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Chlorpyrifos: Common Pesticide Tied to Brain Damage in Children

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Chlorpyrifos, a widely used pesticide, is strongly linked to brain damage in children. These and other health concerns have led several countries and some U.S. states to ban chlorpyrifos, but the chemical is still allowed on food crops in the U.S. after successful lobbying by its manufacturer.

Chlorpyrifos in food

Chlorpyrifos insecticides were introduced by Dow Chemical in 1965 and have been used widely in agricultural settings. Commonly known as the active ingredient in the brand names Dursban and Lorsban, chlorpyrifos is an organophosphate insecticide, acaricide and miticide used primarily to control foliage and soil-borne insect pests on a variety of food and feed crops. Products come in liquid form as well as granules, powders, and water-soluble packets, and may be applied by either ground or aerial equipment.

Chlorpyrifos is used on a wide variety of crops including apples, oranges, strawberries, corn, wheat, citrus and other foods families and their children eat daily. USDA's *Pesticide Data Program* found chlorpyrifos residue on citrus and melons even after being washed and peeled. By volume, chlorpyrifos is most used on corn and soybeans, with over a million pounds applied annually to each crop. The chemical is not allowed on organic crops.

Non-agricultural uses include golf courses, turf, green houses, and utilities.

Human health concerns

The American Academy of Pediatrics, which represents more than 66,000 pediatricians and pediatric surgeons, has warned that continued use of chlorpyrifos puts developing fetuses, infants, children and pregnant women at great risk.

Scientists have found that prenatal exposures to chlorpyrifos are associated with lower birth weight, reduced IQ, the loss of working memory, attention disorders, and delayed motor development. Key studies are listed below.

See these comments to regulators from the Endocrine Society citing "ample evidence that chlorpyrifos has extensive effects on neurological and endocrine systems with demonstrated evidence of harm to humans and wildlife."

Chlorpyrifos is also linked to acute pesticide poisoning and can cause convulsions, respiratory paralysis, and sometimes, death.

FDA says food and drinking water exposures unsafe

Chlorpyrifos is so toxic that the European Food Safety Authority banned sales of the chemical as of January 2020, finding that there is no safe exposure level. Some U.S. states have also banned chlorpyrifos from farming use, including California and Hawaii.

The U.S. Environmental Protection Agency (EPA) reached agreement with Dow Chemical in 2000 to phase out all residential uses of chlorpyrifos because of scientific research showing the chemical is dangerous to the developing brains of babies and young children. It was banned from use around schools in 2012.

In October 2015, the EPA said it planned to revoke all food residue tolerances for chlorpyrifos, meaning it would no longer be legal to use it in agriculture. The agency said "expected residues of chlorpyrifos on food crops exceed the safety standard under the Federal Food, Drug, and Cosmetic Act." The move came in response to a petition for a ban from the Natural Resources Defense Council and Pesticide Action Network.

In November 2016, the EPA released a revised human health risk assessment for chlorpyrifos confirming it was unsafe to allow the chemical to continue in use in agriculture. Among other things, the EPA said all food and drinking water exposures were unsafe, especially to children 1-2 years old. The EPA said the ban would take place in 2017.

Trump EPA delays ban

Following the election of Donald Trump as President of the United States, the proposed chlorpyrifos ban was delayed. In March 2017, in one of his first formal actions as the nation's top environmental official, EPA Administrator Scott Pruitt rejected the petition by environmental groups and said the ban on chlorpyrifos would not go forward.

The Associated Press reported in June 2017 that Pruitt had met with Dow CEO Andrew Liveris 20 days before halting the ban. Media also reported that Dow contributed $1 million to Trump's inaugural activities.

In February of 2018, EPA reached a settlement requiring Syngenta to pay a $150,000 fine and train farmers in pesticide use after the company failed to warn workers to avoid fields where chlorpyrifos was recently sprayed and several workers who entered the fields were sickened and required medical care. The Obama EPA had initially proposed a fine nearly nine times larger.

In February 2020, after pressure from consumer, medical, scientific groups and in face of growing calls for bans around the world, Corteva AgriScience (formerly DowDuPont) said it would phase out production of chlorpyrifos, but the chemical remains legal for other companies to make and sell.

According to an analysis published in July 2020, U.S. regulators relied on falsified data

provided by Dow Chemical to allow unsafe levels of chlorpyrifos into American homes for years. The analysis from University of Washington researchers said the inaccurate findings were the result of a chlorpyrifos dosing study done in the early 1970s for Dow.

In September 2020 the EPA issued its third risk assessment on chlorpyrifos, saying "despite several years of study, peer review, and public process, the science addressing neurodevelopmental effects remains unresolved," and it still could be used in food production.

The decision came after multiple meetings between the EPA and Corteva.

Groups and states sue EPA

Following the Trump administration's decision to delay any ban until at least 2022, Pesticide Action Network and Natural Resources Defense Council filed suit against the EPA in April 2017, seeking to force the government to follow through with the Obama administration's recommendations to ban chlorpyrifos. In August 2018, a federal appeals court found that the EPA broke the law by continuing to allow use of chlorpyrifos, and ordered EPA to finalize its proposed ban within two months. After more delays, EPA Administrator Andrew Wheeler announced in July 2019 that EPA would not ban the chemical.

Several states have sued the EPA over its failure to ban chlorpyrifos, including California, New York, Massachusetts, Washington, Maryland, Vermont and Oregon. The states argue in court documents that chlorpyrifos should be banned in food production due to the dangers associated with it.

Earthjustice has also filed a lawsuit in the U.S. Court of Appeals for the Ninth Circuit Court seeking a nationwide ban on behalf of groups advocating for environmentalists, farmworkers and people with learning disabilities.

On April 29, 2021, the U.S. Judge Jed S. Rakoff of the Ninth Circuit issued a decision, finding the EPA had engaged in an "egregious delay" that exposed a generation of American children to unsafe levels of chlorpyrifos." He ordered the EPA to issue a final regulation within 60 days that modifies or revokes the registration for chlorpyrifos.

Medical and scientific studies

Developmental neurotoxicity

> "The epidemiological studies reviewed herein have reported statistically significant correlations between prenatal exposures to CPF [chlorpyrifos] and postnatal neurological complications, particularly cognitive deficits that are also associated with disruption of the structural integrity of the brain.... Various preclinical research groups throughout the world have consistently demonstrated that CPF is a developmental neurotoxicant. The developmental CPF neurotoxicity, which is well supported by studies using different animal models, routes of exposure, vehicles, and testing methods, is generally characterized by cognitive deficits and disruption of the structural integrity of the brain." Developmental neurotoxicity of the organophosphorus insecticide chlorpyrifos: from clinical findings to preclinical models and potential mechanisms. Journal of Neurochemistry, 2017.

> "Since 2006, epidemiological studies have documented six additional developmental neurotoxicants—manganese, fluoride, chlorpyrifos, dichlorodiphenyltrichloroethane, tetrachloroethylene, and the polybrominated diphenyl ethers." Neurobehavioural effects of developmental toxicity. Lancet Neurology, 2014.

Childrens' IQ & cognitive development

Longitudinal birth cohort study of inner-city mothers and children found that "higher prenatal CPF [chlorpyrifos] exposure, as measured in umbilical cord blood plasma, was associated with decreases in cognitive functioning on two different WISC-IV indices, in a sample of urban minority children at 7 years of age…the Working Memory Index was the most strongly associated with CPF exposure in this population." Seven-Year Neurodevelopmental Scores and Prenatal Exposure to Chlorpyrifos, a Common Agricultural Pesticide. Environmental Health Perspectives, 2011.

Birth cohort study of predominantly Latino farmworker families in California associated a metabolite of organophosphate pesticides found in the urine in pregnant women with poorer scores in their children for memory, processing speed, verbal comprehension, perceptual reasoning and IQ. "Our findings suggest that prenatal exposure to OP [organophosphate] pesticides, as measured by urinary DAP [dialkyl phosphate] metabolites in women during pregnancy, is associated with poorer cognitive abilities in children at 7 years of age. Children in the highest quintile of maternal DAP concentrations had an average deficit of 7.0 IQ points compared with those in the lowest quintile. Associations were linear, and we observed no threshold." Prenatal Exposure to Organophosphate Pesticides and IQ in 7-Year-Old Children. Environmental Health Perspectives, 2011.

Prospective cohort study of women and their children findings "suggest that prenatal exposure to organophosphates is negatively associated with cognitive development, particularly perceptual reasoning, with evidence of effects beginning at 12 months and continuing through early childhood." Prenatal Exposure to Organophosphates, Paraoxonase 1, and Cognitive Development in Childhood. Environmental Health Perspectives, 2011.

Prospective cohort study of an inner-city population found that children with high levels of exposure to chlorpyrifos "scored, on average, 6.5 points lower on the Bayley Psychomotor Development Index and 3.3 points lower on the Bayley Mental Development Index at 3 years of age compared with those with lower levels of exposure. Children exposed to higher, compared with lower, chlorpyrifos levels were also significantly more likely to experience Psychomotor Development Index and Mental Development Index delays, attention problems, attention-deficit/hyperactivity disorder problems, and pervasive developmental disorder problems at 3 years of age." Impact of Prenatal Chlorpyrifos Exposure on Neurodevelopment in the First 3 Years of Life Among Inner-City Children. Journal of the American Academy of Pediatrics, 2006.

Longitudinal birth cohort study in an agricultural region of California extends "previous findings of associations between PON1 genotype and enzyme levels and certain domains of neurodevelopment through early school age, presenting new evidence that adverse associations between DAP [dialkyl phosphate]levels and IQ may be strongest in children of mothers with the lowest levels of PON1 enzyme." Organophosphate pesticide exposure, PON1, and neurodevelopment in school-age children from the CHAMACOS study. Environmental Research, 2014.

Autism and other neurodevelopmental disorders

Population based case-control study found that, "Prenatal or infant exposure to a priori selected pesticides—including glyphosate, chlorpyrifos, diazinon, and permethrin—were associated with increased odds of developing autism spectrum disorder." Prenatal and infant exposure to ambient pesticides and autism spectrum disorder in children: population based case-control study. BMJ, 2019.

Population-based case-control study "observed positive associations between ASD [autism spectrum disorders] and prenatal residential proximity to organophosphate pesticides in the second (for chlorpyrifos) and third trimesters (organophosphates overall)". Neurodevelopmental Disorders and Prenatal Residential Proximity to Agricultural Pesticides: The CHARGE Study. Environmental Health Perspectives, 2014.

See also: Tipping the Balance of Autism Risk: Potential Mechanisms Linking Pesticides and Autism. Environmental Health Perspectives, 2012.

Brain anomalies

> "Our findings indicate that prenatal CPF [chlorpyrifos] exposure, at levels observed with routine (nonoccupational) use and below the threshold for any signs of acute exposure, has a measureable effect on brain structure in a sample of 40 children 5.9–11.2 y of age. We found significant abnormalities in morphological measures of the cerebral surface associated with higher prenatal CPF exposure....Regional enlargements of the cerebral surface predominated and were located in the superior temporal, posterior middle temporal, and inferior postcentral gyri bilaterally, and in the superior frontal gyrus, gyrus rectus, cuneus, and precuneus along the mesial wall of the right hemisphere". Brain anomalies in children exposed prenatally to a common organophosphate pesticide. Proceedings of the National Academy of Sciences, 2012.

Fetal growth

This study "saw a highly significant inverse association between umbilical cord chlorpyrifos levels and both birth weight and birth length among infants in the current cohort born prior to U.S. EPA regulatory actions to phase out residential uses of the insecticide." Biomarkers in assessing residential insecticide exposures during pregnancy and effects on fetal growth. Toxicology and Applied Pharmacology, 2005.

Prospective, multiethnic cohort study found that "when the level of maternal PON1 activity was taken into account, maternal levels of chlorpyrifos above the limit of detection coupled with low maternal PON1 activity were associated with a significant but small reduction in head circumference. In addition, maternal PON1 levels alone, but not PON1 genetic polymorphisms, were associated with reduced head size. Because small head size has been found to be predictive of subsequent cognitive ability, these data suggest that chlorpyrifos may have a detrimental effect on fetal neurodevelopment among mothers who exhibit low PON1 activity." In Utero Pesticide Exposure, Maternal Paraoxonase Activity, and Head Circumference. Environmental Health Perspectives, 2003.

Prospective cohort study of minority mothers and their newborns "confirm our earlier findings of an inverse association between chlorpyrifos levels in umbilical cord plasma and birth weight and length...Further, a dose-response relationship was additionally seen in the

present study. Specifically, the association between cord plasma chlorpyrifos and reduced birth weight and length was found principally among newborns with the highest 25% of exposure levels." Prenatal Insecticide Exposures and Birth Weight and Length among an Urban Minority Cohort. Environmental Health Perspectives, 2004.

Lung Cancer

In an evaluation of over 54,000 pesticide applicators in the Agricultural Health Study, scientists at the National Cancer Institute reported that the incidence of lung cancer was associated with chlorpyrifos exposure. "In this analysis of cancer incidence among chlorpyrifos-exposed licensed pesticide applicators in North Carolina and Iowa, we found a statistically significant trend of increasing risk of lung cancer, but not of any other cancer examined, with increasing chlorpyrifos exposure." Cancer Incidence Among Pesticide Applicators Exposed to Chlorpyrifos in the Agricultural Health Study. Journal of the National Cancer Institute, 2004.

Parkinson's Disease

Case-control study of people living in California's Central Valley reported that ambient exposure to 36 commonly used organophosphate pesticides separately increased the risk of developing Parkinson's disease. The study "adds strong evidence" that organophosphate pesticides are "implicated" in the etiology of idiopathic Parkinson's disease. The association between ambient exposure to organophosphates and Parkinson's disease risk. Occupational & Environmental Medicine, 2014.

Birth outcomes

Multiethnic parent cohort of pregnant women and newborns found that chlorpyrifos "was associated with decreased birth weight and birth length overall ($p = 0.01$ and $p = 0.003$, respectively) and with lower birth weight among African Americans ($p = 0.04$) and reduced birth length in Dominicans ($p < 0.001$)". Effects of Transplacental Exposure to Environmental Pollutants on Birth Outcomes in a Multiethnic Population. Environmental Health Perspectives, 2003.

Neuroendocrine disruption

> "Through the analysis of complex sex-dimorphic behavioral patterns we show that neurotoxic and endocrine disrupting activities of CPF [chlorpyrifos] overlap. This widely diffused organophosphorus pesticide might thus be considered as a neuroendocrine disruptor possibly representing a risk factor for sex-biased neurodevelopmental disorders in children." Sex dimorphic behaviors as markers of neuroendocrine disruption by environmental chemicals: The case of chlorpyrifos. NeuroToxicology, 2012.

Tremor

> "The present findings show that children with high prenatal exposure to chlorpyrifos were significantly more likely to show mild or mild to moderate tremor in one or both arms when assessed between the ages of 9 and 13.9 years of age....Taken together, growing evidence suggests that prenatal exposure to CPF [chlorpyrifos], at current standard usage levels, is associated with a range of persistent and inter-related developmental problems." Prenatal exposure to the organophosphate pesticide

chlorpyrifos and childhood tremor. NeuroToxicology, 2015.

Cost of chlorpyrifos

Cost estimates of exposure to endocrine-disrupting chemicals in the European Union found that "Organophosphate exposures were associated with 13.0 million (sensitivity analysis, 4.24 million to 17.1 million) lost IQ points and 59 300 (sensitivity analysis, 16 500 to 84 400) cases of intellectual disability, at costs of €146 billion (sensitivity analysis, €46.8 billion to €194 billion)." Neurobehavioral Deficits, Diseases, and Associated Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union. Journal of Clinical Endocrinology & Metabolism, 2015.

Thyroid in mice

> "The present study showed that exposure of CD1 mice, during critical windows of prenatal and postnatal development, at CPF [chlorpyrifos] dose levels below those inhibiting brain AchE, can induce alterations in thyroid." Developmental Exposure to Chlorpyrifos Induces Alterations in Thyroid and Thyroid Hormone Levels Without Other Toxicity Signs in Cd1 Mice. Toxicological Sciences, 2009.

Problems with industry studies

> "In March 1972, Frederick Coulston and colleagues at the Albany Medical College reported results of an intentional chlorpyrifos dosing study to the study's sponsor, Dow Chemical Company. Their report concluded that 0.03 mg/kg-day was the chronic no-observed-adverse-effect-level (NOAEL) for chlorpyrifos in humans. We demonstrate here that a proper analysis by the original statistical method should have found a lower NOAEL (0.014 mg/kg-day), and that use of statistical methods first available in 1982 would have shown that even the lowest dose in the study had a significant treatment effect. The original analysis, conducted by Dow-employed statisticians, did not undergo formal peer review; nevertheless, EPA cited the Coulston study as credible research and kept its reported NOAEL as a point of departure for risk assessments throughout much of the 1980′s and 1990′s. During that period, EPA allowed chlorpyrifos to be registered for multiple residential uses that were later cancelled to reduce potential health impacts to children and infants. Had appropriate analyses been employed in the evaluation of this study, it is likely that many of those registered uses of chlorpyrifos would not have been authorized by EPA. This work demonstrates that reliance by pesticide regulators on research results that have not been properly peer-reviewed may needlessly endanger the public." Flawed analysis of an intentional human dosing study and its impact on chlorpyrifos risk assessments. Environment International, 2020.

> "In our review of raw data on a prominent pesticide, chlorpyrifos, and a related compound, discrepancies were discovered between the actual observations and the conclusions drawn by the test laboratory in the report submitted for authorization of the pesticide." Safety of Safety Evaluation of Pesticides: developmental neurotoxicity of chlorpyrifos and chlorpyrifos-methyl. Environmental Health, 2018.

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