomach, and breast. Not only have the studies of specific sites been lamentably too few, but only a small number of nutrients have been evaluated. To make matters worse, we have little notion as to the competing risk of different cancers and of other diseases associated with various nutrients. There may be factors that enhance the risk of some diseases at the same time they reduce the risk of others. It is not outside the realm of possibility that the relationship discovered to date with regard to serum cholesterol, heart disease, and cancer may continue to be replicated and may be found related to ingestion of dietary fats. If such should be the case, and the potential is there, we would need to weigh the risks associated with reducing dietary fats for cancer as well as for coronary disease. Questions will need to be answered. For example, what is the optimum level of serum cholesterol to lower the risk of heart disease and at the same time not to enhance the risk of cancer. The same may be said for the association of alcohol with the risk of coronary disease compared to the risk of cancer of the upper alimentary tract.

Gray,G.M. and J.K.Hammitt. 2000. "Risk/risk trade-offs in pesticide regulation: an exploratory analysis of the public health effects of a ban on organophosphate and carbamate pesticides." Risk Anal. 20:665-680.
Abstract: Efforts to reduce pesticide-related risks to consumers and farmworkers often neglect the possibility that measures to reduce the target risk may introduce or enhance countervailing risks. These may arise from substitute pesticides or pest-control practices, from increased levels of pests or pest-related hazards, from increased levels of toxic natural pesticides in plants, from increased costs and decreased consumption of health-enhancing fruits and vegetables, or from direct income effects on consumers and farmers. The effect of the countervailing risks may partially or completely offset the reduction in the target risk. A risk-trade-off analysis was conducted of a potential ban on the use of organophosphate and carbamate (OP/Carbamate) insecticides in U.S. agriculture. Although this scenario is extreme, it has the analytic virtue of dispensing with the infinite number of "next-best" OP/Carbamates that might be substituted for specific combinations of crops and pests should only selected uses be banned. The analysis relies on detailed descriptions of the alternative pesticides and pest-control measures that would be used for each of 14 major crops. The effects of pest-control cost changes on prices and consumption and effects on consumer and producer incomes are projected using a general-equilibrium economic model. Several countervailing risks that may be significant were found, including acute toxicity to farmworkers from substitute pesticides, cancer and noncancer risks from substitute pesticides, and mortality induced by changes in disposable income. Other countervailing risks are more difficult to estimate or weigh. Potential increases in natural plant pesticides following an OP/Carbamate ban are discussed but data are lacking to quantify the effects. Changes in diet following the ban

have both positive and negative effects, and the ultimate change is difficult to estimate. Although a net risk cannot be estimated, several approaches were illustrated that would be useful in risk-trade-off analyses. Key factors complicating comprehensive analysis of risk/risk trade-offs for pesticides were also identified, including data gaps and shortcomings of current risk assessment methods

Gray,L.E., J.Ostby, J.Furr, C.J.Wolf, C.Lambright, L.Parks, D.N.Veeramachaneni, V.Wilson, M.Price, A.Hotchkiss, E.Orlando, and L.Guillette. 2001. "Effects of environmental antiandrogens on reproductive development in experimental animals." Hum.Reprod Update. 7:248-264.
Abstract: Chemicals that act as androgen receptor (AR) agonists and antagonists or inhibit fetal steroidogenesis can induce reproductive malformations in humans and laboratory animals. Several environmental chemicals disrupt development in rats and/or rabbits at fetal concentrations at, or near, exposure levels seen in some segments of the human population. In rats, fetal tissues concentrations of 10-20 p.p.m. of the DDT metabolite, p,p'-DDE, are correlated with reproductive abnormalities in male offspring. These concentrations are similar to those measured in first-trimester human fetal tissues in the late 1960s. The pesticides vinclozolin, procymidone, linuron and DDT are AR antagonists. They reduce male rat anogenital distance, and induce areolas at relatively low dosages. Hypospadias, agenesis of the sex accessory tissues and retained nipples are seen in the middle dosages, while undescended testes and epididymal agenesis are seen in the highest doses. Phthalate esters (PE) inhibit testosterone synthesis during fetal life, but do not appear to be AR antagonists. Prenatal administration of a single low dose of dioxin (50-1,000 ng TCDD/kg) alters the differentiation of androgen-dependent tissues at p.p.t. concentrations, but the mechanism of action likely involves interaction with a hormone-like nuclear transcription factor, the hormone-like receptor AhR, rather than AR. p,p'-DDT and p,p'-DDE, vinclozolin and di-n-butyl phthalate affect reproductive function in rabbits when administered during prenatal and/or neonatal life. Cryptorchidism and carcinoma in situ-like (CIS) testicular lesions were seen in male rabbits treated during development with p,p'-DDT or p,p'-DDE. Extrapolation of effects from rodents to humans would be enhanced if future studies incorporate determination of tissue concentrations of the active metabolites. Knowledge of the tissue concentrations of the active toxicants also would provide an important link to in-vitro studies, which provide more useful mechanistic information when they are executed at relevant concentrations

Gray,L.E., Jr. and J.Ostby. 1998. "Effects of pesticides and toxic substances on behavioral and morphological reproductive development: endocrine versus nonendocrine mechanisms." Toxicol.Ind.Health. 14:159-184.
Abstract: Exposure to toxic substances or pesticides during critical perinatal developmental periods can alter reproductive and central nervous system (CNS) function in a manner that does not compromise the growth and viability of the fetus but causes functional alterations that become apparent later in life. While some "CNS/behavioral teratogens" are mutagenic or alter cell division, other chemicals produce alterations of CNS development via endocrine-mediated mechanisms. The following discussion will focus on studies conducted primarily in our laboratory that describe how pesticides and toxic substances alter development of the reproductive and central nervous systems as a

consequence of organizational or activational exposures. Abnormal behavior and morphology can result from exposure to endocrine-disrupting toxicants by altering organization of the CNS during critical stages of life or activation of behavior after puberty. Some of the toxicants that alter rodent sexual differentiation include xenoestrogens, antiandrogenic pesticides, and dioxin-like toxic substances. Chemicals that alter sex-linked nonreproductive and reproductive CNS development via nonhormonal mechanisms are also discussed in order to demonstrate that multiple mechanisms of action are involved in the development of behavioral abnormalities in pre- and perinatally exposed offspring. The fact that reproductive function (behavioral, biochemical, and morphological) can be altered via such a wide variety of mechanisms indicates that hazard identification in this area cannot rely solely on the detection of endocrine activity

Gray,L.E., Jr., J.Ostby, R.L.Cooper, and W.R.Kelce. 1999. "The estrogenic and antiandrogenic pesticide methoxychlor alters the reproductive tract and behavior without affecting pituitary size or LH and prolactin secretion in male rats." Toxicol.Ind.Health. 15:37-47.
Abstract: This study was designed to determine if long-term exposure to high doses of methoxychlor (M) would alter pituitary or testicular endocrine functions in either an estrogenic or antiandrogenic manner. Weanling male Long-Evans hooded rats were dosed daily with M (po) at 0, 200, 300, or 400 mg kg-1 day-1 for 10 months. Methoxychlor treatment delayed puberty by as much as 10 weeks and reduced fertility and copulatory plug formation in a dose-related manner at the initial mating. During mating, M-treated males exhibited shorter latencies to mount and ejaculate versus control males, but the number of intromissions prior to ejaculation was unaffected, indicating that M enhanced the arousal level in the males in an estrogen-dependent manner. Most treated males eventually mated but time-to-pregnancy was lengthened. Very low sperm counts were associated with infertility, while prolonged delays in puberty reduced fecundity. Methoxychlor treatment with 200 to 400 mg kg-1 day-1 failed to mimic the chronic effects of a sustained (8 months) low dose of estradiol-17 beta (3-mm silastic implants) on pituitary or testicular hormone levels. Estradiol administration increased pituitary weight 4-fold, serum levels of luteinizing hormone (LH) were reduced by almost 50%, and serum prolactin was increased 40-fold, while M did not affect any of these measures. These data demonstrate that M affects the CNS, epididymal sperm numbers, and the accessory sex glands and delays mating without significantly affecting the secretion of LH, prolactin, or testosterone. These data indicate that M did not alter pituitary endocrine function in either an estrogenic or antiandrogenic manner. To our knowledge, these data provide the first in vivo example of such a pronounced degree of target tissue selectivity to an environmental endocrine-disrupting chemical

Gray,L.E., Jr., J.Ostby, E.Monosson, and W.R.Kelce. 1999. "Environmental antiandrogens: low doses of the fungicide vinclozolin alter sexual differentiation of the male rat." Toxicol.Ind.Health. 15:48-64.
Abstract: In humans and rodents, exposure to antiandrogenic chemicals during sexual differentiation can produce malformations of the reproductive tract. Perinatal administration of 100 or 200 mg vinclozolin (V) kg-1 day-1 during sexual differentiation

in rats induces female-like anogenital distance (AGD), retained nipples, cleft phallus with hypospadias, suprainguinal ectopic scrota/testes, a vaginal pouch, epididymal granulomas, and small to absent sex accessory glands in male offspring. Vinclozolin is metabolized to at least two active forms, M1 and M2, that display antiandrogenic activity by binding the androgen receptor (AR). Here, we present information on the reproductive effects of oral treatment with low dosage levels of V during sexual differentiation of the male rat. Vinclozolin was administered to the dam at 0, 3.125, 6.25, 12.5, 25, 50, or 100 mg kg-1 day-1 from gestational day 14 to postnatal day 3 (the period of fetal/neonatal testicular testosterone synthesis and sexual differentiation). At doses of 3.125 mg V kg-1 and above, AGD was significantly reduced in newborn male offspring and the incidence of areolas was increased. These effects were associated with permanent alterations in other androgen-dependent tissues. Ventral prostate weight in one year old male offspring was reduced in all treatment groups (significant at 6.25, 25, 50, and 100 mg kg-1 day-1), and permanent nipples were detected in males at 3.125 (1.4%), 6.25 (3.6%), 12.5 (3.9%), 25 (8.5%), 50 (91%), and 100 (100%) mg V kg-1 day-1. To date, permanent nipples have not been observed in a control male from any study in our laboratory. Vinclozolin treatment at 50 and 100 mg kg-1 day-1 induced reproductive tract malformations and reduced ejaculated sperm numbers and fertility. Even though all of the effects of V likely result from the same initial event (AR binding), the different endpoints displayed a wide variety of dose-response curves and ED50's. The dose-response data for several of the functional endpoints failed to display an obvious threshold. These data demonstrate that V produces subtle alterations in sexual differentiation of the external genitalia, ventral prostate, and nipple tissue in male rat offspring at dosage levels below the previously described no-observed-effect-level (NOEL). These effects occur at a dosage level an order of magnitude below that required to induce malformations and reduce fertility. Hence, multigenerational reproduction studies of antiandrogenic chemicals that were not conducted under the Environmental Protection Agency's new Harmonized Multigenerational Test Guidelines, which include endpoints sensitive to antiandrogens at low dosage levels, could yield a NOEL that is at least an order of magnitude too high

Greene,A. Opportunities to Reduce Children's Exposures to Pesticides: A Truly Grand Challenge. Presented at the 2006 annual meeting of the AAAS . 6 A.D. The Organic Center.
Ref Type: Generic

Greenlee,A.R., T.E.Arbuckle, and P.H.Chyou. 2003. "Risk factors for female infertility in an agricultural region." Epidemiology. 14:429-436.
Abstract: BACKGROUND: Recent studies have suggested that agricultural occupations or exposure to pesticides may impair female fertility. METHODS: The Fertility Risk Factor Study retrospectively examined agricultural and residential exposures and the risk of female infertility. Cases and controls (N = 322 each) came from women who sought treatment at a large group medical clinic in Wisconsin. Women and their male partners provided information on health, occupational and lifestyle exposures in response to a telephone interview during 1997-2001. RESULTS: Mixing and applying herbicides 2 years before attempting conception was more common among infertile women (odds ratio [OR] = 27; 95% confidence interval [CI] = 1.9-380), as was the use of fungicides

(OR = 3.3; CI = 0.8-13). Residing on a farm, ranch or in a rural area during this time period was protective of female fertility. Households supplied with central Wisconsin groundwater were at less risk for infertility than households using municipal sources (OR = 0.6; CI = 0.4-0.9). Behavioral risk factors included alcohol consumption (OR = 1.8; 1.2-2.5), smoking (1.6; 0.9-2.9), passive smoke exposure (1.8; 1.2-2.5), steady weight gain in adult life (3.5; 2.0-6.1), and having a male partner over the age of 40 (4.5; 1.2-16.3). Drinking 3 or more glasses of milk per day was protective of female fertility (0.3; 0.1-0.7). CONCLUSION: These results suggest that certain agricultural, residential and lifestyle choices may modify the risk of female infertility.

"Women's exposure to herbicides at any time during the 2-year period before trying to conceive was associated with an increased risk of infertility (albeit imprecise due to small numbers).... Use of fungicides by either partner in the 20year period prior to attempting conception was also associated with a risk of female infertility.... Living on a farm, ranch or in a rural home before trying to conceive was associated with a reduced risk of infertility. ....
"eHouseholds supplied with central Wisconsin groundwater from private wells were found to be at less risk for infertility than were those households using municipal sources (Table 3). Drinking 3 or more glasses of milk per day was protective against female infertility." (p. 433)

Groth,E., C.M.Benbrook, and Benbrook K.L. Pesticide Residues in Children's Food. Consumers Union of the United States. 2000. Yonkers, NY.
Ref Type: Report

Guillette,E.A., M.M.Meza, M.G.Aquilar, A.D.Soto, and I.E.Garcia. 1998. "An anthropological approach to the evaluation of preschool children exposed to pesticides in Mexico." Environ.Health Perspect. 106:347-353.
Abstract: In this comparative study, we compensated for many of the known variables that influence children's growth and development by selecting two groups of 4-5-year-old Yaqui children who reside in the Yaqui Valley of northwestern Mexico. These children share similar genetic backgrounds, diets, water mineral contents, cultural patterns, and social behaviors. The major difference was their exposure to pesticides. Pesticides have been applied to the agricultural area of the valley since the late 1940s. In 1990, high levels of multiple pesticides were found in the cord blood of newborns and in breast milk. Building on anthropological methods for rapid rural appraisal of problems within the environment, a Rapid Assessment Tool for Preschool Children (RATPC) was developed to measure growth and development. The children of the agrarian region were compared to children living in the foothills, where pesticide use is avoided. The RATPC measured varied aspects of physical growth and abilities to perform, or function in, normal childhood activities. No differences were found in growth patterns. Functionally, the exposed children demonstrated decreases in stamina, gross and fine eye-hand coordination, 30-minute memory, and the ability to draw a person. The RATPC also pointed out areas in which more in-depth research on the toxicology of pesticides would be valuable

Hansen,L.G. 2002. "Persistent organic pollutants in food supplies." Journal of Epidemiology and Community Health. 56:820-821.
Abstract: Persistent organic pollutants (POPs) in various food supplies have important health impacts, but are not as devastating as malnutrition and, perhaps, obesity. POPs should be controlled and the Stockholm Convention is having an accelerating effect on the global decline of POP manufacture and use. Reservoirs from previous misuses are much larger than current manufacture and efforts should be directed at containing these reservoirs, tackling food shortages, and continuing to educate toward following advisories and maintaining a varied diet and food sources

Hardell,L. and M.Eriksson. 1981. "Soft-tissue sarcomas, phenoxy herbicides, and chlorinated phenols." Lancet. 2:250.

Hardell,L., G.Liljegren, G.Lindstrom, B.Vanbavel, K.Broman, M.Fredrikson, H.Hagberg, M.Nordstrom, and B.Johansson. 1996. "Increased concentrations of chlordane in adipose tissue from non-Hodgkins lymphoma patients compared with controls without a malignant disease." International Journal of Oncology. 9:1139-1142.
Abstract: Chlordane is a pesticide which is lipophilic, bioaccumulates, and may cause immunological impairment in exposed subjects. The aim of this study was to determine the concentrations of chlordane and its metabolites in cases with NHL and surgical controls without a malignant disease. Adipose tissue was obtained from the abdominal wall and analysis was performed using gas chromatograph coupled to mass spectrometer. The study included 27 NHL cases of the B-cell type and 17 controls. Significantly increased concentrations were found in NHL patients versus (vs) controls of trans-nonachlor, mean 98.9 vs 47.0, range 24.9-389 vs 16.3-88.2 ng/g lipid ($p = 0.002$), cis-nonachlor, mean 17.1 vs 7.4, range 4.1-68.3 vs 1.7-13.6 ($p = 0.010$), oxy-chlordane, mean 39.7 vs 24.5, range 8.5-144 vs 8.9-49.0, ($p = 0.028$) nonachlor III, mean 18.4 vs 8.7, range 6.3-67.6 vs 3.0-19.3 ($p = 0.002$) and sum of chlordanes, 180 vs 92.8, range 48.3-678 vs 37.0-164 ng/g lipid ($p = 0.002$). For cases with a concentration higher than the median for all subjects significantly increased odds ratios (OR) and 95% confidence intervals (CI) were calculated for trans-nonachlor (OR = 4.1, CI = 1.1-15), nonachlor LII (OR = 6.5, CI = 1.7-25), and sum of chlordanes (OR = 4.1, CI = 1.1-15); median concentrations were 61.2, 11.3, and 119 ng/g lipid, respectively. [References: 40]

Hardell,L. and M.Eriksson. 1999. "A case-control study of non-Hodgkin lymphoma and exposure to pesticides." Cancer. 85:1353-1360.
Abstract: BACKGROUND: The incidence of non-Hodgkin lymphoma (NHL) has increased in most Western countries during the last few decades. Immunodefective conditions are established risk factors. In 1981, the authors reported an increased risk for NHL following exposure to certain pesticides. The current study was designed to further elucidate the importance of phenoxyacetic acids and other pesticides in the etiology of NHL. METHODS: A population-based case-control study in northern and middle Sweden encompassing 442 cases and twice as many controls was performed. Exposure data were ascertained by comprehensive questionnaires, and the questionnaires were supplemented by telephone interviews. In total, 404 cases and 741 controls answered the questionnaire. Univariate and multivariate analyses were performed with the SAS

statistical data program. RESULTS: Increased risk for NHL was found for subjects exposed to herbicides (odds ratio [OR], 1.6; 95% confidence interval [CI], 1.0-2.5) and fungicides (OR, 3.7; 95% CI, 1.1-13.0). Among herbicides, the phenoxyacetic acids dominated (OR, 1.5; 95% CI, 0.9-2.4); and, when subclassified, one of these, 4-chloro-2-methyl phenoxyacetic acid (MCPA), turned out to be significantly associated with NHL (OR, 2.7; 95% CI, 1.0-6.9). For several categories of herbicides, it was noted that only exposure during the most recent decades before diagnosis of NHL was associated with an increased risk of NHL. Exposure to impregnating agents and insecticides was, at most, only weakly related to NHL. CONCLUSIONS: Exposure to herbicides in total, including phenoxyacetic acids, during the decades before NHL diagnosis resulted in increased risk for NHL. Thus, the risk following exposure was related to the latency period. Fungicides also increased the risk for NHL when combined, but this group consisted of several different agents, and few subjects were exposed to each type of fungicide

Hardell,L., M.Eriksson, and M.Nordstrom. 2002. "Exposure to pesticides as risk factor for non-Hodgkin's lymphoma and hairy cell leukemia: pooled analysis of two Swedish case-control studies." Leuk.Lymphoma. 43:1043-1049.
Abstract: Increased risk for non-Hodgkin's lymphoma (NHL) following exposure to certain pesticides has previously been reported. To further elucidate the importance of phenoxyacetic acids and other pesticides in the etiology of NHL a pooled analysis was performed on two case-control studies, one on NHL and another on hairy cell leukemia (HCL), a rare subtype of NHL. The studies were population based with cases identified from cancer registry and controls from population registry. Data assessment was ascertained by questionnaires supplemented over the telephone by specially trained interviewers. The pooled analysis of NHL and HCL was based on 515 cases and 1141 controls. Increased risks in univariate analysis were found for subjects exposed to herbicides (OR 1.75, CI 95% 1.26-2.42), insecticides (OR 1.43, CI 95% 1.08-1.87), fungicides (OR 3.11, CI 95% 1.56-6.27) and impregnating agents (OR 1.48, CI 95% 1.11-1.96). Among herbicides, significant associations were found for glyphosate (OR 3.04, CI 95% 1.08-8.52) and 4-chloro-2-methyl phenoxyacetic acid (MCPA) (OR 2.62, CI 95% 1.40-4.88). For several categories of pesticides the highest risk was found for exposure during the latest decades before diagnosis. However, in multivariate analyses the only significantly increased risk was for a heterogeneous category of other herbicides than above

Heindel,J.J., R.E.Chapin, D.K.Gulati, J.D.George, C.J.Price, M.C.Marr, C.B.Myers, L.H.Barnes, P.A.Fail, T.B.Grizzle, B.A.Schwetz, and R.S.H.Yang. 1994. "Assessment of the reproductive and developmental toxicity of pesticide/fertilizer mixtures based on confirmed pesticide contamination in California and Iowa groundwater." Fundamental & Applied Toxicology. 22:605-621.
Abstract: Pesticides and fertilizers, as used in modern agriculture, contribute to the overall low-level contamination of groundwater sources. In order to determine the potential of pesticide and fertilizer mixtures to produce reproductive or developmental toxicity at concentrations up to 100 x the median level found in groundwater, we prepared and studied two mixtures of pesticides and a fertilizer (ammonium nitrate). One mixture containing aldicarb, atrazine, dibromochloropropane, 1,2-dichloropropane,

ethylene dibromide, and simazine plus ammonium nitrate was considered to be a representative of groundwater contamination in California (CAL). The other, containing of either Swiss CD-1 mice during a Reproductive Assessment by Continuous Breeding study or pregnant Sprague-Dawley rats (gd 6-20) at three dose levels (1x, 10x, and 100x) where 1x was the median concentration of each pesticide component as determined in the groundwater surveys in California or Iowa. Unlike conventional toxicology studies, the purpose of this study was to evaluate the health effects of realistic human concentrations. Thus, the testing concentrations are probably well below the maximally tolerated dose. Propylene glycol was used as the solubilizer for the pesticides in drinking water formulations in both studies. In the reproductive study, neither mixture caused any clinical signs of toxicity, changes in food or water consumption, or body weight in either F0 or F1 mice at doses up to 100x the median groundwater concentrations. There were no treatment-related effects on fertility or any measures of reproductive performance of either the F0 or the F1 generation mice exposed to either CAL or IOWA at up to 100x. Similarly, measures of spermatogenesis, epididymal sperm concentration, percentage motile sperm, percentage abnormal sperm, and testicular and epididymal histology were normal. In the developmental study, CAL- or IOWA-exposed females did not exhibit any significant treatment-related clinical signs of toxicity. No adverse effects of CAL or IOWA were observed for measures of embryo/fetal toxicity, including resorptions per litter, live litter size, or fetal body weight. CAL or IOWA did not cause an increased incidence of fetal malformations or variations. In summary, administration of these pesticide/fertilizer mixtures at levels up to 100-fold greater than the median concentrations in groundwater supplies in California or Iowa did not cause any detectable reproductive (mice), general, or developmental toxicity (rats).

Hill,R.K., S.L.Head, S.Baker, M.Gregg, D.B.Shealy, S.L.Bailey, C.Williams, E.J.Sampson, and L.Needham. Pesticide Residues in Urine of Adults Living in the United States: Reference Range Concentrations. Environmental Research 71, 99-108. 1995.
Ref Type: Generic

Jaga,K. and H.Duvvi. 2001. "Risk reduction for DDT toxicity and carcinogenesis through dietary modification." J R.Soc.Health. 121:107-113.
Abstract: Organochlorine pesticides, including dichlorodiphenyltrichloroethane (DDT), are an environmental hazard due to their persistent nature and potential health effects. DDT and 1,1,dichloro-2,2,bis(p-chlorophenyl)ethylene (DDE) are lipid-soluble pesticides which accumulate in fatty tissues and are, therefore, more present in fat-containing foods such as meat, fish, milk, cheese and oil than in fruit, vegetables and grain. Scientists have for some time been concerned about the human exposure to DDT and the potential risk of breast cancer due to its oestrogenic activity. The introduction of foods containing chemopreventive agents in the diet could inhibit the oestrogenic effects of DDT and the risk of developing cancer. Phytooestrogens are weak oestrogens found in certain plants such as soybean. They compete with DDT for oestrogen receptors and inhibit the oestrogenic effect of DDT on cultured human breast (MCF) cells. Curcumin, a spice widely used in Indian dishes, has anti-carcinogenic and anti-inflammatory properties. It also inhibits the oestrogenic effects of DDT and is synergistic with phytooestrogens.

Indole-3-carbinol, a compound naturally found in cruciferous vegetables, stimulates oestrogen metabolism towards 2-hydroxyoestrone which reduces the oestrogenic response in MCF cells and the risk of breast cancer. Since DDT is lipid soluble and accumulates in adipose tissue it could have a role in lipid metabolism. Would a low fat diet reduce DDT bioaccumulation? A reduction in calories can decrease oestrogen levels and possibly reduce the risk of breast cancer. A dietary modification with the introduction of soy products, curcumin, cruciferous vegetables and low fat could be beneficial in reducing the risk of developing cancer and possibly the effects of DDT

Jedrychowski,W., R.M.Whyatt, D.E.Camann, U.V.Bawle, K.Peki, J.D.Spengler, T.S.Dumyahn, A.Penar, and F.F.Perera. 2003. "Effect of prenatal PAH exposure on birth outcomes and neurocognitive development in a cohort of newborns in Poland. Study design and preliminary ambient data." Int J Occup.Med Environ.Health. 16:21-29. Abstract: Preliminary data suggest an association between infant mortality rates and several measures of ambient air pollution, including dustfall and polycyclic aromatic hydrocarbons (PAH). The effects of airborne PAH components on fetal growth and early childhood development are of primary interest since we have previously demonstrated that these pollutants were associated with significant decrements in birthweight, length and head circumference in Polish newborn babies. The undertaken research combines a state-of-the-art environmental monitoring and molecular approaches with comprehensive neurodevelopment assessments. A further innovation is the incorporation of biomarkers (lead and antioxidants in cord blood) to control for potential confounding of exposure-effect. The mean overall concentrations of specific PAH compounds in Krakow were highest for benzo(b)fluoranthene (23 ng/m3), benzo(a)anthracene (16 ng/m3), indeno(l,2,3-cd)pyrene (14 ng/m3), chyresene (13 ng/m3) and benzo(a)pyrene (12 ng/m3). In general, concentrations of the PAH compounds measured by personal monitoring were considerably higher among the residents of the higher polluted area of the city. The comparison between the Krakow and New York City monitoring ambient data demonstrates that the concentrations and proportions of specific compounds in the total PAH mixture differ widely across these cities. Thus, one may expect that the PAH-related health risks would differ between the two areas not only because exposures are different, but also because the PAH profile differs. Presumably, this different profile is a consequence, at least in part, of variations in the sources of fossil and solid fuels used in production of energy. In Poland, solid fuels such as coal is used to a much greater extent than in New York City, where fossil fuels are the universal source of energy production. Auto emissions for example, are low in benzo(a)pyrene, whereas such emissions from refuse burning are high

Jensen,T.K., E.Carlsen, N.Jørgensen, J.G.Berthelsen, N.Keiding, K.Christensen, J.H.Petersen, L.B.Knudsen, and N.E.Skakkebaek. 2002. "Poor semen quality may contribute to recent decline in fertility rates." Human Reproduction. 17:1437-1440. Abstract: During past decades, we have witnessed a remarkable decline in fertility rates (number of births per 1000 women of reproductive age) in the industrialized world. It seems beyond doubt that the enormous social changes of our societies play the major role in this decline, but can it be attributed to changing social structures alone or is a reduced fecundity in the population also a factor? To address this we have focused on trends in

teenage pregnancies (which to a large extent are unplanned). During the period in question fertility rates among 15- 19 year old Danish women have been falling and the decline in fertility rate is not counterbalanced by an increase in the rate of induced abortion. When seen together with recent results from Denmark, which have shown that more than 30% of 19 year old men from the general population now have sperm counts in the subfertile range, we argue that this fall may not be attributable to social factors, changes in conception practices or diminished sexual activity alone. It seems reasonable also to consider widespread poor semen quality among men as a potential contributing factor to low fertility rates among teenagers. Due to the concern caused by the low sperm count among younger Danish men, the Danish Ministries of Health and Environment have launched a surveillance programme which includes an annual examination of the semen quality in 600 young Danes from the general population. We propose that researchers in other countries with low and falling fertility rates among young women should consider the possibility that semen quality of their younger male cohorts may also have deteriorated.

Jensen,W.D., A.Giwercman, E.Carlsen, T.Scheike, and N.E.Skakkebaek. 1996. "Semen quality among members of organic food associations in Zealand, Denmark." Lancet. 347:1844.
Abstract: Those men eating organically grown food had sperm concentrations 43.1% higher than controls. Seminal volume, total sperm count, and sperm morphology were not statistically significant. Organic: mean 99 million/ml; median 69 million/ml. Controls: mean 69.2 million/ml; median 48.0 million/ml. Confounders and significance discussed

Juhler,R.K., S.B.Larsen, O.Meyer, N.D.Jensen, M.Spano, A.Giwercman, and J.P.Bonde. 1999. "Human semen quality in relation to dietary pesticide exposure and organic diet." Archives of Environmental Contamination & Toxicology. 37:415-423.
Abstract: The objective of the study was to corroborate or refute the hypothesis that farmers having a high intake of organic grown commodities have a high semen quality due to their expected lower level of dietary pesticides intake. Food frequency data and semen were collected from 256 farmers (171 traditional farmers and 85 organic farmers, overall participation rate: 32%) who were selected from central registers. Each farmer delivered one semen sample before the spraying season started. The farmers were divided into three groups where the commodities from organic production contributed no (N, 0%), medium (M, 1-49%), or a high (H, 50-100%) proportion of the fruit and vegetables consumed. Farmers having a high relative intake of organically grown fruit and vegetables also had a high relative consumption of organically produced meat, milk, and bread, and differences were observed comparing the actual mean intake of single commodities, such as rice, potato, and pork meat. The current individual dietary intake of 40 pesticides was estimated using food frequencies and generalized serving size data in combination with data on pesticide concentrations in food commodities as obtained from the National Danish Food Monitoring Program. The estimated pesticide intake was significantly lower among farmers of group H, but for all three groups of farmers the average dietary intake of 40 pesticides was at or below 1% of the acceptable daily intake (ADI) except for the dithiocarbamates (max = 0.21 mu g/kg day = 2.2% ADI), methidathion, (max = 0.01 mu g/kg day = 1.4% ADI), and 2-phenylphenol (max = 0.21

mu g/kg day = 1.1% ADI). The median sperm concentration for the three groups of farmers was not significantly different (p = 0.40, median sperm concentration was N = 62, M = 44, and H = 75 million/ml). The group of men without organic food intake had a significant lower proportion of morphologically normal spermatozoa, but in relation to 14 other semen parameters no significant differences were found between the groups. Intake of 40 individual pesticides was correlated with four semen parameters (concentration, percentage dead spermatozoa, percentage normal sperm heads, and motility [VCL]). Five significant correlations (p value 0.01) were found among the 160 comparisons in relation to percentage dead spermatozoa: azin-phos-methyl, carbaryl, chlorfenson, fenitrothion, and tetradifon. For all of them a lower percentage of dead spermatozoa were found in the groups with a high dietary intake of the specific pesticide. In contrast, for all pesticides evaluated only minor differences were found between the groups when considering spermatozoa concentration, morphology, and motility. In conclusion the estimated dietary intake of 40 pesticides did not entail a risk of impaired semen quality, but precautions should be taken when generalizing this negative result to populations with a higher dietary exposure level or an intake of other groups of pesticides.

Kishi,M. 2002. "Farmers' perceptions of pesticides, and resultant health problems from exposures." Int.J.Occup.Environ.Health. 8:175-181.
Abstract: As part of an evaluation study of the impacts of the Indonesian integrated pest management (IPM) Farmer Field Schools on farmers' health, focus group discussions were conducted with rice farmers who grew shallots in rotation. Farmers who had previously participated in IPM rice field schools and who were at the time participating in IPM shallot field schools were compared with farmers who had had no experience with IPM methods. The study found that farmers' knowledge concerning the health dangers of pesticides is not sufficient to change their behaviors. Their overriding concern is crop damage that leads to economic loss, not health. IPM field-school training offers farmers a viable alternative by concretely demonstrating the health, agricultural, environmental, and economic advantages of eliminating unnecessary pesticide use. If public health professionals aim to change behaviors through interventions, they must employ appropriate methods, meet the community's priorities and values, and offer feasible alternatives

Knox,K. OPP Results Indicators. [Pesticide Program Dialogue Committee Report]. 2005. U.S. Environmental Protection Agency.
Ref Type: Generic

Koch,D., C.Lu, J.Fisker-Andersen, L.Jolley, and R.A.Fenske. 2002. "Temporal association of children's pesticide exposure and agricultural spraying: report of a longitudinal biological monitoring study." Environ.Health Perspect. 110:829-833.
Abstract: We measured organophosphorus (OP) pesticide exposures of young children living in an agricultural community over an entire year and evaluated the impact of agricultural spraying on exposure. We also examined the roles of age, sex, parental occupation, and residential proximity to fields. We recruited 44 children (2-5 years old) through a Women, Infants, and Children clinic. We collected urine samples on a biweekly basis over a 21-month period. Each child provided at least 16 urine samples,

and most provided 26. We analyzed samples for the dialkylphosphate (DAP) metabolites common to the OP pesticides. DAP concentrations were elevated in months when OP pesticides were sprayed in the region's orchards. The geometric means of dimethyl and diethyl DAPs during spray months were higher than those during nonspray months (p = 0.009 for dimethyl; p = 0.018 for diethyl). Dimethyl DAP geometric means were 0.1 and 0.07 micro mol/L for spray months and nonspray months, respectively (57% difference); diethyl DAP geometric means were 0.49 and 0.35, respectively (40% difference). We also observed differences for sex of the child, with male levels higher than female levels (p = 0.005 for dimethyl; p = 0.046 for diethyl). We observed no differences due to age, parental occupation, or residential proximity to fields. This study reports for the first time the temporal pattern of pesticide exposures over the course of a full year and indicates that pesticide spraying in an agricultural region can increase children's exposure in the absence of parental work contact with pesticides or residential proximity to pesticide-treated farmland

Kristensen,P., L.M.Irgens, A.Andersen, A.S.Bye, and L.Sundheim. 1997. "Birth defects among offspring of Norwegian farmers, 1967-1991." Epidemiology. 8:537-544.
Abstract: We investigated birth defects (N = 4,565) reported to the Medical Birth Registry of Norway among 192,417 births between 1967 and 1991 to parents identified as farmers in five agricultural and horticultural censuses between 1969 and 1989. The prevalences at birth of all and specific birth defects deviated little from those among 61,351 births to non-farmers in agricultural municipalities. We classified exposure indicators on the basis of information provided at the agricultural censuses. The main hypotheses were that parental exposure to pesticides was associated with defects of the central nervous system, orofacial clefts, some male genital defects, and limb reduction defects. We found moderate increases in risk for spina bifida and hydrocephaly, the associations being strongest for exposure to pesticides in orchards or greenhouses [spina bifida: 5 exposed cases, odds ratio (OR) = 2.76, 95% confidence interval (CI) = 1.07-7.13; hydrocephaly: 5 exposed cases, OR = 3.49, 95% CI = 1.34-9.09]. Exposure to pesticides, in particular in grain farming, was also associated with limb reduction defects (OR = 2.50; 95% CI = 1.06-5.90). We also saw an;association;with pesticides for cryptorchism and hypospadias. We found less striking associations for other specific defects and pesticide indicators, animal farming, and fertilizer regimens.

Landrigan,P. and C.Benbrook. Impacts of the Food Quality Protection Act on Children's Exposures to Pesticides. Delivered at the 2006 Annual Meeting of the AAAS . 2006. The Organic Center.
Ref Type: Generic

Larsen,S.B., M.Spano, A.Giwercman, and J.P.Bonde. 1999. "Semen quality and sex hormones among organic and traditional Danish farmers." Occupational & Environmental Medicine. 56:139-144.
Abstract: Objectives-To confirm or refute the hypothesis that organic farmers have higher sperm concentrations than traditional farmers. Methods-Traditional and organic farmers were selected randomly from central registers, and 171 traditional farmers and 85 organic farmers delivered one semen sample before the start of the spraying season. The

participation rate was 28.8% among traditional farmers and 42.9% among organic farmers. Results-The median sperm concentration for traditional and organic farmers was 58 million/ml and 64 million/ml, respectively. After adjustment for several confounders, sperm concentration, total count, proportion of non-vital spermatozoa, sperm chromatin structure, and motility variables did not differ significantly between the two groups. The traditional farmers had a significantly lower proportion of normal spermatozoa, but this result was not confirmed in a second sample Organic farmers had slightly higher inhibin B concentration and testosterone/sex hormone binding globulin ratio. Conclusion-Despite slight differences in concentrations of reproductive hormones, no significant differences in conventional measures of semen quality were found between organic and traditional farmers.

Lau,K., W.G.McLean, D.P.Williams, and C.V.Howard. 2005. "Synergistic Interactions Between Commonly Used Food Additives in a Developmental Neurotoxicity Test." Toxicol.Sci.
Abstract: Exposure to non-nutritional food additives during the critical development window has been implicated in the induction and severity of behavioural disorders such as attention deficit hyperactivity disorder (ADHD). Although the use of single food additives at their regulated concentrations is believed to be relatively safe in terms of neuronal development, their combined effects remain unclear. We therefore examined the neurotoxic effects of four common food additives in combinations of two (Brilliant Blue and L-glutamic acid, Quinoline Yellow and aspartame) to assess potential interactions. Mouse NB2a neuroblastoma cells were induced to differentiate and grow neurites in the presence of additives. After 24 h, cells were fixed and stained and neurite length measured by light microscopy with computerised image analysis. Neurotoxicity was measured as an inhibition of neurite outgrowth. Two independent models were used to analyse combination effects: effect additivity and dose additivity. Significant synergy was observed between combinations of Brilliant Blue with L-glutamic acid, and Quinoline Yellow with aspartame, in both models. Involvement of N-methyl-D-aspartate (NMDA) receptors in food additive-induced neurite inhibition was assessed with a NMDA antagonist, CNS-1102. L-glutamic acid- and aspartame-induced neurotoxicity was reduced in the presence of CNS-1102; however the antagonist did not prevent food colour-induced neurotoxicity. Theoretical exposure to additives was calculated based on analysis of content in foodstuff, and estimated percentage absorption from the gut. Inhibition of neurite outgrowth was found at concentrations of additives theoretically achievable in plasma by ingestion of a typical snack and drink. In addition, Trypan Blue dye exclusion was used to evaluate the cellular toxicity of food additives on cell viability of NB2a cells; both combinations had a straightforward additive effect on cytotoxicity. These data have implications for the cellular effects of common chemical entities ingested individually and in combination

Lee,W.Y., W.Lannucci-Berger, B.D.Eitzer, J.C.White, and M.I.Mattina. 2003. "Persistent organic pollutants in the environment: chlordane residues in compost." J Environ.Qual. 32:224-231.
Abstract: The half-lives of some persistent organic pollutants (POPs) in environmental compartments such as soil and air can be as long as decades. In spite of the

hydrophobicity of many POPs, the literature contains reports of their uptake by, and translocation through, a variety of plants. Both these observations prompt the investigation of whether a vegetation-based environmental compartment such as compost contains significant residues of POPs. Previous reports imply that residues of technical chlordane will be found in compost. Due to its physicochemical properties, technical chlordane provides insights into the fate of POPs in the environment, which are not accessible through determinations of other pollutants in this group. Accordingly, we undertook the first comprehensive examination of technical chlordane residues in a variety of composts, specifically, 13 commercial and 39 municipal compost products, to both characterize and quantify the magnitude of this point source of contamination. Using chiral gas chromatography interfaced to ion trap mass spectrometry, the concentration and the compositional and enantiomeric profiles of chlordane components were determined. Of the 13 commercial products, 9 contained detectable chlordane concentrations, ranging from 4.7 to 292 microg/kg (dry wt.), while all 39 municipal products contained chlordane residues ranging from 13.9 to 415 microg/kg (dry wt.). The residue concentrations and profiles suggest possible feedstock sources for the chlordane in the finished compost product. The data also support the conclusion that some composts contribute to anthropogenic cycling of POPs through the biosphere

Leng,A., J.Feldon, and B.Ferger. 2003. "Rotenone increases glutamate-induced dopamine release but does not affect hydroxyl-free radical formation in rat striatum." Synapse. 50:240-250.
Abstract: Impairment of the mitochondrial complex I has been found in Parkinson's disease and recently long-term treatment with the complex I inhibitor rotenone led to neurodegeneration and Lewy body-like inclusions in rats. To investigate the relationship of free radical formation, complex I inhibition, and dopamine release, rotenone (15 mg/kg s.c.) was injected in male Sprague Dawley rats. Complex I inhibition was measured in the striatum and substantia nigra using the lactate accumulation assay. Dopamine release and free radical formation was determined using striatal microdialysis in combination with the salicylate hydroxylation assay. In a second experiment, glutamate (10 mM) stimulation via the microdialysis probe was used to provoke hydroxyl radical formation and dopamine release 60 min after rotenone or vehicle pretreatment. Rotenone significantly increased striatal and nigral lactate levels. However, rotenone did not produce a significant increase in hydroxyl radical formation and dopamine release, but led to a pronounced hypokinesia. In contrast, rotenone in comparison to vehicle pretreatment produced a significant augmentation of glutamate-induced dopamine release (67-fold and 31-fold increase, respectively) and did not affect the glutamate-induced hydroxyl free radical formation (23-fold and 21-fold increase, respectively). The present study demonstrates that a single systemic rotenone administration does not lead to neurotoxicity, but rather to enhanced glutamate-induced dopamine release with no further increase of hydroxyl free radical formation. Thus, acute complex I inhibition in the presence or absence of high extracellular dopamine and glutamate levels is not critically involved in the formation of hydroxyl free radicals

Liu,B., H.M.Gao, and J.S.Hong. 2003. "Parkinson's disease and exposure to infectious agents and pesticides and the occurrence of brain injuries: role of neuroinflammation." Environ.Health Perspect. 111:1065-1073.
Abstract: Idiopathic Parkinson's disease (PD) is a devastating movement disorder characterized by selective degeneration of the nigrostriatal dopaminergic pathway. Neurodegeneration usually starts in the fifth decade of life and progresses over 5-10 years before reaching the fully symptomatic disease state. Despite decades of intense research, the etiology of sporadic PD and the mechanism underlying the selective neuronal loss remain unknown. However, the late onset and slow-progressing nature of the disease has prompted the consideration of environmental exposure to agrochemicals, including pesticides, as a risk factor. Moreover, increasing evidence suggests that early-life occurrence of inflammation in the brain, as a consequence of either brain injury or exposure to infectious agents, may play a role in the pathogenesis of PD. Most important, there may be a self-propelling cycle of inflammatory process involving brain immune cells (microglia and astrocytes) that drives the slow yet progressive neurodegenerative process. Deciphering the molecular and cellular mechanisms governing those intricate interactions would significantly advance our understanding of the etiology and pathogenesis of PD and aid the development of therapeutic strategies for the treatment of the disease

Lo,M. and D.Matthews. Results of routine testing of organic food for ago-chemical residues. Powell et al. Proceedings of the COR Conference. UK Organic Research 2002 . 2002.
Ref Type: Statute

London,L., G.S.de, C.Wesseling, S.Kisting, H.A.Rother, and D.Mergler. 2002. "Pesticide usage and health consequences for women in developing countries: out of sight, out of mind?" Int.J Occup.Environ.Health. 8:46-59.
Abstract: Pesticide exposures of women in developing countries are aggravated by economic policy changes associated with structural adjustment programs and globalization. Women in these countries, particularly in the agricultural sector, are increasingly exposed. Since they are concentrated in the most marginal positions in the formal and informal workforces, and production is organized in a gender-specific way, opportunities for women to control their exposures are limited. Data from developing countries show that: 1) women's exposures to pesticides are significantly higher than is recognized; 2) poisonings and other pesticide-related injuries are greatly underestimated for women; 3) for a given adverse outcome from exposure, the experience of that outcome is gender-discriminatory; 4) erroneous risk perception increases women's exposures. The hiatus in knowledge of gender-specific exposures and effects is related to gender biases in the nature of epidemiologic inquiry and in the literature, and the gendered nature of health workers' practices and surveillance. Recommendations are made for strong, independent organizations that provide opportunities for women to control their environments, and the factors affecting their health, as well as gender-sensitive research to address the particularities of women's pesticide exposures

Longnecker,M.P. and S.J.London. 1993. "Re: Blood levels of organochlorine residues and risk of breast cancer." J.Natl.Cancer Inst. 85:1696-1697.

Longnecker,M.P., L.Bernstein, C.L.Bird, A.K.Yancey, and J.C.Peterson. 1996. "Measurement of organochlorine levels in postprandial serum or in blood collected in serum separator tubes." Cancer Epidemiol.Biomarkers Prev. 5:753-755.
Abstract: Whether organochlorine blood levels in fasting and postprandial specimens provide equivalent measures of exposure and the extent to which collecting blood in tubes containing material to separate serum and blood cells corrupts the specimen are unclear. In this paper, we present data from two studies that address both of these issues. In the first study, 27 women provided fasting blood in plain, silicone-coated Vacutainer tubes (red-topped) and in similar tubes containing serum separator gel (SSTs), as well as a postprandial specimen in a red-topped tube. The specimens collected in SSTs were left to stand overnight, with the gel in contact with the sample. In the second study, the blood of 12 industrial incinerator workers was collected in red-topped tubes and in SSTs. Blood in SSTs was left in contact with the gel for 5 days. Serum organochlorine residue levels ([1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene] (DDE)) and polychlorinated biphenyls) in samples collected in red-topped tubes were highly correlated with levels measured in samples collected in SSTs (all Pearson r values were > or = 0.79). Postprandial and fasting organochlorine levels were also highly correlated (Pearson r values > or = 0.89). Our results indicate that timing of the collection of blood in relation to meals and use of SSTs to collect blood specimens did not greatly affect the relative classification of subjects with respect to serum level of DDE or polychlorinated biphenyls. The longer the specimen was in contact with the SST gel, however, the lower the level of organochlorine that was detected and, at least for DDE, the greater the misclassification caused

Longnecker,M.P., W.J.Rogan, and G.Lucier. 1997. "The human health effects of DDT (dichlorodiphenyltrichloroethane) and PCBS (polychlorinated biphenyls) and an overview of organochlorines in public health." Annu.Rev.Public Health. 18:211-244.
Abstract: Organochlorines are a diverse group of persistent synthetic compounds, some of which are detectable in nearly everyone. Many organochlorines are endocrine disruptors or carcinogens in experimental assays. p,p'-DDE (dichlorodiphenyl-dichloroethene) and PCBs (polychlorinated biphenyls) comprise the bulk of organochlorine residues in human tissues. We reviewed relevant human data cited in the 1991-1995 Medline database and elsewhere. High-level exposure to selected organochlorines appears to cause abnormalities of liver function, skin (chloracne), and the nervous system. Of more general interest, however, is evidence suggesting insidious effects of background exposure. Of particular concern is the finding of neonatal hypotonia or hyporeflexia in relation to PCB exposure. The epidemiologic data reviewed, considered in isolation, provide no convincing evidence that organochlorines cause a large excess number of cancers. A recent risk assessment that considered animal data, however, gives a cancer risk estimate for background exposure to dioxin and dioxin-like compounds (e.g. some PCBs) with an upper bound in the range of 10(-4) per year

Longnecker,M.P., M.A.Klebanoff, B.C.Gladen, and H.W.Berendes. 1999. "Serial levels of serum organochlorines during pregnancy and postpartum." Arch.Environ.Health. 54:110-114.
Abstract: In utero exposure to dichlorodiphenyldichloroethene and polychlorinated biphenyls, within the range found in the general U.S. population, may produce detectable effects in offspring. To design studies of the effects of in utero organochlorine exposure, we obtained data on the relationship between gestational and perinatal maternal levels in females on several occasions. We studied 67 pregnant women in the United States who agreed to have their blood drawn once during each trimester and once postpartum. We examined the Pearson correlation coefficient between the natural logarithm of levels (microg/g serum lipid). The correlation, r, among levels in the first and third trimester was .86 and .77 for dichlorodiphenyldichloroethene and for polychlorinated biphenyls. Correlations among levels determined at other times (i.e., second trimester and postpartum) were similar. On the basis of these results, we suggest that in studies of the effects of in utero or perinatal exposure to the aforementioned compounds, the time when specimens are collected is not critical

Longnecker,M.P. and J.L.Daniels. 2001. "Environmental contaminants as etiologic factors for diabetes." Environ.Health Perspect. 109 Suppl 6:871-876.
Abstract: For both type 1 and type 2 diabetes mellitus, the rates have been increasing in the United States and elsewhere; rates vary widely by country, and genetic factors account for less than half of new cases. These observations suggest environmental factors cause both type 1 and type 2 diabetes. Occupational exposures have been associated with increased risk of diabetes. In addition, recent data suggest that toxic substances in the environment, other than infectious agents or exposures that stimulate an immune response, are associated with the occurrence of these diseases. We reviewed the epidemiologic data that addressed whether environmental contaminants might cause type 1 or type 2 diabetes. For type 1 diabetes, higher intake of nitrates, nitrites, and N-nitroso compounds, as well as higher serum levels of polychlorinated biphenyls have been associated with increased risk. Overall, however, the data were limited or inconsistent. With respect to type 2 diabetes, data on arsenic and 2,3,7,8-tetrachlorodibenzo-p-dioxin relative to risk were suggestive of a direct association but were inconclusive. The occupational data suggested that more data on exposure to N-nitroso compounds, arsenic, dioxins, talc, and straight oil machining fluids in relation to diabetes would be useful. Although environmental factors other than contaminants may account for the majority of type 1 and type 2 diabetes, the etiologic role of several contaminants and occupational exposures deserves further study

Longnecker,M.P., M.A.Klebanoff, H.Zhou, and J.W.Brock. 2001. "Association between maternal serum concentration of the DDT metabolite DDE and preterm and small-for-gestational-age babies at birth." Lancet. 358:110-114.
Abstract: BACKGROUND: DDT (1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane) is highly effective against most malaria-transmitting mosquitoes and is being widely used in malaria-endemic areas. The metabolite, DDE (1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene), has been linked to preterm birth in small studies, but these findings are inconclusive. Our aim was to investigate the association between DDE

exposure and preterm birth. METHODS: Our study was based on the US Collaborative Perinatal Project (CPP). From this study we selected a subset of more than 44000 eligible children born between 1959 and 1966 and measured the DDE concentration in their mothers' serum samples stored during pregnancy. Complete data were available for 2380 children, of whom 361 were born preterm and 221 were small-for-gestational age. FINDINGS: The median maternal DDE concentration was 25 mg/L (range 3-178)- several fold higher than current US concentrations. The adjusted odds ratios (OR) of preterm birth increased steadily with increasing concentrations of serum DDE (ORs=1, 1.5, 1.6, 2.5, 3.1; trend p<0.0001). Adjusted odds of small-for-gestational-age also increased, but less consistently (ORs=1, 1.9, 1.7, 1.6, 2.6; trend p=0.04). After excluding preterm births, the association of DDE with small-for-gestational-age remained. INTERPRETATION: The findings strongly suggest that DDT use increases preterm births, which is a major contributor to infant mortality. If this association is causal, it should be included in any assessment of the costs and benefits of vector control with DDT

Longnecker,M.P., M.A.Klebanoff, J.W.Brock, H.Zhou, K.A.Gray, L.L.Needham, and A.J.Wilcox. 2002. "Maternal serum level of 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene and risk of cryptorchidism, hypospadias, and polythelia among male offspring." American Journal of Epidemiology. 155:313-322.
Abstract: 1,1-Dichloro-2,2-bis(p-chlorophenyl)ethylene (p,p'-DDE) is a metabolite of the insecticide 2,2-bis(p-chlorophenyl)-1,1,1-trichloroethane (DDT) and is a ubiquitous environmental contaminant. Nearly everyone in the United States has a detectable serum level of DDE. DDE was recently found to inhibit binding of androgen to its receptor and to block androgen action in rodents. Normal development of male genitalia in mammals depends on androgen action. The authors used stored serum samples to examine the relation between maternal DDE levels during pregnancy and adjusted odds of cryptorchidism (n = 219), hypospadias (n = 199), and polythelia (extra nipples) (n = 167) among male offspring, using a nested case-control design with one control group (n = 552). Subjects were selected from the Collaborative Perinatal Project, a US birth cohort study begun in 1959-1966, when DDE levels were much higher than they are at present. Compared with boys whose mother's recovery-adjusted serum DDE level was less than 21.4 microg/liter, boys with maternal levels greater than or equal to 85.6 microg/liter had adjusted odds ratios of 1.3 (95% confidence interval (CI): 0.7, 2.4) for crypt-orchidism, 1.2 (95% CI: 0.6, 2.4) for hypospadias, and 1.9 (95% CI: 0.9, 4.0) for polythelia. For cryptorchidism and polythelia, the results were consistent with a modest-to-moderate association, but in no instance was the estimate very precise. The results were inconclusive

Longnecker,M.P. 2005. "Invited Commentary: Why DDT matters now." American Journal of Epidemiology. 162:726-728.

Longnecker,M.P., M.A.Klebanoff, D.B.Dunson, X.Guo, Z.Chen, H.Zhou, and J.W.Brock. 2005. "Maternal serum level of the DDT metabolite DDE in relation to fetal loss in previous pregnancies." Environ.Res. 97:127-133.

Abstract: Use of 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane (DDT) continues in about 25 countries. This use has been justified partly by the belief that it has no adverse consequences on human health. Evidence has been increasing, however, for adverse reproductive effects of DDT, but additional data are needed. Pregnant women who enrolled in the Collaborative Perinatal Project (United States, 1959-1965) were asked about their previous pregnancy history; blood samples were drawn and the serum frozen. In 1997-1999, the sera of 1717 of these women who had previous pregnancies were analyzed for 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE), the major breakdown product of DDT. The odds of previous fetal loss was examined in relation to DDE level in logistic regression models. Compared with women whose DDE level was <15 microg/L, the adjusted odds ratios of fetal loss according to category of DDE were as follows: 15-29 microg/L, 1.1; 30-44 microg/L, 1.4; 45-59 microg/L, 1.6; and 60+ microg/L, 1.2. The adjusted odds ratio per 60 microg/L increase was 1.4 (95% confidence interval 1.1-1.6). The results were consistent with an adverse effect of DDE on fetal loss, but were inconclusive owing to the possibility that previous pregnancies ending in fetal loss decreased serum DDE levels less than did those carried to term

Lotti,M., C.E.Becker, M.J.Aminoff, J.E.Woodrow, J.N.Seiber, R.E.Talcott, and R.J.Richardson. 1983. "Occupational exposure to the cotton defoliants DEF and merphos. A rational approach to monitoring organophosphorous-induced delayed neurotoxicity." J Occup.Med. 25:517-522.

Lourenco,I., S.Rodrigues, E.Figueiredo, M.C.Godinho, C.Marques, F.Amaro, and A.Mexia. 2002. "The effect of crop protection strategy on pest and beneficials incidence in protected crops." Meded.Rijksuniv.Gent Fak.Landbouwkd.Toegep.Biol.Wet. 67:569-573.
Abstract: This study took place in the Oeste region from 1996-1999 and it intended to analyse if the crop protection strategy followed by the farmer influenced the arthropod incidence and the natural control in protected vegetable crops under Mediterranean conditions. The observations were made fortnightly (Autumn/Winter) or weekly (Spring/Summer) in 30-60 plants/parcel (1 plant/35 m2) in order to evaluate incidences. Samples of pests and natural enemies were collected for systematic identification in two greenhouses for each protection strategy (traditional chemical control (TCC), integrated pest management (IPM) and pest control allowed in organic farming (OF)) in lettuce, tomato, green beans and cucumber. Data on incidence of mites, aphids, caterpillars, leafminers, whiteflies, thrips and respective natural enemies were registered as well as phytosanitary treatments performed (farmers' information and/or in loco traces). The leafminers were the pest whose incidence more often presented significant statistical differences between the studied protection strategies. In relation to this pest, the main results obtained were: a higher feeding punctures incidence in TCC than in IPM; higher incidence of adults, mines and feeding punctures in TCC than in OF; and a higher mines' incidence in IPM than in OF. Both in TCC and IPM high percentages of plants with mines were found although without an adult proportional presence. In the first case this was due to the repeatedly phytosanitary treatments applied; in the second case it was due to the natural control, since in IPM and OF greenhouses the collected larvae were mostly parasitized or dead. In spite of the fact these two strategies have as final result a similar

mines and adults incidence, their production and environmental costs are quite different. Significant differences at the beneficials' population level between TCC greenhouses and IPM or OF greenhouses were found. As the farmers did no biological treatments these differences are related to different levels of beneficial populations due to different secondary effects of the pesticides applied

Lu,C. and R.A.Fenske. 1999. "Dermal transfer of chlorpyrifos residues from residential surfaces: comparison of hand press, hand drag, wipe, and polyurethane foam roller measurements after broadcast and aerosol pesticide applications." Environ.Health Perspect. 107:463-467.
Abstract: Indoor residential pesticide applications present the potential for human exposures, particularly for small children. Personal contact with target and nontarget surfaces can result in transfer of pesticides to the skin, but the magnitude of such transfer is uncertain. This research compared surface sampling techniques [wipe and polyurethane foam (PUF) roller] with the removal ability of human skin following broadcast and total aerosol release applications of Dursban (Dow Elanco, Midland, MI), a residential formulation containing the insecticide chlorpyrifos. Hands were washed immediately after surface contact, following a protocol that included a laboratory-generated adjustment factor to account for incomplete removal of chlorpyrifos from skin. Chlorpyrifos transfer was similar for hand press and hand drag techniques, averaging approximately 1-6 ng/cm2 of carpet contacted. These amounts represented < 1% of the amount of chlorpyrifos deposited on the surfaces 3.5 hr earlier. Chlorpyrifos transfer from carpet to skin was 23-24 times lower than for wipe sampling and 33-36 times lower than for PUF roller sampling ($p = 0.0007$ and $p = 0.0006$ for broadcast and aerosol applications, respectively). Hand press sampling removed approximately 4.5 times less chlorpyrifos from nontarget furniture surfaces (12 ng/cm2) than did wipe sampling (56 ng/cm2; $p = 0.009$). Chlorpyrifos residues on carpet were substantially higher after broadcast applications than after aerosol applications, but residues on such nontarget surfaces as furniture were substantially higher for the aerosol application. This study indicates that human skin removes substantially less residue from carpets and furniture than either conventional wipe or PUF roller sampling methods following residential pest control applications of chlorpyrifos. Although this paper focuses on quantifying residue transfer from surface to skin using different surface sampling techniques, no attempt is made to quantify the amount of chlorpyrifos residue that is subsequently absorbed

Lu,C., D.E.Knutson, J.Fisker-Andersen, and R.A.Fenske. 2001. "Biological monitoring survey of organophosphorus pesticide exposure among pre-school children in the Seattle metropolitan area." Environ.Health Perspect. 109:299-303.
Abstract: In this study we assessed organophosphorus (OP) pesticide exposure among children living in two Seattle metropolitan area communities by measuring urinary metabolites, and identified possible exposure risk factors through a parental interview. We recruited children in clinic and outpatient waiting rooms. We obtained spot urine samples in the spring and fall of 1998 from 110 children ages 2-5 years, from 96 households. We analyzed urine samples for six dialkylphosphate (DAP) compounds, the common metabolites of the OP pesticides. Through parental interviews we gathered demographic and residential pesticide use data. At least one of the DAP metabolites was

measured in 99% of the children, and the two predominant metabolites (DMTP and DETP) were measured in 70-75% of the children. We found no significant differences in DAP concentrations related to season, community, sex, age, family income, or housing type. Median concentrations of dimethyl and diethyl DAPs were 0.11 and 0.04 micromol/L, respectively (all children). Concentrations were significantly higher in children whose parents reported pesticide use in the garden (0.19 vs. 0.09 micromol/L for dimethyl metabolites, p = 0.05; 0.04 vs. 0.03 micromol/L for diethyl metabolites, p = 0.02), but were not different based on reported pet treatment or indoor residential use. Nearly all children in this study had measurable levels of OP pesticide metabolites. Some of this exposure was likely due to diet. Garden pesticide use was associated with elevated metabolite levels. It is unlikely that these exposure levels would cause acute intoxication, but the long-term health effects of such exposures are unknown. We recommend that OP pesticide use be avoided in areas where children are likely to play

Lu,C., K.Toepel, R.Irish, R.A.Fenske, D.B.Barr, and R.Bravo. 2006. "Organic diets significantly lower children's dietary exposure to organophosphorus pesticides." Environ.Health Perspect. 114:260-263.
Abstract: We used a novel study design to measure dietary organophosphorus pesticide exposure in a group of 23 elementary school-age children through urinary biomonitoring. We substituted most of children's conventional diets with organic food items for 5 consecutive days and collected two spot daily urine samples, first-morning and before-bedtime voids, throughout the 15-day study period. We found that the median urinary concentrations of the specific metabolites for malathion and chlorpyrifos decreased to the nondetect levels immediately after the introduction of organic diets and remained nondetectable until the conventional diets were reintroduced. The median concentrations for other organophosphorus pesticide metabolites were also lower in the organic diet consumption days; however, the detection of those metabolites was not frequent enough to show any statistical significance. In conclusion, we were able to demonstrate that an organic diet provides a dramatic and immediate protective effect against exposures to organophosphorus pesticides that are commonly used in agricultural production. We also concluded that these children were most likely exposed to these organophosphorus pesticides exclusively through their diet. To our knowledge, this is the first study to employ a longitudinal design with a dietary intervention to assess children's exposure to pesticides. It provides new and persuasive evidence of the effectiveness of this intervention

Lynch,S., D.L.Sexson, C.M.Benbrook, M.Carter, J.A.Wyman, P.Nowak, J.Barzen, S.Diercks, and J.Wallendal. 2000. "Working out the bugs." Choices. 3:28-32.

Ma,X., P.A.Buffler, R.B.Gunier, G.Dahl, M.T.Smith, K.Reinier, and P.Reynolds. 2002. "Critical windows of exposure to household pesticides and risk of childhood leukemia." Environ.Health Perspect. 110:955-960.
Abstract: The potential etiologic role of household pesticide exposures was examined in the Northern California Childhood Leukemia Study. A total of 162 patients (0-14 years old) with newly diagnosed leukemia were rapidly ascertained during 1995-1999, and 162 matched control subjects were randomly selected from the birth registry. The use of

professional pest control services at any time from 1 year before birth to 3 years after was associated with a significantly increased risk of childhood leukemia [odds ratio (OR) = 2.8; 95% confidence interval (CI), 1.4-5.7], and the exposure during year 2 was associated with the highest risk (OR = 3.6; 95% CI, 1.6-8.3). The ORs for exposure to insecticides during the 3 months before pregnancy, pregnancy, and years 1, 2, and 3 were 1.8 (95% CI, 1.1-3.1), 2.1 (95% CI, 1.3-3.5), 1.7 (95% CI, 1.0-2.9), 1.6 (95% CI, 1.0-2.7), and 1.2 (95% CI, 0.7-2.1), respectively. Insecticide exposures early in life appear to be more significant than later exposures, and the highest risk was observed for exposure during pregnancy. Additionally, more frequent exposure to insecticides was associated with a higher risk. In contrast to insecticides, the association between herbicides and leukemia was weak and nonsignificant. Pesticides were also grouped based on where they were applied. Exposure to indoor pesticides was associated with an increased risk, whereas no significant association was observed for exposure to outdoor pesticides. The findings suggest that exposure to household pesticides is associated with an elevated risk of childhood leukemia and further indicate the importance of the timing and location of exposure

MacIntosh,D.L., L.L.Needham, K.A.Hammerstrom, and P.B.Ryan. 1999. "A longitudinal investigation of selected pesticide metabolites in urine." J Expo.Anal.Environ.Epidemiol. 9:494-501.
Abstract: As part of a longitudinal investigation of environmental exposures to selected chemical contaminants, concentrations of the pesticide metabolites 1-naphthol (INAP), 3,5,6-trichloro-2-pyridinol (TCPY), malathion dicarboxylic acid (MDA), and atrazine mercapturate (AM) were measured in repeated samples obtained from 80 individuals in Maryland during 1995-1996. Up to six urine samples were collected from each individual at intervals of approximately 8 weeks over a 1-year period (i.e., one sample per participant in each of six cycles). INAP (median=4.2 microg/l and 3.3 microg/g creatinine) and TCPY (median=5.3 microg/l and 4.6. microg/g creatinine) were present in over 80% of the samples, while MDA and AM were detected infrequently (6.6% and <1% of samples, respectively). Geometric mean (GM) concentrations of INAP in urine did not vary significantly among sampling cycles. In contrast, GM concentrations of TCPY were significantly greater in samples collected during the spring and summer of 1996 than in the preceding fall and winter. Repeated measurements of INAP and TCPY from the same individual over time were highly variable. The average range of INAP and TCPY concentrations from the same individual were approximately 200% and 50% greater than the respective population mean levels. Geometric mean (GM) TCPY concentrations differed significantly between Caucasian (n=42, GM=5.7 microg/g creatinine) and African-American (n=11, GM=4.0 microg/g) participants and among education levels, but were not significantly different among groups classified by gender, age, or household income. In future research, environmental measurements of the parent compounds and questionnaire data collected concurrently with the biomarker data will be used to characterize the determinants of variability in the urinary pesticide metabolite levels

Magnusson,M.K., A.Arvola, U.K.Hursti, L.Aberg, and P.O.Sjoden. 2003. "Choice of organic foods is related to perceived consequences for human health and to environmentally friendly behaviour." Appetite. 40:109-117.
Abstract: We designed a questionnaire concerned with attitudes and behaviour towards organic foods, environmentally friendly behaviour (EFB), and perceived consequences of organic food choice in terms of human health, the environment and animal welfare. It was mailed in 1998 to a random nation-wide sample of 2000 Swedish citizens, ages 18-65 years, and 1154 (58%) responded. Self-reported purchase of organic foods was most strongly related to perceived benefit for human health. Performance of EFBs such as refraining from car driving was also a good predictor of purchase frequency. The results indicate that egoistic motives are better predictors of the purchase of organic foods than are altruistic motives

March of Dimes. Leading categories of birth defects. 2004.
Ref Type: Electronic Citation
Abstract: Estimated incidence of 18 birth defects, and links to sources of summary data.

Marcus,M., J.Kiely, F.J.Xu, M.McGeehin, R.Jackson, and T.Sinks. 1998. "Changing sex ratio in the United States, 1969-1995." Fertility & Sterility. 70:270-273.
Abstract: Objective: To determine if the sex ratio of live births in the United States has changed during the 27 years from 1969 through 1995. Design: Regression analysis of secular trends in sex ratios. Setting: Population-based data. Patient(s): Liveborn infants in the United States 1969-1995. Main Outcome Measure(s): Sex of liveborn infant. Result(s): The sex ratio (number of male births divided by number of female births) declined significantly among whites during the 27 years under study. Among black newborns, the sex ratio significantly increased during the same time period. Conclusion(s): These secular trends could not be explained by changing maternal or paternal age, or by changing proportions of specific birth orders. Possible explanations for the observed changes in sex ratio include random fluctuations in sex ratio over time, changes in demographic characteristics of the population (other than the characteristics controlled for in this analysis), and changes in frequency or timing of intercourse. Environmental exposures are unlikely to account for the observed trends.

Mattina,M.I., W.Iannucci-Berger, L.Dykas, and J.Pardus. 1999. "Impact of Long-Term Wathering, Mobility and Land Use on Chlordane Residues in Soil." Environ.Sci.Technol. 33:2425-2431.

Mattina,M.J., W.Iannucci-Berger, and L.Dykas. 2000. "Chlordane uptake and its translocation in food crops." J Agric Food Chem. 48:1909-1915.
Abstract: Chlordane is a member of the persistent organic pollutants (POPs), a group of chemicals characterized by extremely long residence in the environment after application. Technical chlordane, composed of a large number of components, is a synthetic organochlorine substance that was used primarily as an insecticide. Uptake by root crops of persistent soil residues of chlordane was noted early in the chronology of the material. The present report is the first comprehensive study of the uptake of weathered soil residues of chlordane and its translocation throughout the tissues of food crops under

both greenhouse and field conditions. The data show that for all 12 crops chlordane is not limited to root tissue but is translocated from the root to some of the aerial tissues. Chlordane accumulation in edible aerial tissue appears to be dependent on plant physiology. As expected, chlordane was detected in the edible root tissue of the three root crops examined, carrots, beets, and potatoes. In the remaining crops chlordane was detected in the edible aerial tissue of spinach, lettuce, dandelion, and zucchini, whereas it was not detected in edible aerial tissue of tomatoes, peppers, and corn; trace amounts of chlordane were detected in the edible aerial tissue of bush beans and eggplant. Under the conditions of the field trial the data indicate that for weathered chlordane residues, the soil-to-plant uptake route dominates over the air-to-plant uptake route. This is the case even when the soil concentration of the recalcitrant, weathered residues, for which volatilization is expected to be minimal, is as high as it would be directly following application. Greenhouse trials confirm this observation for zucchini, a member of the Cucurbitaceae family, which bioaccumulates weathered chlordane very efficiently in its edible fruits

Meeker,J.D., L.Ryan, D.B.Barr, R.F.Herrick, D.H.Bennett, R.Bravo, and R.Hauser. 2004. "The relationship of urinary metabolites of carbaryl/naphthalene and chlorpyrifos with human semen quality." Environ.Health Perspect. 112:1665-1670.
Abstract: Most of the general population is exposed to carbaryl and other contemporary-use insecticides at low levels. Studies of laboratory animals, in addition to limited human data, show an association between carbaryl exposure and decreased semen quality. In the present study we explored whether environmental exposures to 1-naphthol (1N), a metabolite of carbaryl and naphthalene, and 3,5,6-trichloro-2-pyridinol (TCPY), a metabolite of chlorpyrifos and chlorpyrifos-methyl, are associated with decreased semen quality in humans. Subjects (n=272) were recruited through a Massachusetts infertility clinic. Individual exposures were measured as spot urinary concentrations of 1N and TCPY adjusted using specific gravity. Semen quality was assessed as sperm concentration, percent motile sperm, and percent sperm with normal morphology, along with sperm motion parameters (straight-line velocity, curvilinear velocity, and linearity). Median TCPY and 1N concentrations were 3.22 and 3.19microg/L, respectively. For increasing 1N tertiles, adjusted odds ratios (ORs) were significantly elevated for below-reference sperm concentration (OR for low, medium, and high tertiles = 1.0, 4.2, 4.2, respectively; p-value for trend =0.01) and percent motile sperm (1.0, 2.5, 2.4; p-value for trend = 0.01). The sperm motion parameter most strongly associated with 1N was straight-line velocity. There were suggestive, borderline-significant associations for TCPY with sperm concentration and motility, whereas sperm morphology was weakly and nonsignificantly associated with both TCPY and 1N. The observed associations between altered semen quality and 1N are consistent with previous studies of carbaryl exposure, although suggestive associations with TCPY are difficult to interpret because human and animal data are currently limited

Meeker,J.D., N.P.Singh, L.Ryan, S.M.Duty, D.B.Barr, R.F.Herrick, D.H.Bennett, and R.Hauser. 2004. "Urinary levels of insecticide metabolites and DNA damage in human sperm." Hum.Reprod. 19:2573-2580.

Abstract: BACKGROUND: Members of the general population are exposed to non-persistent insecticides at low levels. The present study explored whether environmental exposures to carbaryl and chlorpyrifos are associated with DNA damage in human sperm. METHODS: Subjects (n=260) were recruited through a Massachusetts infertility clinic. Individual exposures were measured as spot urinary metabolite concentrations of chlorpyrifos [3,5,6-trichloro-2-pyridinol (TCPY)] and carbaryl [1-naphthol (1N)], adjusted using specific gravity. Sperm DNA integrity was assessed by neutral comet assay and reported as comet extent, percentage DNA in comet tail (Tail%) and tail distributed moment (TDM). RESULTS: A statistically significant increase in Tail% was found for an interquartile range (IQR) increase in both 1N [coefficient=4.1; 95% confidence interval (CI) 1.9-6.3] and TCPY (2.8; 0.9-4.6), while a decrease in TDM was associated with IQR changes in 1N (-2.2; -4.9 to 0.5) and TCPY (-2.5; -4.7 to -0.2). A negative correlation between Tail% and TDM was present only when stratified by comet extent, suggesting that Tail% and TDM may measure different types of DNA damage within comet extent strata. CONCLUSIONS: Environmental exposure to carbaryl and chlorpyrifos may be associated with increased DNA damage in human sperm, as indicated by a change in comet assay parameters

Meeker,J.D., D.B.Barr, L.Ryan, R.F.Herrick, D.H.Bennett, R.Bravo, and R.Hauser. 2005. "Temporal variability of urinary levels of nonpersistent insecticides in adult men." J.Expo.Anal.Environ.Epidemiol. 15:271-281.
Abstract: Widespread application of contemporary-use insecticides results in low-level exposure for a majority of the population through a variety of pathways. Urinary insecticide biomarkers account for all exposure pathways, but failure to account for temporal within-subject variability of urinary levels can lead to exposure misclassification. To examine temporal variability in urinary markers of contemporary-use insecticides, nine repeated urine samples were collected over 3 months from 10 men participating in an ongoing study of male reproductive health. These 90 samples were analyzed for urinary metabolites of chlorpyrifos (3,5,6-trichloro-2-pyridinol (TCPY)) and carbaryl (1-naphthol (1N)). Volume- based (unadjusted), as well as creatinine (CRE)- and specific gravity (SG)-adjusted concentrations were measured. TCPY had low reliability with an intraclass correlation coefficient between 0.15 and 0.21, while 1N was moderately reliable with an intraclass correlation coefficient between 0.55 and 0.61. When the 10 men were divided into tertiles based on 3-month geometric mean TCPY and 1N levels, a single urine sample performed adequately in classifying a subject into the highest or lowest exposure tertiles. Sensitivity and specificity ranged from 0.44 to 0.84 for TCPY and from 0.56 to 0.89 for 1N. Some differences in the results between unadjusted metabolite concentrations and concentrations adjusted for CRE and SG were observed. Questionnaires were used to assess diet in the 24 h preceding the collection of each urine sample. In mixed-effects models, TCPY was significantly associated with season as well as with consuming grapes and cheese, while 1N levels were associated with consuming strawberries. In conclusion, although a single sample adequately predicted longer-term average exposure, a second sample collected at least 1 month following the first sample would reduce exposure measurement error

Meeker,J.D., L.Ryan, D.B.Barr, and R.Hauser. 2006. "Exposure to nonpersistent insecticides and male reproductive hormones." Epidemiology. 17:61-68.
Abstract: BACKGROUND: Urinary metabolites of several nonpersistent insecticides have been measured in a high percentage of men in the general population, suggesting widespread environmental exposures to these compounds. The present study explored the association of urinary concentrations of 3,5,6-trichloro-2-pyridinol (TCPY), a metabolite of chlorpyrifos and chlorpyrifos-methyl, and 1-naphthol (1N), a metabolite of carbaryl and naphthalene, with serum reproductive hormone levels in adult men. METHODS: Subjects (n = 268) were the male partners in couples presenting to a Massachusetts infertility clinic in years 2000 through 2003. TCPY and 1N were measured in a spot urine sample from each subject and adjusted for dilution using specific gravity. Reproductive hormones (follicle-stimulating hormone, leuteinizing hormone, inhibin B, testosterone, and sex hormone-binding globulin) were measured in serum collected from subjects during the same clinic visit. RESULTS: Multiple linear regression models showed an inverse association between TCPY and testosterone concentration. An interquartile range (IQR) increase in TCPY was associated with a decline of 25 ng/dL (95% confidence interval = -40 to -10) in testosterone concentration. The association appeared to be dose-dependent when exposure was divided into quintiles. The highest TCPY quintile was associated with a testosterone decline of 83 ng/dL (-128 to -39) compared with the lowest TCPY quintile. We also found inverse associations between TCPY and free androgen index and between 1N and testosterone, and suggestive inverse associations between TCPY and leuteinizing hormone and between 1N and free androgen index. CONCLUSION: In adult men, TCPY and 1N were associated with reduced testosterone levels. On a population level, these reductions are of potential public health importance because of widespread exposure to these nonpersistent insecticides

Metcalf,R.L., I.P.Kapoor, P.Y.Lu, C.K.Schuth, and P.Sherman. 1973. "Model ecosystem studies of the environmental fate of six organochlorine pesticides." Environ.Health Perspect. 4:35-44.

Miller,D.B. 1982. "Neurotoxicity of the pesticidal carbamates." Neurobehav.Toxicol.Teratol. 4:779-787.
Abstract: The carbamates, stabilized derivatives of carbamic acid, are potent biological agents used extensively in applications ranging from agriculture to medicine and industry. This review covers the two major classes of pesticidal carbamates: (1) cholinesterase-inhibiting carbamates which include monomethyl- and dimethylcarbamates (used primarily as insecticides); and (2) non-cholinesterase inhibiting, sulfur containing carbamates, the dithiocarbamates (used primarily as fungicides and herbicides). The dithiocarbamates include four major classes; (a) methyldithiocarbamates, (b) dimethyldithiocarbamates, (c) diethyldithio carbamates, (d) ethylenebisdithiocarbamates. For the purposes of this review neurotoxicity is defined as any unwanted change in the functional status of the organism which can be characterized in terms of behavioral, neurochemical, electrophysiological, or neuropathological indices. Neurotoxicity associated with methyl- and dimethylcarbamates has been characterized in terms of their reversible cholinesterase-inhibiting properties. The dithiocarbamates can have neurotoxic effects. However, a complete characterization of the neurotoxicity of

these compounds has not been attempted. The neurotoxic actions of the dithiocarbamates may be related to their metal-chelating and enzyme-inhibiting properties

Mills,P.K. and S.Kwong. 2001. "Cancer incidence in the United Farmworkers of America (UFW), 1987-1997." Am.J Ind.Med. 40:596-603.
Abstract: BACKGROUND: The purpose of this study was to evaluate cancer incidence in the membership a largely Hispanic farmworker labor union in California, the United Farmworkers of America (UFW) and to examine cancer-site specific distributions as well as histology and stage of cancer at diagnosis in this group. METHODS: An electronic record linkage was conducted between a membership roster of the UFW and the database of the California Cancer Registry, the population-based cancer registry in California for the years 1987-1997. Based upon the results of the linkage, morbidity odds ratios were calculated using the distribution of cancer in the California Hispanic population as the reference to determine if risk of specific cancers was higher or lower in the UFW. Time since first joining the union was evaluated, as was the proportional distribution of histologic subtypes and stage at diagnosis, again comparing the experience of the UFW membership to the California Hispanic population. RESULTS: Several types of cancer were elevated in the UFW membership in comparison to the California Hispanic population. Morbidity odds ratios and 95% confidence limits were elevated for leukemia (O.R. = 1.59: 95% C.I. = 1.07-2.37), stomach cancer (O.R. = 1.69: 95% C.I. = 1.24-2.27), uterine cervix cancer (O.R. = 1.63: 95% C.I. = 1.11-2.44) and uterine corpus cancer (O.R. = 1.68: 95% C.I. = 1.05-2.67). Brain cancer was also elevated although not significantly so (O.R. = 1.57: 95% C.I. = 0.96-2.53). CONCLUSIONS: Risk of leukemia, stomach, cervix and uterine cancers was elevated in California farmworkers. The histologic distribution of leukemia and brain cancers within the UFW membership did not differ from the distribution in the general California population although small numbers of cancers in the UFW hindered interpretation of these results. Members of the UFW experienced later stage of disease at diagnosis in comparison to California Hispanics for most major cancer sites but not for breast cancer

Mills,P.K. and S.H.Zahm. 2001. "Organophosphate pesticide residues in urine of farmworkers and their children in Fresno County, California." Am.J Ind.Med. 40:571-577.
Abstract: BACKGROUND: Childhood cancer, notably leukemia, brain cancer, non-Hodgkin's lymphoma, soft tissue sarcoma, and Hodgkin's disease, has been associated with pesticide exposure, often with greater relative risks than among exposed adults, suggesting greater susceptibility in children. These differences in risk may be due to developmental factors or differences in pesticide exposure. METHODS: A feasibility study was conducted to determine levels of pesticide metabolites in urine of adults (n = 18) and children (n = 9) in Fresno County, California, an intensely agricultural county in the Central San Joaquin Valley. Spot urine samples were obtained and analyzed for six metabolites of organophosphate (OP) pesticides using gas chromatography with flame photometric detection methods. The metabolites of OP pesticides included DMP, DEP, DMTP, DMDTP, DETP, and DEDTP. RESULTS: Levels were generally low for both adults and children for most metabolites tested. Frequencies of detection ranged from 0 to 37%, with mean levels ranging from non-detectable to 13.22 ppb. However, levels of

several metabolites were higher in children than in adults. The most frequently detected metabolite, DMP, was found among 44% of the children and 33% of the adults. DMTP was detected among 33% of the children and 28% of the adults. CONCLUSIONS: These results are difficult to interpret given the sampling variation associated with the small sample size. Nevertheless, because OP pesticides have been associated with increased cancer risk in animal and human studies, these results indicate a need to closely monitor children's exposure to environmental chemicals

Mineau,P., A.Baril, B.T.Collins, J.Duffe, G.Joerman, and R.Luttik. 2001. "Pesticide acute toxicity reference values for birds." Rev.Environ.Contam Toxicol. 170:13-74.

Mineau,P. 2002. "Estimating the probability of bird mortality from pesticide sprays on the basis of the field study record." Environ.Toxicol.Chem. 21:1497-1506.
Abstract: The outcome of avian field studies was examined to model the likelihood of mortality. The data were divided into clusters reflecting the type of pesticide application and bird guilds present on site. Logistic regression was used to model the probability of a bird kill. Four independent variables were tested for their explanatory power: a variable reflecting acute oral toxicity and application rate; a variable reflecting the relative oral to dermal toxicity of the pesticides; Henry's law constant; and a variable reflecting possible avoidance of contaminated food items, the hazard factor (HF). All variables except for HF significantly improved model prediction. The relative dermal to oral toxicity, especially, was shown to have a major influence on field outcome and clearly must be incorporated into future avian risk assessments. The probability of avian mortality could be calculated from a number of current pesticide applications and the conclusion was made that avian mortality occurs regularly and frequently in agricultural fields

Monosson,E., W.R.Kelce, C.Lambright, J.Ostby, and L.E.Gray, Jr. 1999. "Peripubertal exposure to the antiandrogenic fungicide, vinclozolin, delays puberty, inhibits the development of androgen-dependent tissues, and alters androgen receptor function in the male rat." Toxicol.Ind.Health. 15:65-79.
Abstract: Vinclozolin is a well-characterized antiandrogenic fungicide. It produces adverse effects when administered during sexual differentiation, and it alters reproductive function in adult male rats by acting as an androgen-antagonist. Two active metabolites of vinclozolin, M1 and M2, compete with natural androgens for the rat and human androgen receptors (ARs), an effect that blocks androgen-induced gene expression in vivo and in vitro. In addition to their effects during perinatal life, androgens play a key role in pubertal maturation in young males. In this regard, the present study was designed to examine the effects of peripubertal oral administration of vinclozolin (0, 10, 30, or 100 mg kg-1 day-1) on morphological landmarks of puberty, hormone levels, and sex accessory gland development in male rats. In addition, as binding of the M1 and M2 to AR alter the subcellular distribution of AR by inhibiting AR-DNA binding, we examined the effects of vinclozolin on AR distribution in the target cells after in vivo treatment. We also examined serum levels of vinclozolin, M1, and M2 in the treated males so that these could be related to the effects on the reproductive tract and AR distribution. Vinclozolin treatment delayed pubertal maturation (at 30 and 100 mg kg-1 day-1) and retarded sex accessory gland and epididymal growth. Serum luteinizing hormone (LH; significant at

all dosage levels) and testosterone and 5 alpha-androstane, 3 alpha, 17 beta-diol (at 100 mg kg-1 day-1) levels were increased. Testis size and sperm production, however, were unaffected. It was apparent that these effects were concurrent with subtle alterations in the subcellular distribution of AR. In control animals, most AR were in the high salt cell fraction, apparently bound to the natural ligand and DNA. Vinclozolin treatment reduced the amount of AR in the high salt (bound to DNA) fraction and it increased AR levels in the low salt (inactive, not bound to DNA) fraction. M1 and M2 were found in the serum of animals from the two highest dosage groups, but they were present at levels well below their K1 values. In summary, these results suggest that when the vinclozolin metabolites occupy a small percentage of AR in the cell, this prevents maximal AR-DNA binding and alters in vivo androgen-dependent gene expression and protein synthesis, which in turn results in obvious alterations of morphological development and serum hormone levels. It is noteworthy that similar exposures during prenatal life result in a high incidence of malformations in male rats

Mushak,E.W. and W.T.Piver. 1992. "Agricultural chemical utilization and human health." Environ.Health Perspect. 97:269-274.
Abstract: The public is justifiably concerned about the human health effects of agricultural chemicals. The many gaps in information about the mechanisms of toxic action, human exposures, and the nature and extent of human health effects are large. Very few older pesticides, in particular, have been tested for human health effects. Workers who produce, harvest, store, transport, process, and prepare food and fibers are exposed to many chemicals that are potentially hazardous and that are used in agriculture. The occupational health of these workers has not been adequately studied, and protective efforts have sometimes been minimal. Valid and accurate risk assessment is best based on sound information about how chemicals, in this case agricultural chemicals, are involved in toxic events--their mechanisms of action. These health effects include tumor promotion, chronic and acute neurotoxicity, immunotoxicity, and reproductive and developmental toxicity. Another key part of risk assessment is exposure assessment. Fundamental studies of the toxicology of target organisms and nontarget organisms exposed to agricultural chemicals are needed to discover and develop better solutions to the problems of agricultural pest control, including better formulations, optimal application rates and public education in safety and alternative agricultural practices. The large number of pesticides that have never been adequately tested for effects on human health is particularly worrisome in light of emerging information about delayed nervous system effects

National Center for Health Statistics? "Table 23. Infant mortality rates, fetal mortality rates, and perinatal mortality rates, according to race: United States, selected years 1950-1999." Health United States, 2001. National Center for Health Statistics. 1 p.

National Center for Health Statistics. Table 31. Infant, neonatal, and postneonatal mortality rates by race and sex: United States, 1940, 1950, 1960, 1970, and 1975-2001. 52 (3), 92-93. 2003.
Ref Type: Generic

National Center for Health Statistics. Table 32. Number of infant deaths and infant mortality rates for 130 selected causes by race and sex: United States, 2001. 52 (3), 94-96. 2003.
Ref Type: Generic

National Center for Health Statistics. Infant Deaths/Mortality. 2004.
Ref Type: Generic
Abstract: infant mortality rate, U.S. 2001: 6.8/1000 live births

National Center for Health Statistics. Fetal Deaths. 2004.
Ref Type: Generic

National Research Council. Regulating Pesticides in Food: The Delaney Paradox. 1987. Washington, D.C., National Academy Press.
Ref Type: Generic

National Research Council. 1993. Pesticides in the Diets of Infants and Children. National Academy Press. Washington D.C.

Nazarko,O.M., R.C.Van Acker, M.H.Entz, A.Schoofs, and G.Martens. 2003. "Pesticide Free Production of Field Crops: Results of an On-Farm Pilot Project." Agronomy Journal. 95:1262-1273.
Abstract: Existing strategies for pesticide use reduction in the northern Great Plains have suffered from limited adoption. A novel approach, Pesticide Free Production (PFP), was recently developed in Manitoba, Canada. A participatory, on-farm study was conducted to assess the potential of PFP to be implemented on typical farms and the level of success farmers experienced with PFP. Pesticide Free Production prohibits the use of in-crop pesticide and seed treatments during one crop year as well as prior use of residual pesticides. Synthetic fertilizer use is permitted, as are pre-emergent applications of nonresidual pesticides. A total of 71 farmers, representing 120 fields and 11 crops, participated in the study. Fields and farmers were grouped based on whether or not fields (i) achieved PFP certification and (ii) were in transition to organic production. Certification was achieved for 83% of the participating area. Spring cereals were the most likely crops to achieve PFP certification. Yields in all groups were slightly lower than conventional averages in Manitoba but were not significantly different among groups. Weed densities were higher (P = 0.065) in noncertifiable fields than in certifiable fields. Most farmers reported manageable weed densities in the year following PFP. Soil conservation practices were used on a high proportion of PFP fields. Management practices associated with PFP included the use of delayed seeding, forages in rotation, and increased seeding rates. Agronomic and demographic characteristics of participating fields and farmers were typical for Manitoba. Pesticide Free Production demonstrates considerable potential to be successfully adopted by mainstream farmers

Office of Pesticide Programs. Pesticide Reregistration -- Chemical Status. US Environmental Protection Agency. 2002. Washington, D.C.
Ref Type: Data File

Oliva,A., A.Giami, and L.Multigner. 2002. "Environmental agents and erectile dysfunction: a study in a consulting population." J.Androl. 23:546-550.
Abstract: We evaluated chemical and physical environmental agents as risk factors for erectile dysfunction among a consulting population. We studied 199 men who sought medical help for erectile disorders between 1996 and 1998 in 3 andrology units in the Litoral Sur region of Argentina. Patients were evaluated by monitoring nocturnal penile tumescence and rigidity, and were classified as having normal (n = 26), irregular (dissociation, short episode or low amplitude, n = 146), or flat erectile pattern (n = 26). Exposure to environmental agents was assessed by a detailed interview, and 4 groups were constituted: nonexposed, pesticide-exposed, solvent-exposed, and heat-exposed. A multivariate polytomous logistic regression model was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for association between quality of nocturnal erections and exposure groups adjusted for confounding factors. Exposure to environmental agents was a risk factor for a flat erectile pattern (OR 7.1, 95% CI 1.5-33.0 for pesticides; OR 12.2, 95% CI 1.2-124.8 for solvents; and OR 1.7, 95% CI 0.3-9.4 for heat). Associations were much weaker for an irregular erectile pattern (OR 1.8, 95% CI 0.5-6.7 for pesticides; OR 2.1, 95% CI 0.3-17.9 for solvents; and OR 1.2, 95% CI 0.4-4.0 for heat). Our results suggest that environmental agents constitute a risk factor for erectile dysfunction by interfering with erectile ability

Pang,Y., D.L.MacIntosh, D.E.Camann, and P.B.Ryan. 2002. "Analysis of aggregate exposure to chlorpyrifos in the NHEXAS-Maryland investigation." Environ.Health Perspect. 110:235-240.
Abstract: As part of the National Human Exposure Assessment Survey (NHEXAS) in Maryland, we collected indoor air, carpet dust, exterior soil, and duplicate diet samples from a stratified random sample of 80 individuals to evaluate aggregate daily exposure, contributions of specific pathways of exposure, and temporal variation in exposure to chlorpyrifos. We collected samples from each participant in up to six equally spaced sampling cycles over a year and analyzed them for chlorpyrifos. We used chlorpyrifos concentrations in each medium and self-reported rates of time spent inside at home, time and frequency of contact with carpet, frequency of contact with soil, and weights of the duplicate diet samples to derive exposure to chlorpyrifos from each medium as well as average daily aggregate exposure (nanograms per day). The mean aggregate daily exposure to chlorpyrifos of 36 measurements obtained from 31 people was 1,390 ng/day (SD, 2,770 ng/day). Exposure from inhalation of indoor air accounted for 84.7% of aggregate daily exposure to chlorpyrifos on average. Chlorpyrifos concentrations in indoor air and carpet dust and the corresponding exposure rates were significantly correlated. Repeated short-term measurements of chlorpyrifos in carpet dust from individual residences were strongly correlated over time (reliability coefficient, R = 0.90), whereas the short-term measurements of chlorpyrifos in indoor air (R = 0.55) and solid food (R = 0.03) had moderate to weak reliability. Exposure to chlorpyrifos through those media and in aggregate based on direct measurements reported in this study can be used to understand better the accuracy of pesticide safety assessments

Panganiban,L., N.Cortes-Maramba, C.Dioquino, M.L.Suplido, H.Ho, A.Francisco-Rivera, and A.Manglicmot-Yabes. 2004. "Correlation between blood ethylenethiourea and thyroid gland disorders among banana plantation workers in the Philippines." Environmental Health Perspectives. 112:42-45.
Abstract: Ethylenebisdithiocarbamates (EBDCs) are metabolized into ethylenethiourea (ETU), a possible human carcinogen and an antithyroid compound. In this study our goal was to correlate ETU levels with the incidence of thyroid gland disorders among banana plantation workers exposed to EBDC. We randomly selected 57 directly exposed workers and 31 indirectly exposed workers from four banana plantations and 43 workers from an organic farm; all subjects underwent complete medical examinations and laboratory tests. Results showed a higher mean thyroid-stimulating hormone measurement among exposed workers compared with the control group, although the levels were well within normal range. Nine of the exposed farmers had abnormal thyroid ultrasound findings, consisting mostly of solitary nodules, compared with three among the control group. Analysis of variance showed significantly different blood ETU levels among the directly exposed, indirectly exposed, and control groups ($p < 0.001$), but ETU levels in urine were not significantly different ($p = 0.10$). Environmental ETU levels were below the U.S. Environmental Protection Agency remediation levels. Among farmers with solitary thyroid nodules, we found a very good direct correlation between the size of the nodule and blood ETU level. In this study we showed that blood ETU is a more reliable biomarker for EBDC exposure than urinary ETU; therefore, the determination of blood ETU should be part of medical surveillance efforts among workers exposed to EBDC to detect occurrences of thyroid gland disorders.

Pastore,L.M., I.Hertz-Picciotto, and J.J.Beaumont. 1997. "Risk of stillbirth from occupational and residential exposures." Occupational & Environmental Medicine. 54:511-518.
Abstract: Objectives-To analyse the risk of stillbirth from 12 residential and occupational maternal exposures during pregnancy. Methods-Stillbirths and neonatal deaths in 1984 within 24 hours of birth from 10 California counties were identified from death certificates. Controls were randomly selected from live births born in 1984 and frequency matched to cases by maternal age and county. Data sources included vital statistics and a self administered postal questionnaire. regression and proportional modelling were performed; the proportional hazards considered the truncated opportunity for exposure among cases. Special focus was given to two cause of death groups: congenital anomalies (12% of deaths) and complications of the placenta, cord, and membranes (37% of deaths). Results-Occupational exposure to pesticides during the first two months of gestation was positively associated with stillbirths due to congenital anomalies (odds ratio (OR) 2.4, 95% confidence interval (95% CI) 1.0 to 5.9), and during the first and second trimesters with stillbirths due to all causes of death (risk ratios (RR) 1.3-1.4, 95% CI 1.0 to 1.7) and stillbirths due to complications of the placenta, cord, and membranes (RR 1.6-1.7, 95% CI 1.1 to 2.3). Occupational exposure to video display terminals in the third trimester was found to have a modest inverse association with stillbirths (RR 0.7, 95% CI 0.6, 0.9). Home pesticide exposure was positively associated with stillbirths due to congenital anomalies (OR 1.7, 95% CI 1.0 to 2.9). Conclusions-Occupational exposure to pesticides, especially during early pregnancy, had a clear positive association with

stillbirths regardless of cause of death. Methodologically, this study of stillbirths is unique in its analysis of specific causes of death and use of time specific exposure windows.

Perera,F.P., V.Rauh, R.M.Whyatt, D.Tang, W.Y.Tsai, J.T.Bernert, Y.H.Tu, H.Andrews, D.B.Barr, D.E.Camann, D.Diaz, J.Dietrich, A.Reyes, and P.L.Kinney. 2005. "A summary of recent findings on birth outcomes and developmental effects of prenatal ETS, PAH, and pesticide exposures." Neurotoxicology. 26:573-587.
Abstract: Inner-city minority populations are high-risk groups for adverse birth outcomes and also more likely to be exposed to environmental contaminants, including environmental tobacco smoke (ETS), benzo[a]pyrene B[a]P, other ambient polycyclic aromatic hydrocarbons (global PAHs), and residential pesticides. The Columbia Center for Children's Environmental Health (CCCEH) is conducting a prospective cohort study of 700 northern Manhattan pregnant women and newborns to examine the effects of prenatal exposure to these common toxicants on fetal growth, early neurodevelopment, and respiratory health. This paper summarizes results of three published studies demonstrating the effects of prenatal ETS, PAH, and pesticides on birth outcomes and/or neurocognitive development [Perera FP, Rauh V, Whyatt RM, Tsai WY, Bernert JT, Tu YH, et al. Molecular evidence of an interaction between prenatal environment exposures on birth outcomes in a multiethnic population. Environ Health Perspect 2004;12:630-62; Rauh VA, Whyatt RM, Garfinkel R, Andrews H, Hoepner L, Reyes A, et al. Developmental effects of exposure to environmental tobacco smoke and material hardship among inner-city children. Neurotoxicol Teratol 2004;26:373-85; Whyatt RM, Rauh V, Barr DB, Camann DE, Andrews HF, Garfinkel R, et al. Prenatal insecticide exposures, birth weight and length among an urban minority cohort. Environ Health Perspect, in press]. To evaluate the effects of prenatal exposure to ETS, PAHs, and pesticides, researchers analyzed questionnaire data, cord blood plasma (including biomarkers of ETS and pesticide exposure), and B[a]P-DNA adducts (a molecular dosimeter of PAHs). Self-reported ETS was associated with decreased head circumference ($P = 0.04$), and there was a significant interaction between ETS and adducts such that combined exposure had a significant multiplicative effect on birth weight ($P = 0.04$) and head circumference ($P = 0.01$) after adjusting for confounders. A second analysis examined the neurotoxic effects of prenatal ETS exposure and postpartum material hardship (unmet basic needs in the areas of food, housing, and clothing) on 2-year cognitive development. Both exposures depressed cognitive development ($P < 0.05$), and there was a significant interaction such that children with exposure to both ETS and material hardship exhibited the greatest cognitive deficit (7.1 points). A third analysis found that cord chlorpyrifos, and a combined measure of cord chlorpyrifos, diazinon, and propoxur-metabolite, were inversely associated with birth weight and/or length ($P < 0.05$). These results underscore the importance of policies that reduce exposure to ETS, air pollution, and pesticides with potentially adverse effects on fetal growth and child neurodevelopment

Pesticide Residue Committee. Annual Report of the Pesticide Residue Committee 2001. 2001. United Kingdom Food Standards Agency.
Ref Type: Generic

Petrini,J., K.Damus, and R.B.Johnston, Jr. 1998. "Trends in infant mortality attributable to birth defects -- United States, 1980-1995." Morbidity & Mortality Weekly Report. 47:773-778.
Abstract: 1980 vs 1995 rates of infant mortality associated with birth defects, and % change. Most drastic reductions (according to map): Oregon, Vermont, Maryland, which went from 2.7-3.2 down to 1.1-1.4 per 1000 live births.

Pfleeger,T.G. 2003. "Pesticides: Problems, Improvements, Alternatives." Journal of Environmental Quality. 32:2445.

Qiao,D., F.J.Seidler, S.Padilla, and T.A.Slotkin. 2002. "Developmental neurotoxicity of chlorpyrifos: what is the vulnerable period?" Environ.Health Perspect. 110:1097-1103.
Abstract: Previously, we found that exposure of neonatal rats to chlorpyrifos (CPF) produced brain cell damage and loss, with resultant abnormalities of synaptic development. We used the same biomarkers to examine prenatal CPF treatment so as to define the critical period of vulnerability. One group of pregnant rats received CPF (subcutaneous injections in dimethyl sulfoxide vehicle) on gestational days (GD) 17-20, a peak period of neurogenesis; a second group was treated on GD9-12, the period of neural tube formation. In the GD17-20 group, the threshold for a reduction in maternal weight gain was 5 mg/kg/day; at or below that dose, there was no evidence (GD21) of general fetotoxicity as assessed by the number of fetuses or fetal body and tissue weights. Above the threshold, there was brain sparing (reduced body weight with an increase in brain/body weight ratio) and a targeting of the liver (reduced liver/body weight). Indices of cell packing density (DNA per gram of tissue) and cell number (DNA content) similarly showed effects only on the liver; however, there were significant changes in the protein/DNA ratio, an index of cell size, in fetal brain regions at doses as low as 1 mg/kg, below the threshold for inhibition of fetal brain cholinesterase (2 mg/kg). Indices of cholinergic synaptic development showed significant CPF-induced defects but only at doses above the threshold for cholinesterase inhibition. With earlier CPF treatment (GD9-12), there was no evidence of general fetotoxicity or alterations of brain cell development at doses up to the threshold for maternal toxicity (5 mg/kg), assessed on GD17 and GD21; however, augmentation of cholinergic synaptic markers was detected at doses as low as 1 mg/kg. Compared with previous work on postnatal CPF exposure, the effects seen here required doses closer to the threshold for fetal weight loss; this implies a lower vulnerability in the fetal compared with the neonatal brain. Although delayed neurotoxic effects of prenatal CPF may emerge subsequently in development, our results are consistent with the preferential targeting of late developmental events such as gliogenesis, axonogenesis, and synaptogenesis

Qiao,D., F.J.Seidler, C.A.Tate, M.M.Cousins, and T.A.Slotkin. 2003. "Fetal chlorpyrifos exposure: adverse effects on brain cell development and cholinergic biomarkers emerge postnatally and continue into adolescence and adulthood." Environ.Health Perspect. 111:536-544.
Abstract: Fetal and childhood exposures to widely used organophosphate pesticides, especially chlorpyrifos (CPF), have raised concerns about developmental neurotoxicity.

Previously, biomarkers for brain cell number, cell packing density, and cell size indicated that neonatal rats were more sensitive to CPF than were fetal rats, yet animals exposed prenatally still developed behavioral deficits in adolescence and adulthood. In the present study, we administered CPF to pregnant rats on gestational days 17-20, using regimens devoid of overt fetal toxicity. We then examined subsequent development of acetylcholine systems in forebrain regions involved in cognitive function and compared the effects with those on general biomarkers of cell development. Choline acetyltransferase, a constitutive marker for cholinergic nerve terminals, showed only minor CPF-induced changes during the period of rapid synaptogenesis. In contrast, hemicholinium-3 binding to the presynaptic choline transporter, which is responsive to nerve impulse activity, displayed marked suppression in the animals exposed to CPF; despite a return to nearly normal values by weaning, deficits were again apparent in adolescence and adulthood. There was no compensatory up-regulation of cholinergic receptors, as m2-muscarinic cholinergic receptor binding was unchanged. CPF also elicited delayed-onset alterations in biomarkers for general aspects of cell integrity, with reductions in cell packing density, increases in relative cell size, and contraction of neuritic extensions; however, neither the magnitude nor timing of these changes was predictive of the cholinergic defects. The present findings indicate a wide window of vulnerability of cholinergic systems to CPF, extending from prenatal through postnatal periods, occurring independently of adverse effects on general cellular neurotoxicity

Reganold,J.P., J.D.Glover, P.K.Andrews, and H.R.Hinman. 2001. "Sustainability of three apple production systems." Nature. 410:926-930.
Abstract: Escalating production costs, heavy reliance on non-renewable resources, reduced biodiversity, water contamination, chemical residues in food, soil degradation and health risks to farm workers handling pesticides all bring into question the sustainability of conventional farming systems. It has been claimed, however, that organic farming systems are less efficient, pose greater health risks and produce half the yields of conventional farming systems. Nevertheless, organic farming became one of the fastest growing segments of US and European agriculture during the 1990s. Integrated farming, using a combination of organic and conventional techniques, has been successfully adopted on a wide scale in Europe. Here we report the sustainability of organic, conventional and integrated apple production systems in Washington State from 1994 to 1999. All three systems gave similar apple yields. The organic and integrated systems had higher soil quality and potentially lower negative environmental impact than the conventional system. When compared with the conventional and integrated systems, the organic system produced sweeter and less tart apples, higher profitability and greater energy efficiency. Our data indicate that the organic system ranked first in environmental and economic sustainability, the integrated system second and the conventional system last

Rosso,S.B., A.O.Caceres, A.M.de Duffard, R.O.Duffard, and S.Quiroga. 2000. "2,4-Dichlorophenoxyacetic acid disrupts the cytoskeleton and disorganizes the Golgi apparatus of cultured neurons." Toxicol.Sci. 56:133-140.
Abstract: 2,4-Dichlorophenoxyacetic acid (2,4-D) is a potent neurotoxic herbicide widely used in agriculture. The basic mechanisms by which 2,4-D produces cell damage have

not yet been determined. In this study we have examined the effects of 2,4-D in primary cultures of cerebellar granule cells in order to obtain insights into the possible mechanisms underlying the toxic effects of this herbicide. The results obtained indicate that a 24-hour exposure to 2,4-D produces a striking and dose-dependent inhibition of neurite extension. This phenomenon is paralleled by a significant reduction in the cellular content of both dynamic and stable microtubules, a disorganization of the Golgi apparatus, and an inhibition in the synthesis of complex gangliosides. Interestingly, 2,4-D inhibits the in vitro polymerization of purified tubulin. Taken together, the present observations raise the possibility that at least one basic mechanism underlying 2,4-D neurotoxicity involves an inhibition of microtubule assembly. That event may cause a decreased neurite outgrowth response, and could also explain the observed differences in the pattern of ganglioside biosynthesis and/or the disorganization of the Golgi apparatus

Savitz,D.A., T.Arbuckle, D.Kaczor, and K.M.Curtis. 1997. "Male pesticide exposure and pregnancy outcome." American Journal of Epidemiology. 146:1025-1036.
Abstract: Potential health effects of agricultural pesticide use include reproductive outcomes. For the Ontario Farm Family Health Study, the authors sampled Ontario farms from the 1986 Canadian Census of Agriculture, identified farm couples, and obtained questionnaire data concerning farm activities, reproductive health experience, and chemical applications, Male farm activities in the period from 3 months before conception through the month of conception were evaluated in relation to miscarriage, preterm delivery, and small-for-gestational-age births. Among the 1,898 couples with complete data (64% response), 3,984 eligible pregnancies were identified. Miscarriage was not associated with chemical activities overall but was increased in combination with reported use of thiocarbamates, carbaryl, and unclassified pesticides on the farm, Preterm delivery was also not strongly associated with farm chemical activities overall, except for mixing or applying yard herbicides (odds ratio = 2.1, 95% confidence interval 1.0-4.4), Combinations of activities with a variety of chemicals (atrazine, glyphosate, organophosphates, 4-[2,4-dichlorophenoxy] butyric acid, and insecticides) generated odds ratios of two or greater, No associations were found between farm chemicals and small-for-gestational-age births or altered sex ratio. Based on these data, despite limitations in exposure assessment, the authors encourage continued evaluation of male exposures, particularly in relation to miscarriage and preterm delivery.

Schafer,K.S. and S.E.Kegley. 2002. "Persistent toxic chemicals in the US food supply." Journal of Epidemiology and Community Health. 56:813-817.
Abstract: Persistent organic pollutants (POPs) have spread throughout the global environment to threaten human health and damage ecosystems, with evidence of POPs contamination in wildlife, human blood, and breast milk documented worldwide. Based on data from the US Food and Drug Administration, this article provides a brief overview of POPs residues in common foods in the United States food supply. The analysis focuses on 12 chemical compounds now targeted for an international phase out under the Stockholm Convention on POPs. The available information indicates that POPs residues are present in virtually all categories of foods, including baked goods, fruit, vegetables, meat, poultry, and dairy products. Residues of five or more persistent toxic chemicals in a single food item are not unusual, with the most commonly found POPs being the

pesticides DDT (and its metabolites, such as DDE) and dieldrin. Estimated daily doses of dieldrin alone exceed US Environmental Protection Agency and US Agency for Toxic Substances Disease Control reference dose for children. Given the widespread occurrence of POPs in the food supply and the serious health risks associated with even extremely small levels of exposure, prevention of further food contamination must be a national health policy priority in every country. Implementation of the Stockholm Convention will prevent further accumulation of persistent toxic chemicals in food. Early ratification and rapid implementation of this treaty should be an urgent priority for all governments

Schreinemachers,D.M., J.P.Creason, and V.F.Garry. 1999. "Cancer mortality in agricultural regions of Minnesota." Environ.Health Perspect. 107:205-211.
Abstract: Because of its unique geology, Minnesota can be divided into four agricultural regions: south-central region one (corn, soybeans); west-central region two (wheat, corn, soybeans); northwest region three (wheat, sugar beets, potatoes); and northeast region four (forested and urban in character). Cancer mortality (1980-1989) in agricultural regions one, two, and three was compared to region four. Using data compiled by the National Center for Health Statistics, cancer mortality was summarized by 5-year age groups, sex, race, and county. Age-standardized mortality rate ratios were calculated for white males and females for all ages combined, and for children aged 0-14. Increased mortality rate ratios and 95% confidence intervals (CIs) were observed for the following cancer sites: region one--lip (men), standardized rate ratio (SRR) = 2.70 (CI, 1.08-6.71); nasopharynx (women), SRR = 3.35 (CI, 1.20-9.31); region two--non-Hodgkin's lymphoma (women), SRR = 1.35 (CI, 1.09-1.66); and region three--prostate (men), SRR = 1.12 (CI, 1.00-1.26); thyroid (men), SRR = 2.95 (CI, 1.35-6.44); bone (men), SRR = 2.09 (CI, 1. 00-4.34); eye (women), SRR = 5.77 (CI, 1.90-17.50). Deficits of smoking-related cancers were noted. Excess cancers reported are consistent with earlier reports of agriculturally related cancers in the midwestern United States. However, reports on thyroid and bone cancer in association with agricultural pesticides are few in number. The highest use of fungicides occurs in region three. Ethylenebisdithiocarbamates, whose metabolite is a known cause of thyroid cancer in rats, are frequently applied. This report provides a rationale for evaluation of the carcinogenic potential of this suspect agent in humans

Schreinemachers,D.M. 2000. "Cancer mortality in four northern wheat-producing states." Environ.Health Perspect. 108:873-881.
Abstract: Chlorophenoxy herbicides are used both in cereal grain agriculture and in nonagricultural settings such as right-of-ways, lawns, and parks. Minnesota, North Dakota, South Dakota, and Montana grow most of the spring and durum wheat produced in the United States. More than 90% of spring and durum wheat is treated with chlorophenoxy herbicides, in contrast to treatment of approximately 30% of winter wheat. In this ecologic study I used wheat acreage as a surrogate for exposure to chlorophenoxy herbicides. I investigated the association of chlorophenoxy herbicides with cancer mortality during 1980-1989 for selected counties based on level of agriculture ([greater and equal to] 20%) and rural population ([greater and equal to] 50%). Age-standardized cancer mortality rates were determined for grouped counties based on tertiles of wheat acreage per county or for individual counties for frequently

occurring cancers. The cancer sites that showed positive trends of increasing cancer mortality with increasing wheat acreage were esophagus, stomach, rectum, pancreas, larynx, prostate, kidney and ureter, brain, thyroid, bone, and all cancers (men) and oral cavity and tongue, esophagus, stomach, liver and gall bladder and bile ducts, pancreas, cervix, ovary, bladder, and other urinary organs, and all cancers (women). Rare cancers in men and women and cancers in boys and girls were studied by comparing counties above and below the median of wheat acreage per county. There was increased mortality for cancer of the nose and eye in both men and women, brain and leukemia in both boys and girls, and all cancers in boys. These results suggest an association between cancer mortality and wheat acreage in counties of these four states

Schreinemachers,D.M. 2003. "Birth malformations and other adverse perinatal outcomes in four U.S. Wheat-producing states." Environ.Health Perspect. 111:1259-1264.
Abstract: Chlorophenoxy herbicides are widely used in the United States and Western Europe for broadleaf weed control in grain farming and park maintenance. Most of the spring and durum wheat produced in the United States is grown in Minnesota, Montana, North Dakota, and South Dakota, with more than 85% of the acreage treated with chlorophenoxy herbicides such as 2,4-dichlorophenoxyacetic acid (2,4-D) and 4-chloro-2-methylphenoxyacetic acid (MCPA). Rates of adverse birth outcomes in rural, agricultural counties of these states during 1995-1997 were studied by comparing counties with a high proportion of wheat acreage and those with a lower proportion. Information routinely collected and made available by federal agencies was used for this ecologic study. Significant increases in birth malformations were observed for the circulatory/respiratory category for combined sexes [odds ratio (OR) = 1.65; 95% confidence interval (CI), 1.07-2.55]. A stronger effect was observed for the subcategory, which excluded heart malformations (OR = 2.03; 95% CI, 1.14-3.59). In addition, infants conceived during April-June--the time of herbicide application--had an increased chance of being diagnosed with circulatory/respiratory (excluding heart) malformations compared with births conceived during other months of the year (OR = 1.75; 95% CI, 1.09-2.80). Musculoskeletal/integumental anomalies increased for combined sexes in the high-wheat counties (OR = 1.50; 95% CI, 1.06-2.12). Infant death from congenital anomalies significantly increased in high-wheat counties for males (OR = 2.66; 95% CI, 1.52-4.65) but not for females (OR = 0.48; 95% CI, 0.20-1.15). These results are especially of concern because of widespread use of chlorophenoxy herbicides

Sever,L.E., T.E.Arbuckle, and A.Sweeney. 1997. "Reproductive and developmental effects of occupational pesticide exposure: the epidemiologic evidence." Occup.Med. 12:305-325.
Abstract: There is increasing evidence for reproductive and developmental effects of both maternal and paternal pesticide exposures. Here is a summary of the epidemiologic data, culled from studies in humans, with significant attention to Agent Orange

Sharpe,R.M. and D.S.Irvine. 2004. "How strong is the evidence of a link between environmental chemicals and adverse effects on human reproductice health?" British Medical Journal. 328:447-451.

Abstract: [overview of the current evidence for reproductive effects relusting from exposure to environmental synthetic chemicals]

Shaw,G.M., C.R.Wasserman, C.D.O'Malley, V.Nelson, and R.J.Jackson. 1999. "Maternal pesticide exposure from multiple sources and selected congenital anomalies." Epidemiology. 10:60-66.
Abstract: We explored the relation between various potential sources of maternal periconceptional pregnancy exposures to pesticides and congenital anomalies in offspring. Data were derived from a case-control study of fetuses and liveborn infants with orofacial clefts, neural tube defects, conotruncal defects, or limb anomalies, among 1987-1989 California births and fetal deaths. We conducted telephone interviews with mothers of 662 (85% of eligible) orofacial cleft cases, 265 (84%) neural tube defect cases, 207 (87%) conotruncal defect cases, 165 (84%) limb cases, and 734 (78%) nonmalformed controls. The odds ratio (OR) estimates did not indicate increased risk for any of the studied anomaly groups among women whose self-reported occupational tasks were considered by an industrial hygienist likely to involve pesticide exposures. Paternal occupational exposure to pesticides, as reported by the mother, revealed elevated ORs for only two of the cleft phenotypes {OR = 1.7 [95% confidence interval (CI) = 0.9-3.4] for multiple cleft lip with/without cleft palace and OR = 1.6 [95% CI = 0.7-3.4] for multiple cleft palate}. Use of pesticide products for household gardening, by mothers or by professional applicators, was associated with ORs greater than or equal to 1.5 for most of the studied anomalies. Use of pesticide products for the control of pests in or around homes was not associated with elevated risks for most of the studied anomalies, although women who reported that a professional applied pesticides to their homes had increased risks for neural tube defect-affected pregnancies [OR = 1.6 (95% CI = 1.1-2.5)] and limb anomalies [OR = 1.6 (95% CI = 1.0-2.7)]. Having a pet cat or dog and treating its fleas was not associated with increased anomaly risk. Women who reported living within 0.25 miles of an agricultural crop revealed increased risks for offspring with neural tube defects [OR = 1.5 (95%CI = 1.1-2.1)]. For many of the comparisons, data were sparse, resulting in imprecise effect estimation. Despite our investigating multiple sources of potential pesticide exposures, without more specific information on chemical and level of exposure, we could not adequately discriminate whether the observed effects are valid, whether biased exposure reporting contributed to the observed elevated risks, or whether nonspecific measurement of exposure was responsible for many of the observed estimated risks not being elevated.

Smirle,M.J., D.T.Lowery, and C.L.Zurowski. 2003. "Susceptibility of leafrollers (Lepidoptera: Tortricidae) from organic and conventional orchards to azinphosmethyl, spinosad, and Bacillus thuringiensis." J.Econ.Entomol. 96:879-884.
Abstract: Populations of obliquebanded leafroller, Choristoneura rosaceana Harris, and three-lined leafroller, Pandemis limitata Robinson, were obtained from seven sites in the Okanagan and Similkameen Valleys of British Columbia and assayed for their responses to three insecticides using a leaf disk bioassay. Lethal concentration ratios (LCRs) were calculated for all populations compared with a susceptible laboratory colony of C. rosaceana; significant variation was detected in response to all three insecticides. LCRs were 0.86-15.52 for azinphosmethyl, 0.38-2.37 for spinosad (Success), and 0.58-4.89 for

Bacillus thuringiensis (Foray). Correlation analysis indicated no cross-resistance among the three insecticides. Leafroller populations obtained from apple orchards managed with organic production practices were more susceptible to azinphosmethyl than leafrollers obtained from conventionally managed sites. Conversely, the highest levels of tolerance to B. thuringiensis were observed in the populations from organic sites, possibly reflecting usage patterns; B. thuringiensis is one of the few insecticides allowed under organic production guidelines. All populations were highly susceptible to spinosad, which may be a useful tool for resistance management programs if used judiciously

Solomon,G.M. and A.M.Huddle. 2002. "Low levels of persistent organic pollutants raise concerns for future generations." J Epidemiol Community Health. 56:826-827.
Abstract: Bans and regulation in many countries have reduced the environmental levels of many persistent organic pollutants (POPs). Despite these declines, there is still evidence of exposures in a range associated with adverse health effects. This seeming paradox is a result of the realisation that levels once presumed safe can cause subtle but important health effects. For example, levels of PCBs now shown to affect human brain development are nearly one million-fold lower than levels previously believed safe. These findings add urgency to efforts to globally eliminate these chemicals, and carry lessons for persistent pollutants that are still in widespread use today, such as the polybrominated diphenyl ethers (PBDEs) and synthetic musks

Stoker,T.E., J.M.Goldman, and R.L.Cooper. 1993. "The dithiocarbamate fungicide thiram disrupts the hormonal control of ovulation in the female rat." Reproductive Toxicology. 7:211-218.
Abstract: Thiram has been reported to inhibit dopamine b-hydroxylase (DbH), thereby affecting norepinephrine (NE) synthesis. Because NE is a neurotransmitter that is known to play an important role in the hypothalamic regulation of pituary function, the acute effects of the thiram on the hormonal control of ovulation in the rat were investigated. Ovariectomized, estrogen primed female rats were given a single injection of thiram (0,6,12,25,50 and 100 mg/kg, i.p.) at 1100 h and serum LH was measured in serial bleeds. Thiram at 100 and 50 mg/kg completely blocked the LH surge in all rats tested, while 12 and 25 mg/kg blocked the surge in 40 and 75% of the treated animals, respectively. Six mg/kg had no effect. Ovulation was then assessed in intact, proestrus females in response to thiram administration (0,12,25, or 50 mg/kg) at 0900, 1100, 1300 or 1800 h. Ovulation was blocked by 25 and 50 mg/kg at 1300 h in all rats, but when injected at 1100 h only the 50 mg/kg dose was effective. No such blockade was found with 50mg/kg injected at 0900 and 1800 h. To assess the influence of thiram on the LH surge in intact rats, additional females were dosed at 1300 h on the day of proestrus and blood collected over that same day. Thiram at 50mg/kg blocked the LH surge in all rats, while 25 mg/kg blocked the surge in 60% of the females tested. No effect occurred with 12 mg/kg. These data show that thiram is able to block the LH surge and inhibit subsequent ovulation if administered during a sensitive period prior to the initiation of the surge. The effect likely involves a disruption in catecholamine synthesis and requires larger doses as the temporal distance from a time of heightened sensitivity increases.

Stoker,T.E., R.L.Cooper, J.M.Goldman, and J.E.Andrews. 1996. "Characterization of pregnancy outcome following thiram-induced ovulatory delay in the female rat." Neurotoxicology & Teratology. 18:277-282.
Abstract: A single injection of the dithiocarbamate fungicide, thiram, suppresses the proestrous surge of LH and delays ovulation for 24 h. In this study, we examined fertility after a thiram-induced delayed ovulation. Females were injected with thiram (50 mg/kg, IF) on proestrus (1300 h) and mated on the following evening. Control and thiram-treated, but nondelayed, females were injected and mated on the same day. The number of females in the thiram-delayed group that became pregnant was reduced and litter size on GD 20 was reduced; however, no obvious morphological anomalies were seen. The number of pregnant females and litter size was not altered in the thiram-nondelayed rats, indicating that it is the thiram-induced delay in ovulation and nor the exposure to thiram per se that was responsible for altered pregnancy outcome. On GD 7 and 11, the number of live fetuses per litter was reduced in the delayed females, but the number of implantation sites was not different hom controls. On GD 11 the mean developmental score, head length, crown-rump length, and somite number in the delayed group were also reduced, indicating retarded development of live embryos. These results demonstrate that delayed ovulation induced by a single thiram exposure does not alter the number of oocytes released or the number that implant. However, the concepti h om these females are compromised during midgestation.

Swan,S.H., C.Brazil, E.Z.Drobris, F.Liu, R.L.Kruse, M.Hatch, J.B.Rdmon, C.Wang, J.W.Overstreet, and The Study for Future Families Research Group. 2003. "Geographic differences in semen quality of fertile U.S. males." Environmental Health Perspectives. 111:414-420.
Abstract: Although geographic variation in semen quality has been reported, this is the first study in the United States to compare semen quality among study centers using standardized methods and strict quality control. We evaluated semen specimens from partners of 512 pregnant women recruited through prenatal clinics in four U.S. cities during 1999-2001; 91% of men provided two specimens. Sperm concentration, semen volume, and motility were determined at the centers, and morphology was assessed at a central laboratory. Study protocols were identical across centers, and quality control was rigorously maintained. Sperm concentration was significantly lower in Columbia, Missouri, than in New York, New York; Minneapolis, Minnesota; and Los Angeles, California. Mean counts were 58.7, 102.9, 98.6, and 80.8 x 106/mL (medians 53.5, 88.5, 81.8, and 64.8 x106/mL) in Missouri, New York, Minnesota, and California, respectively. The total number of motile sperm was also lower in Missouri than in other centers: 113, 196, 201, and 162 x106 in Missouri, New York, Minnesota, and California, respectively. Semen volume and the percent morphologically normal sperm did not differ appreciably among centers. These between-center differences remained significant in multivariate models that controlled for abstinence time, semen analysis time, age, race, smoking, history of sexually transmitted disease, and recent fever (all p-values < 0.01). Confounding factors and differences in study methods are unlikely to account for the lower semen quality seen in this mid-Missouri population. These data suggest that sperm concentration and motility may be reduced in semirural and agricultural areas relative to more urban and less agriculturally exposed areas.

Swartz,W.J. and V.P.Eroschenko. 1998. "Neonatal exposure to technical methoxychlor alters pregnancy outcome in female mice." Reproductive Toxicology. 12:565-573. Abstract: This study was designed to determine the ability of female mice who were exposed neonatally to the pesticide methoxychlor (MXC) to mate, ovulate, and become pregnant upon reaching sexual maturity. One-day-old female mice (5 to 8/group) were exposed daily by intraperitoneal (ip) injection for 14 d to either sesame oil or 10 mu g estradiol-17 beta or 0.1, 0.5 or 1.0 mg MXC suspended in sesame oil. The MXC exposures corresponded to 14 to 71, 68 to 357, or 135 to 714 mg/kg body weight, respectively, Three months later, female mice were placed with proven breeder males and checked daily for vaginal plugs. Mated female mice were sacrificed 18 d after the appearance of a vaginal plug to evaluate pregnancy. Uteri were examined for the presence of living fetuses and/or resorption sites. Ovaries were removed and prepared for histologic evaluation and tabulation of corpora lutea, All mice from all three MXC-treated groups did in fact mate, in comparison with only one of those exposed neonatally to estradiol, Increasing the dose of MXC produced a decreased number of pregnant animals at 18 d following mating. The mean number of five fetuses/litter was reduced in the 0.5 and 1.0 mg MXC-treated groups. Corpora lutea were significantly reduced in ovaries from only the 1.0 mg MXC group and the estradiol group. No effects of treatment were seen at 0.1 mg MXC, It is concluded that neonatal exposure to MXC does not interfere with mating. Instead, significant alterations are seen in initiating and/or maintaining pregnancy. The deleterious effects on pregnancy may be due to the influence of neonatal MXC treatments on the hypothalamic-pituitary-ovarian axis as well as on possible alteration of the uterine environment.

Thamsborg,S.M., A.Roepstorff, and M.Larsen. 1999. "Integrated and biological control of parasites in organic and conventional production systems." Vet.Parasitol. 84:169-186. Abstract: Organic and other non-intensive animal production systems are of growing importance in several countries worldwide. In contrast to conventional farms, parasite control on organic farms is affected by several of the prescribed changes in management e.g. access to the outdoors in the summer and in most countries, a ban on preventive medication, including use of anti-parasiticides. Organic animal production relies heavily on grazing, and pasture or soil related parasites are thus of major importance. Several studies in northern temperate climate have indicated that outdoor production of pigs, primarily sows, and laying hens results in heavier and more prevalent helminth infections compared to conventional intensive production under indoor conditions. In organic dairy cattle, parasitic gastroenteritis in heifers may be more prevalent. In a short to medium term perspective, integrated control may combine grazing management with biological control using nematophagous micro-fungi, selected crops like tanniferous plants and on conventional farms, limited use of anti-parasiticides. At present, the non-chemotherapeutic control of pasture related infections is based mainly on grazing management strategies. Preventive strategies, where young, previously unexposed stock, are turned out on parasite-free pastures, can be used for grazing first season dairy heifers and in all-in-all-out poultry production. Evasive strategies aim at avoiding disease producing infections of a contaminated area by moving to a clean area and may be relevant for ruminants and pigs. In cattle, effective control of nematodes can be achieved

by repeated moves of the herd or alternate grazing with other species. High stocking rates seem to be an important risk factor. In pig production, the effect of paddock rotation on parasite infections is largely unknown and studies are warranted. Control of nematodes by larvae-trapping fungi, or perhaps in the future by egg-destroying fungi, looks promising for ruminants and certain monogastric animals but delivery systems and practical dosing regimes integrated with grazing management have to be developed. In conclusion, good prospects are expected for acceptable parasite control without a heavy reliance on anti-parasiticides through integration of the above mentioned procedures but future studies are needed to confirm their efficacy under practical farming conditions

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Ref Type: Report

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Ref Type: Report

Thompson,B., G.D.Coronado, J.E.Grossman, K.Puschel, C.C.Solomon, I.Islas, C.L.Curl, J.H.Shirai, J.C.Kissel, and R.A.Fenske. 2003. "Pesticide take-home pathway among children of agricultural workers: study design, methods, and baseline findings." J Occup.Environ.Med. 45:42-53.
Abstract: Farmworkers are exposed to pesticides and may take home pesticide residues to their families. In this paper, self-reported pesticide exposure and home practices to reduce the amount of pesticide residues taken home were examined among 571 farmworkers. Urine samples from a subsample of farmworkers and children and dust samples from households and vehicles also assessed pesticide exposure. Overall, 96% of respondents reported exposure to pesticides at work. Many employers did not provide resources for hand washing. Farmworkers' protective practices to keep pesticide residues out of the home were at a low level. In a subset of respondents, pesticide levels above the limit of quantitation were seen in the urine of children and adults and in house and vehicle dust. The results support the take-home pathway of pesticide exposure. Ways must be found to reduce this pesticide exposure among children of farmworkers

Toppari,J., J.C.Larsen, P.Christiansen, A.Giwercman, P.Grandjean, L.J.Guillette, Jr., B.Jegou, T.K.Jensen, P.Jouannet, N.Keiding, H.Leffers, J.A.McLachlan, O.Meyer, J.Muller, E.Rajpert-De Meyts, T.Scheike, R.Sharpe, J.Sumpter, and N.E.Skakkebaek. 1996. "Male reproductive health and environmental xenoestrogens." Environ.Health Perspect. 104 Suppl 4:741-803.
Abstract: Male reproductive health has deteriorated in many countries during the last few decades. In the 1990s, declining semen quality has been reported from Belgium, Denmark, France, and Great Britain. The incidence of testicular cancer has increased during the same time incidences of hypospadias and cryptorchidism also appear to be increasing. Similar reproductive problems occur in many wildlife species. There are marked geographic differences in the prevalence of male reproductive disorders. While the reasons for these differences are currently unknown, both clinical and laboratory

research suggest that the adverse changes may be inter-related and have a common origin in fetal life or childhood. Exposure of the male fetus to supranormal levels of estrogens, such as diethlylstilbestrol, can result in the above-mentioned reproductive defects. The growing number of reports demonstrating that common environmental contaminants and natural factors possess estrogenic activity presents the working hypothesis that the adverse trends in male reproductive health may be, at least in part, associated with exposure to estrogenic or other hormonally active (e.g., antiandrogenic) environmental chemicals during fetal and childhood development. An extensive research program is needed to understand the extent of the problem, its underlying etiology, and the development of a strategy for prevention and intervention

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Ref Type: Art Work

US Environmental Protection Agency. OPP Revised OP Risk Assessment - Distribution of OP and Carbamate Residues in Composite Peach Samples Compared to Single Servings Tested by the USDA's Pesticide Data Program (PDP) in 2000. 2003. BCS Summary Tables.
Ref Type: Art Work

US Environmental Protection Agency. OPP Revised OP Risk Assessment - Major Ongoing and/or Risk Trading Concerns Among Supported and/or Foreign Uses of High-Risk Organophosphates. 2003. BCS Summary Tables.
Ref Type: Art Work

US Environmental Protection Agency. OPP Revised OP Risk Assessment - Frequency of Foods Appearing in the Diets of Children 1-2 Years Old at the 99.8th to 100th Percentile of the Risk Distribution. 2003. BCS Summary Tables.
Ref Type: Art Work

US Environmental Protection Agency. OPP Revised OP Risk Assessment - Toxicity of OP Insecticides Ranked by aPAD: Acute and Chronic PADs and NOAELs and Relative POtency Factors (Reference Chemical is Methamidophos). 2003. BCS Summary Tables.
Ref Type: Art Work

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Ward,M.H., S.H.Zahm, D.D.Weisenburger, G.Gridley, K.P.Cantor, R.C.Saal, and A.Blair. 1994. "Dietary factors and non-Hodgkin's lymphoma in Nebraska (United States)." Cancer Causes Control. 5:422-432.
Abstract: Little is known about dietary factors and non-Hodgkin's lymphoma (NHL) risk, although high intakes of animal protein and milk have been associated with NHL in two previous studies. As part of a population-based case-control study of agricultural and other risk factors for NHL in eastern Nebraska (USA), we examined the self- and proxy-reported frequency of consumption of 30 food items by 385 White men and women with NHL and 1,432 controls. Animal protein intake was not associated significantly with the risk of NHL, however, there was a nonsignificantly elevated risk of NHL among men with high milk consumption. Vitamin C, carotene, citrus fruit, and dark green vegetable intakes were inversely significantly related to the risk of NHL for men, but not for women. Among men, the odds ratios for the highest quartiles of both vitamin C and carotene intake were 0.6 (95% confidence intervals = 0.3-1.0). There were no meaningful differences in the associations of nutrient intakes and NHL risk between B- and T-cell lymphomas and histologic types. Risks for low intakes of vitamin C and carotene were greater among men and women with a family history of cancer, particularly a history of lymphatic or hematopoietic cancer among first-degree relatives

Ward,M.H., S.D.Mark, K.P.Cantor, D.D.Weisenburger, A.Correa-Villasenor, and S.H.Zahm. 1996. "Drinking water nitrate and the risk of non-Hodgkin's lymphoma." Epidemiology. 7:465-471.
Abstract: The increasing incidence of non-Hodgkin's lymphoma (NHL) in the United States is only partially explained by known risk factors. Nitrate is a contaminant of

drinking water in many rural areas. We evaluated its association with NHL after accounting for dietary nitrate intake. For 156 cases and 527 controls who used Nebraska community supplies, average nitrate exposure was estimated from 1947 through 1979. Longterm consumption of community water with average nitrate levels in the highest quartile (> or = 4 mg per liter nitrate-nitrogen) was positively associated with risk [odds ratio (OR) = 2.0; 95% confidence interval (CI) = 1.1-3.6]. Dietary nitrate, which came mainly from vegetables, was not associated with NHL risk, after adjusting for vitamin C and carotene intakes. Persons with a lower intake of vitamin C were at slightly higher risk of developing NHL than persons whose daily intake was > or = 130 mg, for all levels of intake of drinking water nitrate; our findings were similar for the combined effect of water nitrate and carotene intake. Nitrate levels in private wells were measured at the time of the interview for 51 cases and 150 controls but were not associated with the risk of NHL after adjusting for pesticide use on the farm. These findings indicate that longterm exposure to elevated nitrate levels in drinking water may contribute to the risk of NHL

Ward,M.H., J.R.Prince, P.A.Stewart, and S.H.Zahm. 2001. "Determining the probability of pesticide exposures among migrant farmworkers: results from a feasibility study." Am.J Ind.Med. 40:538-553.
Abstract: BACKGROUND: Migrant and seasonal farmworkers are exposed to pesticides through their work with crops and livestock. Because workers are usually unaware of the pesticides applied, specific pesticide exposures cannot be determined by interviews. We conducted a study to determine the feasibility of identifying probable pesticide exposures based on work histories. METHODS: The study included 162 farm workers in seven states. Interviewers obtained a lifetime work history including the crops, tasks, months, and locations worked. We investigated the availability of survey data on pesticide use for crops and livestock in the seven pilot states. Probabilities of use for pesticide types (herbicides, insecticides, fungicides, etc.) and specific chemicals were calculated from the available data for two farm workers. The work histories were chosen to illustrate how the quality of the pesticide use information varied across crops, states, and years. RESULTS: For most vegetable and fruit crops there were regional pesticide use data in the late 1970s, no data in the 1980s, and state-specific data every other year in the 1990s. Annual use surveys for cotton and potatoes began in the late 1980s. For a few crops, including asparagus, broccoli, lettuce, strawberries, plums, and Christmas trees, there were no federal data or data from the seven states before the 1990s. CONCLUSIONS: We conclude that identifying probable pesticide exposures is feasible in some locations. However, the lack of pesticide use data before the 1990s for many crops will limit the quality of historic exposure assessment for most workers

Weibel,F.P., R.Bickel, S.Leuthold, and T.Alfoldi. 2001. "Are organically grown apples tastier and healthier? A comparative field study using conventional and alternative methods to measure fruit quality." ISHS Acta Horticulutrae. 517.

Welshons,W.V., K.A.Thayer, B.M.Judy, J.A.Taylor, E.M.Curran, and F.S.Vom Saal. 2003. "Large effects from small exposures. I. Mechanisms for endocrine-disrupting chemicals with estrogenic activity." Environ.Health Perspect. 111:994-1006.

Abstract: Information concerning the fundamental mechanisms of action of both natural and environmental hormones, combined with information concerning endogenous hormone concentrations, reveals how endocrine-disrupting chemicals with estrogenic activity (EEDCs) can be active at concentrations far below those currently being tested in toxicological studies. Using only very high doses in toxicological studies of EEDCs thus can dramatically underestimate bioactivity. Specifically: a) The hormonal action mechanisms and the physiology of delivery of EEDCs predict with accuracy the low-dose ranges of biological activity, which have been missed by traditional toxicological testing. b) Toxicology assumes that it is valid to extrapolate linearly from high doses over a very wide dose range to predict responses at doses within the physiological range of receptor occupancy for an EEDC; however, because receptor-mediated responses saturate, this assumption is invalid. c) Furthermore, receptor-mediated responses can first increase and then decrease as dose increases, contradicting the assumption that dose-response relationships are monotonic. d) Exogenous estrogens modulate a system that is physiologically active and thus is already above threshold, contradicting the traditional toxicological assumption of thresholds for endocrine responses to EEDCs. These four fundamental issues are problematic for risk assessment methods used by regulatory agencies, because they challenge the traditional use of extrapolation from high-dose testing to predict responses at the much lower environmentally relevant doses. These doses are within the range of current exposures to numerous chemicals in wildlife and humans. These problems are exacerbated by the fact that the type of positive and negative controls appropriate to the study of endocrine responses are not part of traditional toxicological testing and are frequently omitted, or when present, have been misinterpreted

Whyatt,R.M., D.B.Barr, D.E.Camann, P.L.Kinney, J.R.Barr, H.F.Andrews, L.A.Hoepner, R.Garfinkel, Y.Hazi, A.Reyes, J.Ramirez, Y.Cosme, and F.P.Perera. 2003. "Contemporary-use pesticides in personal air samples during pregnancy and blood samples at delivery among urban minority mothers and newborns." Environ.Health Perspect. 111:749-756.
Abstract: We have measured 29 pesticides in plasma samples collected at birth between 1998 and 2001 from 230 mother and newborn pairs enrolled in the Columbia Center for Children's Environmental Health prospective cohort study. Our prior research has shown widespread pesticide use during pregnancy among this urban minority cohort from New York City. We also measured eight pesticides in 48-hr personal air samples collected from the mothers during pregnancy. The following seven pesticides were detected in 48-83% of plasma samples (range, 1-270 pg/g): the organophosphates chlorpyrifos and diazinon, the carbamates bendiocarb and 2-isopropoxyphenol (metabolite of propoxur), and the fungicides dicloran, phthalimide (metabolite of folpet and captan), and tetrahydrophthalimide (metabolite of captan and captafol). Maternal and cord plasma levels were similar and, except for phthalimide, were highly correlated ($p < 0.001$). Chlorpyrifos, diazinon, and propoxur were detected in 100% of personal air samples (range, 0.7-6,010 ng/m(3)). Diazinon and propoxur levels were significantly higher in the personal air of women reporting use of an exterminator, can sprays, and/or pest bombs during pregnancy compared with women reporting no pesticide use or use of lower toxicity methods only. A significant correlation was seen between personal air level of

chlorpyrifos, diazinon, and propoxur and levels of these insecticides or their metabolites in plasma samples (maternal and/or cord, $p < 0.05$). The fungicide ortho-phenylphenol was also detected in 100% of air samples but was not measured in plasma. The remaining 22 pesticides were detected in 0-45% of air or plasma samples. Chlorpyrifos, diazinon, propoxur, and bendiocarb levels in air and/or plasma decreased significantly between 1998 and 2001. Findings indicate that pesticide exposures are frequent but decreasing and that the pesticides are readily transferred to the developing fetus during pregnancy

Whyatt,R.M., V.Rauh, D.B.Barr, D.E.Camann, H.F.Andrews, R.Garfinkel, L.A.Hoepner, D.Diaz, J.Dietrich, A.Reyes, D.Tang, P.L.Kinney, and F.P.Perera. 2004. "Prenatal insecticide exposures and birth weight and length among an urban minority cohort." Environ.Health Perspect. 112:1125-1132.
Abstract: We reported previously that insecticide exposures were widespread among minority women in New York City during pregnancy and that levels of the organophosphate chlorpyrifos in umbilical cord plasma were inversely associated with birth weight and length. Here we expand analyses to include additional insecticides (the organophosphate diazinon and the carbamate propoxur), a larger sample size (n = 314 mother-newborn pairs), and insecticide measurements in maternal personal air during pregnancy as well as in umbilical cord plasma at delivery. Controlling for potential confounders, we found no association between maternal personal air insecticide levels and birth weight, length, or head circumference. For each log unit increase in cord plasma chlorpyrifos levels, birth weight decreased by 42.6 g [95% confidence interval (CI), -81.8 to -3.8, $p = 0.03$] and birth length decreased by 0.24 cm (95% CI, -0.47 to -0.01, $p = 0.04$). Combined measures of (ln)cord plasma chlorpyrifos and diazinon (adjusted for relative potency) were also inversely associated with birth weight and length ($p < 0.05$). Birth weight averaged 186.3 g less (95% CI, -375.2 to -45.5) among newborns with the highest compared with lowest 26% of exposure levels ($p = 0.01$). Further, the associations between birth weight and length and cord plasma chlorpyrifos and diazinon were highly significant ($p <$ or $= 0.007$) among newborns born before the 2000-2001 U.S. Environmental Protection Agency's regulatory actions to phase out residential use of these insecticides. Among newborns born after January 2001, exposure levels were substantially lower, and no association with fetal growth was apparent ($p > 0.8$). The propoxur metabolite 2-isopropoxyphenol in cord plasma was inversely associated with birth length, a finding of borderline significance ($p = 0.05$) after controlling for chlorpyrifos and diazinon. Results indicate that prenatal chlorpyrifos exposures have impaired fetal growth among this minority cohort and that diazinon exposures may have contributed to the effects. Findings support recent regulatory action to phase out residential uses of the insecticides

Whyatt,R.M., D.Camann, F.P.Perera, V.A.Rauh, D.Tang, P.L.Kinney, R.Garfinkel, H.Andrews, L.Hoepner, and D.B.Barr. 2005. "Biomarkers in assessing residential insecticide exposures during pregnancy and effects on fetal growth." Toxicol.Appl.Pharmacol. 206:246-254.
Abstract: The Columbia Center for Children's Environmental Health is using a combination of environmental and biologic measures to evaluate the effects of prenatal insecticide exposures among urban minorities in New York City. Of the 571 women

enrolled, 85% report using some form of pest control during pregnancy and 46% report using exterminators, can sprays, and/or pest bombs. Chlorpyrifos, diazinon, and propoxur were detected in 99.7-100% of 48-h personal air samples collected from the mothers during pregnancy (n = 394) and in 39-70% of blood samples collected from the mothers (n = 326) and/or newborns (n = 341) at delivery. Maternal and newborn blood levels are similar and highly correlated (r = 0.4-08, P < 0.001). Levels of insecticides in blood samples and/or personal air samples decreased significantly following the 2000-2001 U.S. Environmental Protection Agency's regulatory actions to phase out residential use of chlorpyrifos and diazinon. Among infants born prior to 1/1/01, birth weight decreased by 67.3 g (95% confidence interval (CI) -116.6 to -17.8, P = 0.008) and birth length decreased by 0.43 centimeters (95% CI, -0.73 to -0.14, P = 0.004) for each unit increase in log-transformed cord plasma chlorpyrifos levels. Combined measures of (ln)cord plasma chlorpyrifos and diazinon (adjusted for relative potency) were also inversely associated with birth weight and length (P </= 0.007). Birth weight averaged 215.1 g less (95% CI -384.7 to -45.5) among those with the highest exposures compared to those without detectable levels. No association was seen between birth weight and length and cord plasma chlorpyrifos or diazinon among newborns born after 1/1/01 (P > 0.8). Results support recent regulatory action to phase out residential uses of these insecticides

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Abstract: Analysis of new government information on pesticide residues in food shows that washing, peeling and otherwise preparing food for consumption does not remove or decrease the number of pesticides present in fresh fruits and vegetables. These findings are based on an original analysis of data from the Pesticide Data Program (PDP) of the United States Department of Agriculture (USDA 1994).

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Abstract: We studied the exposure and effect of the organophosphate insecticides azinphos-methyl and diazinon on adult California quail (Callipepla californica) in an apple orchard in the Okanagan Valley, British Columbia. Cholinesterase activity was measured in plasma samples (n = 65) collected from 54 individuals either prior to spraying, immediately (< 24 hours) or 10 days after three spray events. Mean plasma cholinesterase levels declined significantly (P < 0.05, n = 12) to 61% of pre-spray mean activity (controls) immediately following the first spray event, but by ten days had recovered to 86% of mean control activity. Subsequent spray events caused no significant declines in mean plasma cholinesterase activity. Four of the 26 quail sampled within 24 h of a spray event exhibited plasma-ChE inhibition exceeding 50% inhibition. Radio-tagged quail (n = 25) were monitored throughout the breeding season to determine use of orchards and detect changes in use patterns resulting from the spraying of insecticides.

Use of orchards by quail varied over the summer, with the highest use occurring in May, declining to very low use by July. Quail exhibited a diurnal pattern, roosting in sparsely forested uplands at night, travelling to orchard areas to feed early each morning and returning to roosts at dusk. Orchard use by quail differed during spray events compared to non-spray times. During the three hour period immediately after spraying (0530-0800), 14-20% of observed quail were in the orchard, after which use declined to < 4%, and returned to 12% by the next day. During non-spray times, 3-13% of radio-tagged the quail were observed in orchard habitat, with the heaviest use (13%) occurring later in the day (0830-1700 h). Seven radio-tagged quail were predated during the study period. However, no deaths could be attributed to insecticide poisoning as carcasses were not in suitable condition for testing. It was concluded that adult quail using orchard habitat early in the summer may be acutely poisoned by anti-cholinesterase insecticides, but the risk of exposure declined over the summer

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Abstract: Records of eagles, coyotes (Canis latrans), and red foxes (Vulpes vulpes) necropsied at the Western College of Veterinary Medicine, Saskatoon, Saskatchewan, Canada, between 1967 and 2002 were reviewed for cases suggestive of anticholinesterase poisoning. From 1993 to 2002, 54 putative poisoning incidents involving 70 bald eagles (Haliaeetus leucocephalus) and 10 golden eagles (Aquila chrysaetus) were identified. Of these, 50 incidents occurred in Saskatchewan, two were in Manitoba, and one occurred in each of Alberta and the Northwest Territories. The diagnosis was confirmed in eight instances by demonstration of pesticide in ingesta from eagles or known use of pesticide at the site together with brain cholinesterase (AChE) reduction of >50% in at least one animal. A presnmptive diagnosis of poisoning was made in 33 incidents based on brain AChE reduction of >50% in at least one animal; 13 incidents were considered suspicious because of circumstantial evidence of the death of eagles in association with other species and limited AChE reduction. Other wild species were found dead in 85% of the incidents involving eagles. Coyotes, foxes, black-billed magpies (Pica pica), and striped skunks (Mephitis mephitis) were associated with 34, six, six, and three incidents, respectively. There were eight additional incidents that did not involve eagles in which poisoning was diagnosed in coyotes. Carbofuran was identified in nine incidents. Carbamate poisoning was indicated on the basis of reactivation of brain AChE activity in two additional incidents. Brain AChE activity was not reduced from normal in eagles in four of seven incidents in which carbofuran was identified. The organophosplorous insecticide terbufos was found together with carbofuran in one incident. Brain AChE activity was measured in wild canids and in eagles in 15 incidents; in all of these incidents, brain AChE was redulced by >50% in at least one mammal, whereas this level of reduction occrred in eagles in only four incidents. Use of anticholinesterase pesticides to poison coyotes is illegal, but the practice continues and secondary poisoning of eagles is a problem of unknown proportions in western North America

Wolf,C.J., A.Hotchkiss, J.S.Ostby, G.A.LeBlanc, and L.E.Gray, Jr. 2002. "Effects of prenatal testosterone propionate on the sexual development of male and female rats: a dose-response study." Toxicol.Sci. 65:71-86.
Abstract: Testosterone plays a major role in male sexual development. Exposure of females to testosterone in utero can induce masculine characteristics such as anovulation, increased anogenital distance (AGD), absence of nipples, retention of male-like tissues, and agenesis of the lower vagina. In addition, high levels of androgens during fetal development can lead to toxic effects such as reduced litter size and viability. The study of the effects of testosterone administration during sexual differentiation provides a foundation for understanding the effects of environmental androgens on fetuses, a sensitive subpopulation. In the current study, we investigated the ability of a range of concentrations of testosterone propionate (TP) administered prenatally to masculinize female and alter male offspring, and measured maternal and fetal T levels. Pregnant Sprague-Dawley rats were dosed by sc injection on gestational day (GD) 14-19 (GD 1= day of plug) with either corn oil (vehicle; 0.1 ml/rat) or with 0.1 ml of TP solution at 0.1, 0.5, 1, 2, 5, or 10 mg/0.1 ml. Parturition was delayed at 2, 5, and 10 mg TP, litter size was reduced at 5 and 10 mg TP, and pup weight was significantly reduced in both sexes at 0.5 mg TP and higher doses. Viability of offspring was unaffected at any dosage level. Androgenic effects seen at 0.5 mg TP in females included increased AGD at weaning and adulthood, reduced number of areolas and nipples, cleft phallus, small vaginal orifice, and presence of prostate tissue. This dose of TP elevated maternal T levels 10x but had no effect on fetal T levels. At 1 mg TP and above, female AGD on postnatal day (PND) 2 (or postcoital day 24 [gestation length = 22(1/2)]) was increased; areolas and nipples were virtually eliminated; levator ani muscle, bulbourethral glands, and seminal vesicles (2 mg TP and above) were present; none of the females developed a vaginal orifice and many females in the 1 and 2 mg TP dose groups developed a greatly distended, fluid-filled uterus after puberty. Maternal T levels at 1 mg TP were elevated 30x, and female fetal T levels showed an 80% increase. Male offspring displayed a reduced AGD and body weight on PND 2 at 0.5 mg TP and higher doses. These effects were not evident by weaning and male offspring displayed no malformations. We conclude that gestational administration of 0.5 and 1 mg TP masculinizes female offspring without greatly affecting pup viability or pregnancy of the dam. This study provides a useful model for in utero testing of environmental androgens for their potential to induce developmental abnormalities

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Zahm,S.H., M.H.Ward, and A.Blair. 1997. "Pesticides and cancer." Occup.Med. 12:269-289.
Abstract: The authors discuss pesticide exposure in both agricultural and nonagricultural occupations, referring to a variety of studies on the cancer risks of specific pesticides. Adult and childhood cancer are addressed, and direction for future research efforts is offered

Zahm,S.H. and M.H.Ward. 1998. "Pesticides and childhood cancer." Environ.Health Perspect. 106 Suppl 3:893-908.
Abstract: Children are exposed to potentially carcinogenic pesticides from use in homes, schools, other buildings, lawns and gardens, through food and contaminated drinking water, from agricultural application drift, overspray, or off-gassing, and from carry-home exposure of parents occupationally exposed to pesticides. Parental exposure during the child's gestation or even preconception may also be important. Malignancies linked to pesticides in case reports or case-control studies include leukemia, neuroblastoma, Wilms' tumor, soft-tissue sarcoma, Ewing's sarcoma, non-Hodgkin's lymphoma, and cancers of the brain, colorectum, and testes. Although these studies have been limited by nonspecific pesticide exposure information, small numbers of exposed subjects, and the potential for case-response bias, it is noteworthy that many of the reported increased risks are of greater magnitude than those observed in studies of pesticide-exposed adults, suggesting that children may be particularly sensitive to the carcinogenic effects of pesticides. Future research should include improved exposure assessment, evaluation of risk by age at exposure, and investigation of possible genetic-environment interactions. There is potential to prevent at least some childhood cancer by reducing or eliminating pesticide exposure