

Human Health Threats | Biodiversity | Climate

The dire health, biodiversity, and climate crises and their link to petrochemical pesticide and fertilizer use (and related production, transportation, storage, and disposal) support nothing less than systemic change to the practices and policies that have brought on a confluence of never-before-seen threats to life. This section on science tracks the independent, peer-reviewed scientific literature that links pesticides to a dizzying array of health and environmental effects. This science empowers calls for change that, going beyond typical pesticide mitigation and reduction measures or specific chemical phaseouts, adopt strategies to eliminate toxic pesticide dependency and embrace organic practices and policies. The science reflects a pattern of pesticide-induced illness and disease throughout ecosystems that is generational and escalating exponentially, as captured in this section and on the Beyond Pesticides website.



CHILDREN'S HEALTH | MOTOR SKILL DEFICIENCY | JANUARY 5, 2022 HOUSEHOLD Pesticide Use Harms Infant Motor Skill Development

ousehold pesticide use is associated with harmful impacts to infant motor development, according to a study published late last year in the journal Pediatric and Perinatal Epidemiology. The research focuses on primarily low-income Hispanic women located in Los Angeles, California, enrolled in an ongoing study referred to as Maternal and Developmental Risks from Environmental and Social Stressors (MADRES). Low-income, people of color communities are disproportionately in contact with toxic pesticides and other pollutants, resulting in exposures that can start early and affect health over the course of one's lifetime.

Overall, roughly 22% of mothers reported pesticide use in their home during the first months of their children's lives. The analysis reveals that 21 of the infants tested fall below the cut-off for the screening tool that suggests further evaluation by a health professional. "In adjusted models, infants whose mothers reported household use of rodent or insect pesticides had 1.30 (95% CI 1.05, 1.61) times higher expected gross motor scores than infants in households with no reported household pesticide use, with higher scores indicating decreasing gross motor performance," the study indicates.

Women enrolled in the MADRES cohort are over the age of 18 and speak English or Spanish fluently. For the present study, roughly 300 MADRES participants met the criteria for enrollment and completed household pesticide use questionnaires at a three-month postnatal visit. The questionnaire generally inquires whether pesticides had been used in one's home since their child was born. After another three months, researchers also tested infants' motor development using an Ages and Stages-3 protocol screening tool, which evaluates a child's ability to execute muscle movements.

Household pesticide use over the last decade has generally shifted away from the use of older organophosphate chemistries to the use of synthetic pyrethroid insecticides. But this switch has not resulted in safer exposures; a growing body of literature is finding that synthetic pyrethroids can cause a range of adverse health impacts, particularly in children. Multiple studies have been published linking synthetic pyrethroids to developmental problems in children. Most recently, a 2019 Danish study finds that higher concentrations of pyrethroid insecticides corresponds to higher rates of attentiondeficit/hyperactivity disorder (ADHD) in children. Pesticide exposure at a young age can have far-reaching effects. In addition to motor skills and learning development, young boys exposed to synthetic pyrethroids are more likely to experience early onset of puberty.

These data are all the more concerning in the context of findings that show how synthetic pyrethroids can persist as residue on hard surfaces in one's home for over a year. This persistent residue can result in multiple re-exposures, turning what an individual may consider a one-time use into a chronic exposure event. Unfortunately, for many low-income residents in the U.S., pesticide use in and around one's home or apartment is not a decision they can make. Many property management companies, landlords, and public housing authorities have ongoing service contracts with chemical pest control companies. This outdated and dangerous approach to pest management, which often includes service visits that prophylactically spray toxic pesticides without considering need, results in disproportionate exposure to low-income individuals who may otherwise be keeping a spotless home. It is little wonder why studies can match disease risk to zip code, with individuals in low-income, indigenous and people of color communities at greatest risk of developing pesticide and other environmentallyinduced diseases.

What to do: While research finds that feeding kids an organic diet improves scores on tests measuring memory and intelligence, the additional use of pesticides in one's home can undermine those benefits. Ultimately, everyone should have access to healthy food grown without pesticides and be able to live a life without mandated exposure to toxic pesticides that undermine your and your family's health. For assistance on stopping household pesticide use and managing household pests without chemicals, see Beyond Pesticides' ManageSafe webpage, or reach out at info@beyondpesticides.org.

SOURCE: Hernandez-Castro, I, Eckel, SP, Chavez, T, et al. Household pesticide exposures and infant gross motor development in the MADRES cohort. *Paediatr Perinat xEpidemiol.* 2022; 36: 220–229.doi: 10.1111/ppe.12850.



CHILDREN'S HEALTH | PRENATAL EXPOSURE AND EAR INFECTIONS | FEBRUARY 9, 2022 Pesticide Use During Pregnancy Increases Childhood Risk of Ear Infections

nsecticide use during pregnancy significantly increases the occurrence of Otitis Media (OM), an infection of the space behind the ear drum, in infants, according to research published in *Scientific Reports* from a team of Japanese researchers in January. While most infections go away on their own, some children experience pain, fever, and in some cases complications that

result in hearing loss. This research underscores the myriad of dangers and diseases that pesticide use can precipitate, which are not considered under risk assessments conducted by the U.S. Environmental Protection Agency (EPA).

Scientists collected their initial data from the ongoing Japan Environment and Children's Study, a national birth cohort study that evaluates environmental factors affecting children's health in Japan. Data recorded include factors such as maternal age, birth weight, and gestation weeks, and mothers provided answers to a range of questionnaires, including one relating to exposure to insecticides during pregnancy. Study authors utilize a range of other covariates to control for further risk factors, such as family history of OM, living with other siblings, nursery attendance, parental smoking habits, and others.

The study determined that OM during an infant's first year of life is most closely associated with insecticide use more than one time per week between conception and the first trimester of pregnancy. Insecticide use in the second and third trimester is not associated with OM. Researchers speculate that insecticide use causes OM due to weakened immune function in exposed individuals.

This is the first study to show a connection between ear infections in young children and pesticide exposure during pregnancy. Prior research, however, has provided some indication that pesticides can harm the ears and affect hearing. A 2020 study published in the Annals of Work Exposures and Health found that farmworkers exposed to a combination of pesticides and noise from agricultural machinery were at increased risk of hearing loss.

Roughly 1 in 5 children experience several episodes of OM in short spans during early life. The cost of these treatments can add up significantly, accounting for several billion dollars in health care costs. Additionally, "Preventing OM decreases the burden that is placed on parents who have to visit clinics and take time off work," the authors indicate. This is the first study to show a connection between ear infections in young children and pesticide exposure during pregnancy. Prior research has provided some indication that pesticides can harm hearing.

Results highlight the hidden risks that individuals tacitly accept when applying a substance intended to kill life. Chemicals like the increasingly common synthetic pyrethroid class of insecticides can remain on hard surfaces for over a year, providing continual, chronic exposure. These exposures can weaken immune system functioning and make individuals more susceptible to infection and other diseases.

Pregnant mothers, fetuses, and young children are at greatest risk from household pesticide use, as evidenced by a large and growing body of research. Exposure during and after pregnancy has been associated with increased risk of cancers, including infant leukemia and childhood brain tumors. Pregnant mothers exposed to pesticides are more likely to have preterm births and low birth weight, children with motor development problems, as well as children who go on to develop ADHD. These impacts are perhaps unsurprising given studies that show over 100 different chemicals detectable in pregnant women, including new or unknown compounds.

What to do: Pregnant women and households with young children are strongly encouraged to avoid all use or exposure to any pesticide products. Eating healthy, organic food is another factor that can reduce exposure and improve children's well-being. New and expecting families can find more resources to keep your home child-safe on the Materials for New Parents webpage. For more information on the range of diseases associated with pesticide use, see Beyond Pesticides' Pesticide Induced Diseases Database.

SOURCE: Utsunomiya, T., Taniguchi, N., Taniguchi, Y. *et al.* Association between maternal insecticide use and otitis media in one-year-old children in the Japan Environment and Children's Study. *Sci Rep* 12, 1365 (2022). https://doi.org/10.1038/s41598-022-05433-2 Image Source: Luca Prasso, Flikr

CHILDREN'S HEALTH | RESPIRATORY DISEASE | MARCH 3, 2022 Study Confirms Children's Exposure to Mosquito Pesticides Increases Risk of Respiratory Disease

hildren's exposure to synthetic pyrethroid insecticides, particularly during the course of mosquito control operations, is associated with increased occurrence of certain respiratory diseases, finds research published in the journal *Thorax* in February. With a respiratory virus pandemic continuing to spread throughout the world, it has become increasingly important to avoid environmental exposures that can harm lung health. This research underscores

the critical need for homeowners, farmers, and vector control officials to shift away from chemical use as the first line of defense against pest problems in order to safeguard children's health.

A total of 303 women and their children participated in the study, which tracked pesticide exposure during pregnancy and then at age five. All participants in the study lived within roughly three miles of a banana plantation. A structured questionnaire captured a range of variables, from socioeconomic status to medical history, local environmental conditions, occupation, and demographics. Researchers collected urine samples from pregnant mothers during the first visit, and their children during the five-year follow-up.

Urine samples were analyzed for metabolites concerning a range of insecticides, including chlorpyrifos, synthetic pyrethroids, the fungicides mancozeb, pyrimethanil, and thiabendazole, and



the herbicide 2,4-D. During the second follow-up, mothers filled out another questionnaire regarding their children's respiratory and allergic outcomes.

Of the pesticides tested, 80% are frequently detected within tested mothers, and 68% within children during the course of the study. Researchers thus differentiated between high and low levels of pesticide concentration in making their findings.

Current pesticide use is associated with a range of respiratory and allergic complications in children. High levels of metabolites from the fungicide mancozeb are correlated with increased incidence of lower respiratory tract infections. However, synthetic pyrethroid insecticides are the primary offenders, associated with higher rates of current asthma, passed asthma diagnosis, recent lower respiratory tract infections, and cough. The strongest association between pyrethroids and adverse health impacts is for wheeze. Increased exposure exhibits stronger correlations, with each 10x increase showing a greater likelihood of developing asthma, wheeze, lower respiratory tract infections, and itchy rash.

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particularly in children, have grown over the last decade. While researchers did not find links between prenatal pyrethroid use and childhood respiratory problems, a 2012 study looking at PBO (piperonyl butoxide), a pesticide "synergist" often combined with synthetic pyrethroids in consumer products was found to be linked to childhood cough after a mother's exposure. In 2015, a study at the University of California, Berkeley found that general exposure to organophosphates (not only chlorpyrifos) corresponds with a measurable decrease in lung function.

Agricultural workers and their families are at greatest risk from these health hazards. A 2016 study linked an astounding 78 pesticides to allergic and non-allergic wheeze among male farmers. Agricultural work with toxic pesticides was associated with an increased risk of the potentially deadly diseases idiopathic pulmonary fibrosis (IPF) in a 2021 study, and chronic obstructive pulmonary disease (COPD) in a recent February 2022 report. Unsurprisingly, a comprehensive literature review published in 2020 finds pesticide exposure to be strongly correlated with the development of respiratory diseases.

What to do: Current laws do not adequately protect local residents from toxic pesticide exposure coming from farms, community and school pesticide use, and mosquito control operations. Through collective action, we can stop the regular use of hazardous, lungharming pesticides in homes, on farms, and in mosquito management. Reach out to Beyond Pesticides for assistance with your local advocacy efforts. For more information about the link between pesticides and respiratory health, see Beyond Pesticides Pesticide-Induced Diseases Database.

SOURCE: Islam JY, Hoppin J, Mora AM, *et al.* Respiratory and allergic outcomes among 5-year-old children exposed to pesticides. *Thorax*, 2023;78:41-49.



CHILDREN'S HEALTH | OXIDATIVE STRESS, DNA DAMAGE, AND CANCER | APRIL 28, 2022 Glyphosate Breakdown Product Associated with Oxidative Stress and DNA Damage Among Children

study in Environmental Research finds that the herbicide glyphosate's primary metabolite (breakdown product), aminomethylphosphonic acid (AMPA), induces DNA damage through oxidative stress among subpopulations of primary school children. Although pyrethroid and chlorpyrifos metabolites can induce oxidative stress, this study is the first to investigate AMPA's association with adverse health effects, rather than solely the effects of the active ingredient, glyphosate, in Roundup and other formulations.

Glyphosate is the most commonly used active ingredient worldwide, appearing in many herbicide formulations, readily contaminating soil, water, food, and other resources. Chemical use has been increasing since the inception of crops genetically modified to tolerate glyphosate. However, studies demonstrate glyphosate is among the most prevalent pesticide contributors to human, biotic, and ecosystem harm.

According to research, herbicide toxicity to invertebrates has doubled since 2004. Although research links glyphosate exposure to cancer, specifically non-Hodgkin lymphoma, much less research considers the effects that metabolites have on children who are more vulnerable to chemical exposure. Ecological and health risk assessments primarily focus on active ingredients in pesticide products, overlooking the potential impacts of metabolites. Thus, studies like these highlight the need to assess the implications of metabolite exposure to protect human, animal, and environmental health. The study notes, "Our results indicate that [Cypriot] children are co-exposed to a mixture of pesticides likely originating from both dietary and non-dietary sources. On average, these pesticide exposures appear at higher levels than those typically measured in other EU (European Union) populations. The population health risk associated with

such mixture exposures needs to be further investigated."

The researchers in this study investigated the health of children aged 10 to 11 in Cyprus, using the European Human Biomonitoring Initiative (HBM4EU) to measure urinary concentrations of glyphosate, AMPA, and pyrethroid and chlorpyrifos metabolites. Using an immunological assay, researchers identified oxidative stress using biological markers to assess lipid and DNA damage. Additionally, parents filled out questionnaires gathering data on demographic characteristics, pesticide usage, and diet.

The results find that AMPA, but not glyphosate, has a positive association with DNA damage via oxidation. Moreover, the metabolites of pyrethroids (3-PBA) and chlorpyrifos (TCPy) are also associated with DNA damage and oxidative stress. Lipid damage from oxidative stress did not occur among these pesticides. However, the results suggest parental education levels influence urinary pyrethroid levels.

Decades of extensive glyphosate herbicide use (e.g., Roundup) have put human, animal, and environmental health at risk. The chemical's ubiquity threatens 93 percent of all U.S. endangered species, resulting in biodiversity loss and ecosystem disruption (e.g., soil erosion, loss of services, and trophic cascades). Exposure to glyphosate has implications for the development of various health anomalies, including cancer, Parkinson's disease, and autism. Although the U.S. Environmental Protection Agency (EPA) classifies glyphosate herbicides as "not likely to be carcinogenic to humans," stark evidence demonstrates links to various cancers, including non-Hodgkin lymphoma. EPA's classification perpetuates adverse impacts, especially among vulnerable individuals, like pregnant women, infants, children, and the elderly. Not only do health officials warn that continuous use of glyphosate will perpetuate adverse health effects, but that use also highlights recent concerns over antibiotic resistance. Agrochemical company Bayer/Monsanto patents glyphosate as an antibiotic. Exposure hinders enzymatic pathways in many bacteria and parasites. However, studies find glyphosate exposure disrupts the microbial composition in both soil and animals-including humans-discerningly eliminating beneficial bacteria while preserving

unhealthy microbes. Moreover, resistance to pesticides is also growing at similar rates among genetically engineered (GE) and non-GE chemically grown crops. This increase in resistance is evident among herbicide-tolerant GE crops, including seeds genetically engineered to be glyphosate-tolerant.

This study is one of the first to identify oxidative stress from AMPA exposure among children in a nonoccupational setting. However, glyphosate and its formulations have long been associated with oxidative stress and strong evidence of genotoxicity. Moreover, glyphosate degrades relatively quickly in the environment, between five and 20 days, leaving behind AMPA, which is highly persistent with a half-life of 151 days. Therefore, researchers attribute higher rates of AMPA concentration in children's bodies to relative availability in the environment compared to glyphosate. Additional studies find that 100 percent of adults and children have detectable levels of AMPA in urine samples, with children exhibiting a five times higher bodily concentration than adults. Therefore, researchers suggest that a shift to organic can mitigate exposure to these toxic chemicals, especially among vulnerable populations like children.

It is essential to understand the effects widely used pesticides and their breakdown products may have on the health of current and future generations. Beyond Pesticides challenges the EPA registration of chemicals like glyphosate in court due to their impacts on soil, air, water, and our health. However, emphasis on converting to regenerativeorganic systems and using least-toxic pest control can mitigate harmful exposure concerns. Public policy must advance this shift rather than continue to allow unnecessary reliance on pesticides.

What to do: Purchasing organic food whenever possible-which never allows glyphosate use-can help curb exposure and resulting adverse health effects. Beyond Pesticides provides tools, information, and support to take local action to stop glyphosate use and shift to organic practices: check out our factsheet on glyphosate/Roundup and our report, Monsanto's Roundup (Glyphosate) Exposed. Contact us for help with local efforts and stay informed of developments through our Daily News Blog and our journal, Pesticides and You. Additionally, check out Carey Gillam's talk on Monsanto's corruption on glyphosate/Roundup at Beyond Pesticides' 36th National Forum.

SOURCE: Konstantinos C. Makris, Nikolaos Efthymiou, Corina Konstantinou, Elena Anastasi, Greet Schoeters, Marike Kolossa-Gehring, Andromachi Katsonouri, Oxidative stress of glyphosate, AMPA and metabolites of pyrethroids and chlorpyrifos pesticides among primary school children in Cyprus, Environmental Research, Volume 212, Part B, 2022, 113316, ISSN 0013-9351, https://doi. org/10.1016/j.envres.2022.113316.

CHILDREN'S HEALTH | PEDIATRIC CANCER | JUNE 28, 2022 Pesticides Linked to Adult and Childhood Cancer in Western U.S., with Incidence Varying by County

There is a strong connection between pesticide use and cancer rates in the Western United States, finds research recently published by scientists at University of Idaho and Northern Arizona University. Two studies (here and here) published in the

peer-reviewed journal *GeoHealth* used geospatial data and publicly available pesticide databases to uncover the relationship between chemical heavy agricultural practices and cancer in both adults and children. As the rate of chronic diseases like cancer continue to increase

in the United States, and more and more studies find these diseases to be pesticide-induced, it is imperative for the public to put increased pressure on regulators and lawmakers to enact meaningful measures that eliminate pesticide use and the hazards these chemicals pose.



Of the two studies conducted by the research team, the first study models the connection between pesticide use and cancer incidence for adults and children in 11 western states (Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming), while the second study focuses on childhood cancer rates in Idaho's 44 counties. Both studies utilize databases established by public entities, including U.S. Geological Survey (USGS) Pesticide National Synthesis Project database, EPA Pesticide Industry Sales and Usage Estimates, National Cancer Institute (NCI) State Cancer Profiles, and the Cancer Data Registry of Idaho.

Rather than focus solely on the impacts of pesticide use to farmers or agricultural workers, the studies consider the broader effects of agricultural pesticide use on the public at-large.

For the first study, researchers take the top 25 most used pesticides identified by EPA estimates and cross-reference them with USGS data to determine the amount of each pesticide used by state and county. These data were then modeled against NCI county-level cancer incidence.

At the state level, an association is found between the total amount of all pesticides evaluated and both overall and pediatric cancer incidence. Delving deeper into specific pesticide types, a strong connection is found between the amount of fumigants applied in each state and the rate of pediatric cancers. Specifically, the fumigant pesticide metam sodium has a strong connection between its higher use and total cancer rate. These findings are even more prevalent at the county-level. A cutting edge model regarding fumigant use and cancer rate matches guite closely to currently observed cancer rates in the over 450 counties that comprise the 11 western states.

Notably, the areas where fumigant use is high are those with more vegetable and fruit production, rather than grain crops like corn and soy. Regarding the cancer connection to fumigant use, study coauthor Naveen Joseph, PhD says, "We have not seen it expressed in a fumigant like this before, and it's absolutely striking."

The second study by this research team likewise aimed to create a model able to describe county-level childhood cancer rates. Focusing in on Idaho's 44 counties, researchers this time used groundwater contamination, as recorded by the Idaho Department of Water Resources, as a variable and proxy for children's environmental exposures. The same 25 pesticides as the first study were reviewed, but researchers also include other environmental toxicants like heavy metals, and nitrate/nitrites. These data are consolidated into an Environmental Burden Index (EBI), and overall environmental contamination within each county is subsequently deemed as either low, medium, or high on the EBI.

The model finds that EBI correlates closely with the pediatric cancer rate. Idaho counties with high scores on the EBI have higher rates of childhood cancer. As the study further notes, "The variables predominantly contributing to the environmental burden index were pesticides." Like the first study, a model created by the researchers using these available data was able to accurately predict pediatric cancer incidence currently occurring in Idaho counties.

Geospatial mapping is providing new insights into the hazards presented by pesticide use, uncovering trends in public health that are systemic, yet rarely considered. Case in point is a study published in 2020, which looks at the connection between Parkinson's disease, agricultural pesticide use, and one's zip code in Louisiana. That study found that Parkinson's rates are significantly higher in zip codes with commercial forests, woodlands, and pastures where the pesticides 2,4-D, chlorpyrifos, and paraquat were often sprayed.

As with other systemic injustices, one's zip code and place of residence often determines one's destiny. Uncovering this information and relating it to the public is of critical importance, but oftentimes those in disaffected communities are well aware of the dangers and threats they are exposed to daily. What is needed is action.

What to do: With pesticide use, we have enough evidence to know that we should be rapidly embracing timetested, organic approaches to farming and land care that do not utilize toxic pesticides. Data elucidating the public health ills produced by pesticides must be accompanied by meaningful action from regulators and lawmakers at every level—local, state, and federal. For assistance in changing pesticide practices in your community, reach out to Beyond Pesticides at info@ beyondpesticides.org

SOURCE: Joseph, N., Propper, C. R., Goebel, M., Henry, S., Roy, I., & Kolok, A. S. (2022). Investigation of relationships between the geospatial distribution of cancer incidence and estimated pesticide use in the U.S. West. *GeoHealth*, 6, e2021GH000544. https://doi.org/10.1029/2021GH000544; Joseph, N., & Kolok, A. S. (2022). Assessment of pediatric cancer and its relationship to environmental contaminants: An ecological study in Idaho. *GeoHealth*, 6, e2021GH000548. https://doi.org/10.1029/2021GH000548



CHILDREN'S HEALTH | CHILDHOOD DIABETES | AUGUST 5, 2022 Antibiotics and Neonicotinoid Insecticides Linked to Gut Microbiome Disruption and Childhood Diabetes

study published in World Journal of Pediatrics finds an association between antibiotic and neonicotinoid (neonic) exposure and onset of pediatric (childhood) type 1 diabetes (T1D) through effects on the gut microbiome. Individuals with type 1 diabetes are at higher risk of other autoimmune

disorders, including thyroid and celiac disease. Ample evidence demonstrates environmental contaminants like pesticides and antibiotics negatively affect human mouth and gut microbes. Health officials identify Type 1 diabetes as one of the most common chronic childhood diseases, increasing among children younger than five years old.

Through the gut biome, pesticide exposure can enhance or exacerbate the adverse effects of additional environmental toxicants on the body. Moreover, studies find low levels of pesticide exposure during pregnancy or childhood cause adverse health effects from metabolic/immune disorders to mental and physical disabilities. Children are particularly vulnerable to the impacts of pesticide exposure as their developing bodies cannot adequately combat exposure effects. Although studies show how chemical exposures affect overall human health, more research is now questioning how these toxic chemicals influence gut health and subsequent occurrence of diseases. In children, gut microbiome disruption, or gut dysbiosis, has significant associations with type 1 diabetes development, and disruption of gut microbiota plays a role in type 2 diabetes development.

Over 11 percent (>37 million) of individuals in the U.S. have diabetes, and cases are growing by millions annually. With increasing rates of type 1 and 2 diabetes cases among the global population, studies like these highlight the importance of evaluating how chemical contaminants deregulate normal bodily function through microbiome changes.

There is a lack of understanding of the real-world effects of neonic and antibiotic exposure on gut microbiome changes akin to the onset of T1D. However, studies suggest the structure of gut microbiota in children can differ depending on the level of chemical exposure, leading to disparities in T1D risk. The study researchers highlight, "[M]ost existing studies on the health risks caused by antibiotics and pesticides tend to focus on the effect of high levels of exposure over short periods because relationships between longterm low-dose exposure and health risks are ambiguous and difficult to study. As a result, the mechanisms associated with their adverse effects on health remain unclear."

The researchers evaluate antibiotic and neonic concentrations in the urine of 51 children newly diagnosed with T1D, comparing chemical exposure levels to those of healthy control group children (without T1D). Mass spectrometry measured urine for concentrations of 28 antibiotics and 12 neonics, grouping children based on the type of chemical exposures. Furthermore, The study researchers highlight, "[M]ost existing studies on the health risks caused by antibiotics and pesticides tend to focus on the effect of high levels of exposure over short periods because relationships between long-term low-dose exposure and health risks are ambiguous and difficult to study. As a result, the mechanisms associated with their adverse effects on health remain unclear."

researchers compared gut microbiota in fecal matter to urine samples to determine a correlation between differences in gut microbiota and T1D onset.

The study detects antibiotics in 72.5 percent of children with T1D and 61.2 percent of healthy children, while neonics are present in 70.6 percent of children with T1D and 52.2 percent of healthy children. A child's exposure to one type of antibiotic or two or more types of neonics increases the T1D risk 2.6 and 3.9-fold, respectively. Co-exposure to antibiotics and neonics has an association with T1D, increasing the risk 4.9-fold. Children unexposed to both antibiotics and neonics have a higher abundance of Lachnospiraceae (the core taxa of gut microbiota) than children exposed to antibiotics and neonicotinoids, alone or together.

The gut, also known as the "second brain," shares similar structural and chemical parallels with the brain. Microbiota (i.e., groups of microorganisms, including bacteria, archaea, viruses, and fungi) in the gut play a crucial role in lifelong digestion, detoxification, immune and central nervous system regulation, and other bodily functions. Through the gut biome, pesticide exposure can enhance or exacerbate the adverse effects of additional environmental toxicants on the body. Since the gut microbiome shapes metabolism, it can mediate some toxic effects of environmental chemicals. However, prolonged exposure to various environmental contaminants can induce critical chemical changes in the gut microbes, influencing adverse health outcomes.

The impacts of pesticides on the human gut microbiome represent another pesticide assault on human health as the biome harbors between 10 and 100 trillion symbiotic microbes. The human gastrointestinal tract and its digestive processes (the "gut") mediate the function of several systems. Dysfunction of the gut microbiome is associated with a host of diseases, including cardiovascular disease, some cancers, multiple sclerosis, diabetes, asthma, Crohn's disease, Parkinson's disease, and inflammatory bowel disease, as well as allergies, autism, depression, obesity, and other disorders or syndromes.

Over the past 20 years, neonicotinoids captured the global market of insecticides ahead of organophosphates, carbamates, phenyl-pyrazoles, and pyrethroids. These systemic agricultural pesticides are highly toxic, resembling nicotine and affect the central nervous system of insects, resulting in paralysis and death, even at low doses. Like other pesticides, neonics readily contaminate water and food resources as traditional water waste treatments typically fail to remove the chemical from tap water, and the systemic nature of neonics allows the chemical to accumulate within the product rather than externally. According to the Centers for Disease Control and Prevention (CDC), nearly half the U.S. population encounters at least one type of neonic daily, with children ages three to five having the highest exposure risk. Health impacts of exposure to neonics can include neurotoxicity, reproductive anomalies, hepatic and renal damage, and an increase in gene expression linked to hormone-dependent breast cancer. Additionally, researchers identified the role some neonicotinoids play in the production of an enzyme (aromatase) that stimulates excess estrogen

production, a known event in hormonedependent cancer development.

Antibiotic exposure can allow more resilient bacteria to flourish in the gut microbiome and outcompete other beneficial bacteria. For instance, glyphosate, patented as an antibiotic by manufacturer Bayer/Monsanto, kills bacterial species beneficial to humans and incorporated in probiotics, yet allows harmful bacteria to persist, leading to resistance. Glyphosate's mode of action targets and inactivates an enzyme in the "shikimate [metabolic] pathway" in plants. Although this pathway is not present in animal cells, it exists among bacterial species. However, antibiotic exposure can still impact other metabolic pathways in animals. Antibiotic resistance can trigger longer-lasting infections, higher medical expenses, the need for more expensive or hazardous medications, and the inability to treat life-threatening illnesses.

The study concludes, "[C]hildren with exposure to antibiotics and neonicotinoids had small but critical changes in gut microbiota, characterize[ed} by a lower abundance of butyrate-producing genera, especially *Lachnospiraceae*. Similar changes were also observed in T1D children, which were thought to be associated with the increase of autoimmune level. These findings suggest that exposure to high levels of antibiotics and pesticides in daily life might increase the risk of autoimmune diseases, such as T1D. Future work should focus on relationships between antibiotics and neonicotinoids exposure and the onset of autoimmune diseases in children, as well as the underlying mechanisms."

Current risk assessment methods for pesticides are insufficient as assessment procedures fail to account fully for the sublethal effects of pesticides. With the globe currently going through the Holocene Extinction, Earth's 6th mass extinction, with one million species of plants and animals at risk over the last four decades, action is needed to mitigate our anthropogenic impact on essential ecosystem organisms.

Pesticides themselves can possess the ability to disrupt metabolic function, especially for chronically exposed individuals (e.g., farmworkers) or during critical windows of vulnerability and development (e.g., childhood, pregnancy).

What to do: It is essential to mitigate preventable exposure to diseaseinducing pesticides. For more information on the effects of pesticide exposure on autoimmune and metabolic health, see Beyond Pesticides' Pesticide-Induced Diseases Database pages on diabetes, immune system disorders, endocrine disruption, and more. Replacing dietary exposure to food grown in chemical-intensive agriculture with organic consistently reduces pesticide levels in one's body. Preventive practices like organic can eliminate exposure to toxic autoimmune disrupting pesticides, like neonics. There is an indication that maintaining lower levels of conventional, synthetic pesticides is likely to reduce the risk of developing chronic diseases like type 2 diabetes. In addition to positive impacts on the human microbiome, organically grown food (i.e., milk, meat, strawberries, tomatoes, and a range of other foods) contain a much more diverse bacterial community than their chemically grown counterparts. Organic agriculture represents a safer, healthier approach to crop production that does not necessitate toxic pesticide use. Beyond Pesticides encourages farmers to embrace and consumers to support regenerative, organic practices. A complement to buying organic is contacting various organic farming organizations to learn more about what you can do. Additionally, learn more about the hazards posed to children's health through Beyond Pesticide's Pesticide and You Journal article, "Children and Pesticides Don't Mix."

SOURCE: Xu, ZR., Yuan, XX., Chen, RM. *et al.* Association between new onset type 1 diabetes and real-world antibiotics and neonicotinoids' exposure-related gut microbiota perturbation. *World J Pediatr* 18, 671–679 (2022). https://doi.org/10.1007/s12519-022-00589-3.

CHILDREN'S HEALTH | DEVELOPMENTAL DELAYS | SEPTEMBER 1, 2022 Exposure to Synthetic Pyrethroids During Infancy Associated with Developmental Delays in Toddlers

ow level exposure to synthetic pyrethroid insecticides at six to eight months of age is associated with language development delays in two-year old toddlers, according to research published in *Neurotoxicology* this month. This is the latest study to link this class of chemicals to developmental delays in young children. Despite a

steady drumbeat of concerning research, the U.S. Environmental Protection Agency (EPA) in 2019 removed a crucial "safety factor" intended to protect children's health from synthetic pyrethroids, allowing higher levels of the insecticides to be sprayed on food, in homes, and playing fields around the country. To investigate the impact of synthetic pyrethroids on language development, scientists enrolled 327 expectant mothers in their third trimester. The mothers, all from rural areas of China, were selected if they had no history of significant pesticide exposure or family history of serious disease. Urine samples were taken from the women during pregnancy,



and from infants 6-8 months after birth. Scientists analyzed samples for concentrations of three different synthetic pyrethroid breakdown products (metabolites), including 3-phenoxybenzoic acid (3PBA), 4-fluoro-3-phenoxybenzoic acid (4F3PBA), and cis-2,2dibromovinyl-2,2-dimethylcyclopropane-1-carboxylic acid (DBCA). While 3PBA is a metabolite of many synthetic pyrethroids, 4F3PBA is a more specific metabolite of cypermethrin, and DBCA is a metabolite of deltamethrin. At two years of age, enrolled children were tested for expressive communication, receptive communication, and language composite scores.

Average urinary synthetic pyrethroid concentrations in children aged six to eight months are found to be higher than those taken from their mothers during pregnancy for metabolites 3PBA and 4F3PBA. The cyfluthrin metabolite 4F3PBA correlates with lower receptive communication scores. Every one microgram increase in 4F3PBA exposure during infancy corresponds with a 9% increased chance of not passing the receptive communication test. Yet the strongest association is seen with the deltamethrin metabolite DBCA, which is found to increase risk of language development delay by 4.58 times. This metabolite also increases risk of not passing expressive communication tests by 21%. Young boys in particular experience a statistically significant impact compared to young girls, associated with overall exposure to pyrethroid metabolites. Higher amounts of pesticide metabolites in infant boy's urine is associated with lower scores for receptive communication and language composite tests. The study concludes that, "The probability of toddlers' language development delay may be predicted by PYRs [pyrethroids] metabolites of infants aged 6-8 months."

After EPA identified risks of concerns to children over six months and under six years old from exposure to synthetic pyrethroids, the major manufacturers of the insecticides coordinated under the Council for the Advancement of Pyrethroid Human Risk Assessment (CAPHRA) to come up with a new evaluation process for the impact of pyrethroids on children's health. Unsurprisingly, the model developed by CAPHRA effectively exonerated synthetic pyrethroids from harmful effects, allowing the removal of the childhood safety factor and an explosion in pyrethroid usage. Notwithstanding the risks to children in this age range, EPA did not even entertain the potential for damaging impacts to occur earlier in life. In its reevaluation of the safety factor, the agency wrote, "Furthermore, fetal exposure and exposures to children below six months of age are expected to be negligible because pyrethroid levels in food and drinking water are generally low and there is no or low potential for contact with treated surfaces. After looking at hundreds of peer-reviewed studies in the independent scientific literature, EPA incorporated only two into its determination.

Numerous studies have linked synthetic pyrethroids to developmental harm in children. A 2011 study found that children exposed to higher levels of synthetic pyrethroids are three times as likely to have mental delay compared to less exposed children. A 2014 study associated proximity to pesticide treated agricultural fields in pregnancy to increased risk of autism to children of exposed mothers. Two studies published in 2015 find that deltamethrin increases risk of ADHD in children, with one study finding impacts specifically to boys. Studies published in 2017 found that synthetic pyrethroid exposure increases risk of premature puberty in boys, and another associated the chemicals with externalizing and internalizing disorders. The impacts seen are not all developmental. A 2012 study associates pyrethroid exposure before, during, and after pregnancy with increased risk of infant leukemia. And a 2022 finds that synthetic pyrethroid exposure during mosquito control operations increases risk of respiratory disease and certain allergies. What to do: We must embrace a precautionary approach to pesticide regulation, placing the onus on pesticide manufacturers to prove safety rather than on regulators to prove harm. If peer-reviewed studies indicate the potential for harm to children's health, the precautionary approach rejects this harm in favor of available alternatives. Join in urging U.S. Senators to cosponsor the Protect America's Children From Toxic Pesticides Act, which would make significant progress in reining in the influence of the pesticide industry at EPA. Learn how to use science in advocacy in community decision making to eliminate toxic pesticide use by viewing the 2022 National Pesticide Forum Series, Health, Biodiversity, and Climate: A Path for a Livable Future.

SOURCE: Chen S, Xiao X, Qi Z, Chen L, Chen Y, Xu L, Zhang L, Song X, Li Y. Effects of prenatal and infant daily exposure to pyrethroid pesticides on the language development of 2-year-old toddlers: A prospective cohort study in rural Yunnan, China. Neurotoxicology. 2022 Sep;92:180-190. DOI: 10.1016/ j.neuro.2022.08.002



CHILDREN'S HEALTH | BIOMONITORING OF PREGNANT WOMEN | SEPTEMBER 2, 2022 Compounds in Pesticides Shown to Harm Fetuses and Children with Disproportionate Risk to People of Color

evelations of toxic risks to pregnant people seem to emerge with alarming frequency. In late August a study published in *Chemosphere* finds that the compound melamine, its primary byproduct (cyanuric acid), and four aromatic amines were detected in the urine of nearly all pregnant research

participants. These chemicals are associated with increased risks of cancer, kidney toxicity, and/or developmental harm to the resultant child. Beyond Pesticides has covered a variety of pregnancy risks from pesticides and other toxic chemicals, including these in just the last three years: pesticides and children's sleep disorders; prenatal exposures to a multitude of chemicals; insecticides and childhood leukemia; insecticides and Attention Deficit/ Hyperactivity Disorder.

Those of a certain age may hear "Melamine" and think of the nearly indestructible plastic dinnerware from

the mid-20th century, but "melamine" is an organic chemical compound that, when combined with formaldehyde, forms a durable plastic. Others may remember the 2007-2008 incident in China of contamination of infant formula with melamine, which resulted in six deaths, and kidney and urinary tract harms (ranging from development of kidney stones to acute renal failure) in some 300,000 babies. [A small sidebar explainer: melamine was actually intentionally added to the formula under the notion that it would boost the protein content. And because melamine is a high-nitrogen compound, and the chief test for protein levels at the time assayed nitrogen content, the (false) assumption of more protein, as well as the fact that it is a cheap chemical, drove that tragic and toxic decision.]

After the infant formula incident and others involving melamine-contaminated pet food, the compound was recognized as a kidney toxicant. Yet melamine is found in many commercial products, including synthetic pesticides and fertilizers, dishware, plastics, flooring, cookware, kitchen counters, and others. Cyanuric acid is used as a swimming pool cleaning solvent, disinfectant, and plastic stabilizer; aromatic amines are found in hair coloring, mascara, tattoo ink, paint, tobacco smoke, and diesel exhaust.

Many of these compounds are also used in industrial applications, such as in rubbers, adhesives, oil refining, synthetic polymers, dyes, perfumes, pharmaceuticals, and explosives. Exposures to melamine, cyanuric acid, and aromatic amines can happen via any of multiple vectors that can be contaminated with these compounds; people encounter them by consuming food, breathing air, ingesting household dust, drinking water, or using products that contain plastics or pigments.

The research team, hailing largely from the University of California San Francisco (UCSF) and Johns Hopkins Bloomberg School of Public Health, measured 45 chemicals associated with cancer and other risks, using methods that can capture chemicals, or even traces of them, in urine samples. The sampling period extended from 2008 to 2020, though the bulk of collection happened from 2017 to 2020. Samples were collected across all three trimesters of pregnancy. The subjects comprised a group of 171 women—from New York, New Hampshire, Puerto Rico, California, Illinois, and Georgia—who are part of the National Institutes of Health's (NIH's) Environmental influences on Child Health Outcomes (ECHO) Program.

Not only are these inequities in exposures and body burdens of concern for the women, but also, the presence of these compounds in their bodies during pregnancy raises further alarm for the babies that come of those pregnancies. Because the mothers have been exposed prenatally, there may be a real risk of subsequent developmental impacts.

These participants were, on average, 29.5 years old, and represented a relatively diverse sample of the population: 20% were Black, 34% were White, 40% were Latina, 4% were Asian, and 3% were from other or multiple demographic groups. The study authors note that this is "the largest U.S. study to date of melamine, melamine derivatives, and aromatic amines in a geographically and demographically diverse population of pregnant women," and that previous research on melamine has focused on pregnant women in Asian countries, or been limited to nonpregnant people in the U.S.

More than 60% of the samples show the presence of 12 of the 45 chemicals for which the study looked; five were detected in nearly every sample. Melamine, cyanuric acid, *and* nine aromatic amines show up in more than half of the study participants. Most chemicals found are associated with higher exposures among Black and Hispanic participants, as compared with non-Hispanic whites. The highest levels of melamine and cyanuric acid are found in women of color and those with greater exposure to tobacco. In another example, the levels of 3,4-dichloroaniline (used in the production of dyes and pesticides) are more than 100% higher among Black and Hispanic women than in white women.

Not only are these inequities in exposures and body burdens of concern for the women, but also, the presence of these compounds in their bodies during pregnancy raises further alarm for the babies that come of those pregnancies. Because the mothers have been exposed prenatally, there may be a real risk of subsequent developmental impacts, both because there is the potential for maternal-fetal transfer of toxic chemicals via the placenta and/or breastmilk, and because children may have particular "windows" of developmental vulnerability to any one (or more) of these chemicals. Some animal studies have pointed, for example, to fetal growth restriction, incomplete bone development, and spatial cognitive impairments following exposures to melamine (or its analogs, ammeline, ammelide, and cyanuric acid). Further peril lies in the possibility, as the study authors say, that there could be "synergistic effects . . . when exposed to both melamine and melamine analogs."

Study co-senior author Jessie Buckley, PhD, associate professor at Johns Hopkins Bloomberg School of Public Health, commented: "It's disconcerting that we continue to find higher levels of many of these harmful chemicals in people of color." Johns Hopkins postdoctoral fellow and study coauthor Giehae Choi said, "Our findings raise concerns for the health of pregnant women and fetuses, since some of these chemicals are known carcinogens and potential developmental toxicants. Regulatory action is clearly needed to limit exposure." And study co-senior author and professor of obstetrics, gynecology, and reproductive medicine (and director of the UCSF Program on Reproductive

Health and the Environment) Tracey J. Woodruff, PhD, added, "These chemicals are of serious concern due to their links to cancer and developmental toxicity, yet they are not routinely monitored in the United States."

The research paper explains, "Our data indicate important differences in exposures by race and ethnicity; evaluating potential sources of exposure that may contribute to these inequities is needed. Our larger follow-up study will allow us to better characterize exposures across the U.S. during a critical period of development and further assess influential predictors and demographic differences that we characterized in this initial study. Finally, our study demonstrates the importance of continuous identification of environmental factors that can play an important role in maternal and child health." It concludes that there is critical and broad need for expanded biomonitoring that can identify sources of exposure disparities by race and/or ethnicity, and evaluate potentially harmful health effects.

Beyond Pesticides spends a good deal of its human capacity sharing information on the very broad and harmful impacts of the use of synthetic pesticides (and other toxic chemical compounds). The research on these compounds is widely appreciated, and yet, Beyond Pesticides has asserted: the state of pesticide regulation, and of research into pesticide impacts, is inadequate and like nothing so much as a game of "whack-a-mole." A single pesticide or class of pesticides is studied, a paper is written, and policymakers and regulators may or may not pay attention. Then another one happens, and another, and another, ad infinitum.

The pattern of "progress" is similar on the regulation side: individual pesticides registered (aka, approved) by the U.S. Environmental Protection Agency (EPA) are reviewed "on the regular but only every 15 years, barring an emergent and urgent concern. Given the cascade of discovery of harmful impacts over the past couple of decades, 15 years has become a very long window in which to allow continued use for lack of review.

When there is an urgent concern, EPA may undertake more timely review, but again, one compound at a time. Even more fundamentally, its approach to regulation, in the face of evidence of harm, is often characterized by tweaking the use of toxic pesticides "at the margins"—requiring a change to the text on a pesticide label, reducing the time frame in which a compound can be used, restricting application to trained applicators, or other piecemeal actions that are generally wholly inadequate to reducing the health and environmental harms of these compounds being unleashed into the environment.

EPA also continues to fall short on multiple research and regulatory fronts: looking carefully at synergistic impacts, multiple exposure vectors, and endocrine disruption effects, among others. In addition, the agency is far too dependent on industry-generated research, influenced by agrochemical industry lobbying, and sometimes, in downright cahoots with industry.

What Beyond Pesticides wrote in 2020 holds: "It is unconscionable to continue tweaking restrictions on pesticides with known hazards and broad uncertainties about the effect of mixtures, synergistic effects, and cumulative risk . . . given the availability of organic systems . . . [to] eliminate those hazards economically and solve the looming environmental threats."

Likewise still relevant is a 2019 Daily News Blog article, in which Beyond Pesticides wrote, "Since Rachel Carson stunned the world and ignited the modern environmental movement with [her groundbreaking book,] Silent Spring [60 years ago this year], pesticide regulation has been stuck in a whack-a-mole approach that targets only the most publicly visible, toxic, and researched chemicals for restrictions. By transitioning to organic, not only in food production, but also in the management of pests in lawns and landscapes, and other pest control practices, we can eliminate the broad range of chemicals linked to diseases that are

Beyond Pesticides spends a good deal of its human capacity sharing information on the impacts of synthetic pesticides. And yet, it has asserted—the state of pesticide regulation, and of research into pesticide impacts, is inadequate and like nothing so much as a game of "whack-a-mole."

all too common in today's world, and truly protect public health, wildlife, and the environment."

What to do: Beyond Pesticides continues work on its mission-to transform the nation's approach to pest management in all sectors (agricultural, residential/structural, and broad land management) by eliminating the current dependency on pesticides and advancing organic regenerative approaches that do not rely on toxic inputs. The subject research adds to the evidence supporting our call to eliminate use of synthetic, fossil-fuel-based pesticides within the next decade. With sufficient public engagement and advocacy, combined with the work of health, environment, and biodiversity organizations, we can put a stop to toxic pesticide exposures and embrace an organic systems approach that is precautionary and protective of all that we hold dear.

SOURCES: Giehae Choi, Jordan R. Kuiper, Deborah H. Bennett, Emily S. Barrett, Theresa M. Bastain, Carrie V. Breton, Sridhar Chinthakindi, Anne L. Dunlop, Shohreh F. Farzan, Julie B. Herbstman, Margaret R. Karagas, Carmen J. Marsit, John D. Meeker, Rachel Morello-Frosch, Thomas G. O'Connor, Edo D. Pellizzari, Megan E. Romano, Sheela Sathyanarayana, Susan Schantz Rebecca J. Schmidt, Deborah J. Watkins, Hongkai Zhu, Kurunthachalam Kannan, Jessie P. Buckley, Tracey J. Woodruff, Exposure to melamine and its derivatives and aromatic amines among pregnant women in the United States: The ECHO Program, Chemosphere, Volume 307, Part 2, 2022, 135599, ISSN 0045-6535, https://doi. org/10.1016/j.chemosphere.2022.135599; AAAS press release



CHILDREN'S HEALTH | KIDNEY CANCER | NOVEMBER 10, 2022 Kids and Kidney Cancer: Implication for Prenatal Pesticide Exposure

meta-analysis by University Alberta Hospital, Edmonton, AB, Canada adds to the plethora of research linking prenatal (before birth/during pregnancy) pesticide exposure to carcinogenic (cancer) tumor development. The analysis, published in Human & Experimental Toxicology, finds parental exposure to pesticides during the preconception (before pregnancy) or pregnancy period increases the risk of Wilms' tumor (a type of kidney cancer) occurrence among children. Already, studies find low levels of pesticide exposure during pregnancy or childhood cause adverse health effects, from metabolic disorders to mental and physical disabilities. Although medical advancements in disease survival are more prominent nowadays, childhood cancer remains the leading cause of death from disease among children. Furthermore, childhood cancer survivors can suffer from chronic or long-term health complications that may be life-threatening.

Children are particularly vulnerable to the impacts of pesticide exposure,

as their developing bodies cannot adequately combat exposure effects. Moreover, a pregnant woman's pesticide exposure can have a stronger association with childhood cancer than a child's exposure. Therefore, it is essential to understand how pesticides impact the health and well-being of individuals during critical developmental periods, especially for latent diseases (e.g., cancers).

The researchers performed a systematic review and meta-analysis on case-control studies to determine a link between pesticide exposure and Wilms' tumor occurrence in children. To establish the connection, researchers used monographs (commentary studies) on specific organophosphate insecticides and herbicides from the International Association for the Research on Cancer (IARC) of the World Health Organization (WHO). Researchers systematically reviewed PUBMED, SCOPUS, and Google Scholar studies (1960–2021) following the Preferred Reporting Items for Systematic reviews and

Meta-Analyses (PRISMA) guidelines.

The report also examines occupational versus residential exposure and before-birth (prenatal) versus after-birth (postnatal) exposure. These results strengthen the finding that parental pesticide exposure before or during pregnancy correlates with increased risk for Wilms' tumor in a child. The IRAC/WHO monographs support this conclusion and policies to stop specific pesticide use to prevent future cases of cancer.

The connection between pesticides and cancer is significant as several studies link pesticide use and residues to the illness (e.g., breast cancer, prostate cancer, lung cancer). Sixty-six percent of all cancers have links to environmental factors, especially in occupations of high chemical use. In addition to links between agricultural practices and pesticide-related illnesses, over 65 percent of commonly used lawn pesticides and 70 percent of commonly used school pesticides have links to cancer. Moreover, a 2021 study finds previous maternal exposure to the chemical compound during pregnancy can increase the risk of breast cancer and cardiometabolic disorders (e.g., heart disease, obesity, diabetes) up to three times in successive generations.

This study reinforces the concept of "critical windows of exposure," which suggests that prenatal and early-life exposure to environmental toxicants increase susceptibility to health impacts. While Wilms' tumor generally afflicts children under ten years of age, other early life exposures can take years and even decades before adverse health effects arise. Although 90 percent of kidney tumors among children are Wilms tumors, co-occurring diseases may arise from weakened immune function. Similar to this study, previous research demonstrates that pregnant mothers' exposure to household cleaners, many of which are pesticides, can increase nephroblastoma (kidney cancer) and brain tumor risk in children. The etiology or cause of childhood cancer involves the interaction of multiple components including lifestyle and genetics. However, emerging evidence indicates that environmental contaminants like pesticides (through occupational exposures, air

pollution, pesticides, solvents, diet, etc.) play a role in disease etiology. Pesticide contamination is widespread in all ecosystems, and chemical compounds can accumulate in human tissues resulting in chronic health effects. The study concludes, "Pesticide exposure in household/residential settings seems to contribute to Wilms' tumor etiology. Additional investigations with an extensive sample size are required to conclude more confidently, probably involving low-/middle-income and high-income countries. This may be considered important in the post-pandemic era. In our opinion, there is some compelling evidence to robustly educate parents and/or guardians more regarding the appropriate use of chemical compounds and take necessary precautions to minimize the potential risks associated with their application."

There is a strong consensus among pediatricians that pregnant mothers and young children should avoid pesticide exposure during critical windows of development. The wide availability of non-pesticidal alternative strategies allows for choices in residential and agricultural management to promote a safe and healthy environment, especially among chemically vulnerable individuals. For instance, buying, growing, and supporting organic land management reduces human and environmental contamination from pesticides. Organic agriculture has many health and environmental benefits, which curtail the need for chemicalintensive agricultural practices. Numerous studies find that pesticide metabolite levels in urine significantly decrease when switching to an all-organic diet.

What to do: For more information on how organic is the right choice for both consumers and the farmworkers who grow our food, see the Beyond Pesticides webpage on the Health Benefits of Organic Agriculture. On hazards posed to children, see the Pesticide-Induced Diseases Database (PIDD) pages on cancer, birth/ fetal defects, and other diseases.

SOURCE: Khan A, Feulefack J, Sergi C. Exposure to pesticides and pediatric Wilms' tumor. A meta-analysis on pre-conception and pregnancy parental exposure with an IARC/ WHO commentary. *Human & Experimental Toxicology*. 2022;41. doi:10.1177/ 09603271221136211

CHILDREN'S HEALTH | EARLY ONSET PUBERTY | DECEMBER 8, 2022 Childhood Pesticide Exposure Associated with Early Onset of Puberty

hildren with higher levels of certain pesticide metabolites are more likely to go through early puberty, according to research published in *Environmental Pollution*. The findings by a team of Spanish researchers speak to a need for greater protections for children from toxic pesticide exposure. Children are much more sensitive to pesticide exposure than adults as they take in greater amounts of toxic substances relative to their body weight and have developing organ systems.

Researchers began their investigation with children, ages 7–11, participating in the Spanish state's environment and childhood multicenter birth cohort study, an ongoing project aimed at under-

Children are much more sensitive to pesticide exposure than adults as they take in greater amounts of toxic substances relative to their body weight and have developing organ systems. standing the effect of environmental exposures on pregnancy, fetal, and childhood development in the country. Out of over 3,000 children enrolled in the project, 1,539 had their urine sampled for the presence of pesticide metabolites. Scientists focused on four insecticides breakdown products a chlorpyrifos metabolite "TCPy," a metabolite of the organophosphate diazinon "IMPy," a general organophosphate metabolite "DETP," the pyrethroid metabolite "3-PB," and a metabolite of ethylene-bis-dithiocarbamate fungicides "ETU." Urinary levels of these



pesticide metabolites were then compared with parental-reported stages of pubertal development. Researchers worked to control for confounders, and did explore the further interaction between pubertal development, chemical exposure, and body mass index.

For girls, urinary concentrations of DETP and ETU above the 75th percentile are associated with a greater chance of pubertal development, with ETU fungicide metabolites specifically resulting in greater development among girls who are underweight or normal weight (with odds ratios averaging a 10x increased risk). For boys, any detection of TCPy influences more rapid genital development than boys without evidence of exposure. 3-PBA and ETU above the 75th percentile in boys is associated with greater development in overweight/ obese and underweight/normal weight children, respectively. Interestingly, DETP was found to be associated with lower odds of pubertal development in overweight/obese boys. "[T]hese findings represent a potential cause of concern, due to the widespread exposure to children in the general population to pesticides and the possibility that altered pubertal timing may increase the risks

"[T]hese findings represent a potential cause of concern, due to the widespread exposure to children in the general population to pesticides and the possibility that altered pubertal timing may increase the risks of behavioral disorders during adolescence and of obesity, cardiovascular disease, and endocrine-related cancers later in life," the authors write.

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This area of research has been developing consistently since the turn of the century. In 2008, a study on the synthetic pyrethroid esfenvalerate found that it delays the onset of puberty in rats at doses as much as two times lower than levels EPA classifies as having no adverse effects. Nearly a decade later, another study on synthetic pyrethroids, this time looking directly at the association between urinary levels and puberty onset, found similar results with the insecticide cypermethrin. Not only did this study find an association, it was able to characterize the effects driving the process. In rodent models, researchers find that cypermethrin is accelerating puberty through hormonal release. Rather than a response from the hypothalamus, which controls the release of pituitary luteinizing (affecting the reproductive system) and follicle-stimulating hormones, scientists find that cypermethrin acts directly on cells within the testis and pituitary glands.

What to do: Encourage schools to serve organic food, and work to eliminate the unnecessary use of toxic pesticides on community lawns and landscapes.

SOURCE: Castiello F, Suárez B, Beneito A, Lopez-Espinosa MJ, Santa-Marina L, Lertxundi A, Tardón A, Riaño-Galán I, Casas M, Vrijheid M, Olea N, Fernández MF, Freire C. Childhood exposure to non-persistent pesticides and pubertal development in Spanish girls and boys: Evidence from the INMA (Environment and Childhood) cohort. Environ Pollut. 2023 Jan 1;316 (Pt 2):120571. DOI: 10.1016/j.envpol.2022. 120571.

CHILDREN'S HEALTH | AUTISM | DECEMBER 20, 2022 Mother and Child Health: Learning Disorders and Prenatal Pesticide Exposure Study Results Released

meta-analysis published in Chemosphere finds prenatal pesticide exposure, or pesticide exposure during pregnancy has a positive association with autism spectrum disorder (ASD) and attention deficit/hyperactive disorder (ADHD). Particularly, exposure to the organophosphate (OP) and pyrethroid (PYR) insecticides, in addition to the mother's age during preanancy (\geq 30 years old), increased the risk factor of ASD. ADHD risk increases among offspring whose mothers encountered organochlorine pesticides (OCPs) during gestation. The etiology or cause of ASD and ADHD involves the interaction of multiple components, including lifestyle and genetics. However, emerging evidence indicates that environmental contaminants like pesticides play a role in disease etiology.

While it is a complex disease, and genetics may play a role, no specific genes have been identified, and there is increasing evidence that environmental factors like pesticide exposure facilitate the development of the condition. ADHD is estimated to affect 8-12% of schoolage children worldwide. The U.S. Centers for Disease Control and Prevention (CDC) estimates that 1 in 54 children have been diagnosed with an autism spectrum disorder. Rates of autism have skyrocketed over the last several decades. While some of the rise is due to the increase in testing, and an expansion of the diagnostic criteria for the disorder, this cannot entirely account for the increase in ASD cases. In 1997, 0.1% of children had autism, while in 2010, that number rose to 1%. Considering several studies associate early-life exposure to toxic chemicals with adverse birth/health effects, additional exposure through maternal contamination poses an even greater risk to children's health. The report notes, "The findings indicate that maternal pesticide exposure should be avoided, especially for older pregnant women in agricultural areas, to

protect early brain development in offspring."

Beyond Pesticides has covered a variety of pregnancy risks from pesticides and other toxic chemicals, including these in just the last three years: pesticides and children's sleep disorders; prenatal exposures to a multitude of chemicals; insecticides and childhood leukemia; and, insecticides and Attention Deficit/Hyperactivity Disorder.

The analysis reviews documents from five databases (i.e., *PubMed*, *Embase, Web of Science, Medline, PsycINFO*) related to pesticide exposure during pregnancy and ASD and ADHD in children. Factors considered for ASD and ADHD risk include pesticide type, window of exposure, and mother's age. The review identifies, 949 studies, but opted to use the 19 studies with more robust information. There were 11 studies on ASD, seven studies on ADHD, and one study on both disorders. The analysis confirms that a mother's



exposure to pesticides increases offspring's risk of ASD and ADHD.

Pesticide exposure during pregnancy is of specific concern as health effects for all life stages can be long-lasting. Just as nutrients are transferable between mother and fetus, so are chemical contaminants. Studies find pesticide compounds present in the mother's blood can transfer to the fetus via the umbilical cord. Therefore, pesticide exposure during pregnancy has implications for both the mother and child's health. Many studies indicate prenatal and early-life exposure to environmental toxicants increases susceptibility to disease. A 2020 study finds the first few weeks of pregnancy are the most vulnerable periods during which prenatal exposure to pesticides can increase the risk of the rare fetal disorder holoprosencephaly. This disorder prevents the embryonic forebrain from developing into two separate hemispheres. Moreover, women living near agricultural areas experience higher exposure rates that increase the risk of birthing a baby with abnormalities, including cancers like acute lymphoblastic leukemia.

This determination, and the present study's findings, are supported by previous scientific literature. Similar to this study, a range of research demonstrates that pregnant mothers' exposure to specific pesticides has links to autism, evidenced by laboratory and epidemiological research. Scientific studies have consistently found elevated rates of ASD in areas of high pesticide use. A 2014 study from the University of California, Davis, found that pregnant women living near crops sprayed with organophosphates, like the insecticide chlorpyrifos, increases the chance of their child being diagnosed with ASD by 60%. For women in their second trimester, chlorpyrifos increases ASD odds by 3.3x. Synthetic pyrethroids increased autism risk by 87 percent. Like the aforementioned insecticides, fungicides also have links to autism disorders. A separate study from California researchers connects autism to the herbicide glyphosate, the bannedfor-residential-use insecticide diazinon, the fumigant methyl bromide, and fungicide myclobutanil. Moreover, studies find that higher rates of ADHD have associations with direct exposure in children and pyrethroid metabolites found in children's urine. The Cincinnati Children's Hospital Medical Center found a strong association between urinary pyrethroid concentrations and ADHD, primarily in boys. Any concentrations found above the level of detection corresponded to a three-fold increase in the chance of developing ADHD when compared to boys without detectable levels. Another study from Rutgers University found that, of over 2,000 children who had ever received an ADHD diagnosis, children with

higher urinary pyrethroid metabolite levels were more than twice as likely to be diagnosed with ADHD. The connection between pesticide exposure and learning/developmental disorders has much research. Although more research is needed to further define the connection, there is enough evidence to warrant a precautionary approach and restrictions on hazardous ASD and ADHD-linked pesticides. The study concludes, "Our findings contribute to our understanding of health risks related to maternal pesticide exposure and indicate that the in-utero developmental period is a vulnerable window-of-susceptibility for ASD and ADHD risk in offspring. These findings should guide policies that limit maternal exposure to pesticides, especially for pregnant women living in agricultural areas."

What to do: For more information on how organic is the right choice for both consumers and the farmworkers that grow our food, see the Beyond Pesticides webpage on the Health Benefits of Organic Agriculture.

SOURCE: Yifan Xu, Xu Yang, Danrong Chen, Yadan Xu, Linchen Lan, Shuangshuang Zhao, Qianqi Liu, Antoine M. Snijders, Yankai Xia, Maternal exposure to pesticides and autism or attention-deficit/hyperactivity disorders in offspring: A meta-analysis, Chemosphere, Volume 313, 2023, 137459, ISSN 0045-6535, https://doi.org/10.1016/j.chemosphere. 2022.137459.

GUT MICROBIOME | DISINFECTANT/ANTIMICROBIAL AND INFLAMMATORY BOWEL DISEASE | JANUARY 25, 2022 Common Antimicrobial Pesticides Linked to Altered Gut Microbe Function

Research at the University of North Carolina at Chapel Hill identifies how triclosan (TCS), an antimicrobial agent used in many household products, impacts the microbial communities in the gut, causing inflammation. According to the study published in *Nature Communications*, triclosan worsens the effects of ulcerative colitis, an inflammatory bowel disease (IBD),

through the retention of harmful bacteria. Ample evidence demonstrates environmental contaminants, including pesticides like triclosan, negatively affect microbes in the human mouth and gut. Although studies show how triclosan exposure affects human health, more research is now questioning how exposure to these toxic chemical influences gut health. Therefore, studies like these highlight the importance of evaluating how chemical contaminant deregulates normal bodily function through microbiome changes. Furthermore, the study has significant implications for considerations that should be, but are not currently, a part of pesticide review and registration by the U.S. Environmental Protection Agency (EPA). The researchers note, "Together, our results define a



mechanism by which intestinal microbes contribute to the metabolic activation and gut toxicity of TCS, and highlight the importance of considering the contributions of the gut microbiota in evaluating the toxic potential of environmental chemicals."

Instances of intestinal bowel disease (IBD) — involving the chronic inflammation of intestinal tissues-incidences and prevalence are readily increasing. As many as 3 million U.S. adults suffer from some form of IBD, with the year 1999 representing a 50 percent increase in disease cases. Disease symptoms include stomach pain, diarrhea, rectal bleeding, and an increased risk of developing colorectal cancer. IBD has no cure, and current treatments can have severe side effects. Although the study notes environmental chemical exposure has links to IBD prevalence, the researchers aim to uncover the mechanisms driving gut microbe disruption.

University researchers sought to identify the molecular mechanisms involved in triclosan's toxic effects on the gut. The scientists employed in vitro (artificial environmental), ex vivo (outside the organism), and in vivo (inside the organism) analyses on microbial communities in the gut of mice. Specifically, researchers investigated specific bacterial enzymes involved in triggering triclosan toxicity through metabolization. The study results find that microbial β -glucu-ronidase (GUS enzymes are responsible for metabolically activating triclosan within the colon, driving gut toxicity. Conversely, inhibition of this bacterial enzyme decreases the gut inflammatory effects of triclosan, thus showcasing the impact specific microbes play in chemical toxicity.

Gut microbiota plays a crucial role in lifelong digestion, immune, and central nervous system regulation, as well as other bodily functions. Through the gut biome, pesticide exposure can enhance or exacerbate the adverse effects of additional environmental toxicants on the body. Since the gut microbiome shapes metabolism, it can mediate some toxic effects of environmental chemicals. However, with prolonged exposure to various environmental contaminants, critical chemical-induced changes may occur in the gut microbes, influencing adverse health outcomes. Over 300 chemical contaminants and their byproducts are common in human blood and urine samples. Most chemical contamination affecting the gut comes from a diet reliant on conventional,

pesticide-laden, highly processed foods. In a 2020 study, researchers associated developmental defects, diabetes, cardiovascular disease, liver disease, obesity, thyroid disorders, and improper immune operation with changes to the gut after exposure to environmental contaminants. Despite the growing body of work linking gut bacteria to overall health, pesticide regulators generally overlook the concept. Therefore, regulators must consider the emerging science on the dangers of pesticides beyond the mortality of humans, animals, and plants to include overall health and fitness.

A bioinformatics tool developed by researchers from the University of Turku in Finland indicates that "54% of species in the core human gut microbiome are sensitive to glyphosate." (See Daily News.) Published in the Journal of Hazardous Materials, the researchers' paper states, "The widespread use of glyphosate may have a strong effect on gut microbiomes as well as on human health." Bats foraging in chemicalintensive banana plantations have much less gut diversity than bats foraging in organic banana fields and natural forestland, finds research published this month in the journal Frontiers in Ecology and Evolution. (See Daily News.)

Triclosan is an antimicrobial agent in products regulated by EPA and FDA. However, cumulative exposure to triclosan registered by both agencies poses unacceptable risks to human health and the environment. Many studies identify the various health and environmental effects of triclosan as the chemical absorbs through organs, from the skin to the gastrointestinal tract, and are environmentally persistent. Several independent, peer-reviewed research studies have identified triclosan as an endocrine-disrupting chemical. On top of its endocrine-disrupting effects, recent work shows that triclosan is a possible human carcinogen. Similar to this study, a 2016 peer-reviewed study published in the Annual Review of Pharmacology and Toxicology found that triclosan promotes cancer cell development in mice through pathways shared with humans. Furthermore, like many antimicrobial and antibacterial products, triclosan use increases the persistence of antibiotic-resistant bacteria, a severe public health concern for disease risk. Despite these findings, EPA's evaluation of triclosan fails to address one of the most concerning aspects of its chemical activity concerning human and environmental health.

While people who use triclosan products daily have higher concentrations in their bodies, consumers who do not use triclosan can still encounter the chemical through food, water, and dust. Although FDA banned triclosan from soap products in 2016, other personal care products still contain the chemical. These products include toothpaste, mouthwash, hand sanitizers, cosmetics, and antibacterial/antimicrobial clothing. However, EPA and FDA evaluate different use of triclosan, with EPA responsible for assessing the chemical in various consumer products, marketed as "microban." Therefore, individuals may encounter multiple sources of triclosan, especially on consumer products, such as toothbrush bristles, that tend to accumulate the chemical.

To improve and sustain gut microbiome health, the use of toxic pesticides is problematic. Although EPA denied a petition by Beyond Pesticides and Food and Water Watch to remove remaining triclosan uses in 2015, this study adds to growing evidence demonstrating the danger of this chemical. The data suggests that adequate public health protection requires EPA and FDA to work together to eliminate health risks from ongoing exposure to triclosan. What to do: Beyond Pesticides holds that safer alternatives are available, and organic practices can protect public health and the environment. In addition to positive impacts on the human microbiome, organically grown food (i.e., milk, meat, strawberries, tomatoes, and a range of other foods) contain a much more diverse bacterial community than their conventional counterparts. Moreover, emphasis on converting to regenerative-organic systems and using least-toxic pest control to mitigate harmful exposure to pesticides, restore soil health, and reduce carbon emissions, should be the main focus. Learn more about soil and gut microbiota and its importance via Beyond Pesticide's journal article Sustaining Life: From soil microbiota to gut microbiome. For a complete history of the regulation of triclosan, see Beyond Pesticides' triclosan timeline and webpage on triclosan.

SOURCE: Zhang, J., Walker, M.E., Sanidad, K.Z. *et al.* Microbial enzymes induce colitis by reactivating triclosan in the mouse gastrointestinal tract. *Nat Commun* 13, 136 (2022). https://doi.org/10.1038/s41467-021-27762-y; Science Daily

GUT MICROBIOME | METABOLIC DISTRESS | MAY 12, 2022 Environmental Pesticide Exposure Alters Gut Microbes, Increasing Urgency for Organic Transition

Report published in *Environmental Health* finds that exposure to environmentally relevant concentrations of pesticides can alter gut microbial communities, as demonstrated through fecal samples. Over 300 environmental contaminants and their byproducts, including pesticides, are chemicals commonly present in human blood and urine samples. Ample evidence demonstrates that environmental contaminants, including pesticides, negatively affect the human mouth and

gut microbes. However, fecal samples provide an accurate representation of the microbial community existing in the gut. These toxicants can alter hormone metabolism, which adversely affects health outcomes. Adverse health effects of environmental contaminants include reproductive and developmental defects, diabetes, cardiovascular disease, liver disease, obesity, thyroid disorders, and improper immune operation. Although studies show how chemical exposures affect human health, more research is now questioning how these toxic chemicals influence gut health. Therefore, studies like these highlight the importance of evaluating how chemical contaminants deregulate normal bodily function through microbiome changes. The report notes, "Our results highlight the need for future dietary intervention studies to understand effects of pesticide exposure on the gut microbiome and possible health consequences."

Researchers examined dietary exposure to 186 common pesticide residues



in the fecal excrement to determine impacts on the microbiome among 65 twins in the United Kingdom. Gut microbiota composition has associations with dietary habits, different life stages, geographical location, exercise, antibiotics, and disease states. However, researchers investigated if these associations can also impact concentrations of pesticide residues in excrement to indicate gut health alterations. Using metagenomics and metabolomics, researchers measured the metabolic activity of microbes in fecal matter and pesticides in urine excretion to note any bodily changes.

The report finds all urine samples contain pyrethroid or organophosphate insecticide residues, with 53 percent of urine samples containing glyphosate. Individuals who consume more fruits and vegetables grown with chemicalintensive practices have higher concentrations of organophosphate residues. Although urinary metabolite (pesticide breakdown product) excretion lacks a correlation with gut microbial changes, there are 34 associations between the concentration of pesticide residues and metabolite residues in fecal matter and gut health. Glyphosate excretion in the fecal matter correlates with an increase

in bacterial species richness, fatty acid metabolites, and phosphate concentrations in the gut. For pyrethroids, deltamethrin metabolite, Br2CA, has a positive association with phytoestrogens enterodiol (dietary estrogen) and negative associations with specific amino acids in the gut.

The gut microbiome is a group of microorganisms, including bacteria, archaea, viruses, and fungi, that plays a crucial role in digestion, bodily function, detoxification, and immune and central nervous system regulation. Through the gut biome, pesticide exposure can enhance or exacerbate the adverse effects of additional environmental toxicants on the body. Since the gut microbiome shapes metabolism, it can mediate some toxic effects of environmental chemicals. However, with prolonged exposure to various environmental contaminants, critical chemicalinduced changes may occur in the gut microbes, influencing adverse health outcomes. Like aut microbes, soil microbes are essential for the functionality of the soil ecosystem. Toxic chemicals damage the soil microbiota by decreasing and altering microbial biomass and soil microbiome composition (diversity). Pesticide use contaminates soil and

results in a bacteria-dominant ecosystem causing "vacant ecological niches, so organisms that were rare become abundant and vice versa." The bacteria outcompete beneficial fungi, which improves soil productivity and increases carbon sequestration capacity. The resulting soil ecosystem is unhealthy and imbalanced, with a reduction in the natural cycling of nutrients and resilience. Thus, plants grown in such conditions are more vulnerable to parasites and pathogens. Moreover, the effects of climate change only exacerbate threats to soil health as studies show a link between global climate change and a high loss of microbial organisms in the soil ecosystem.

The findings add to the growing quantity of environmental studies linking pesticide exposure to metabolic distress and the respective health consequences. Although previous studies suggest pesticide exposure in the environment disrupts the gut microbiome, this report is the first to find an association between pesticide excretion and exposure to environmentally relevant concentrations of pesticides. Although most pesticide exposure decreases microbial species richness, some chemicals, like glyphosate, increase bacterial species richness. However, an increase in species richness is not always positive as it cannot measure the function of how these bacteria work together. Studies find functional diversity declines faster with agricultural intensification then species richness. Functional diversity involves the interaction of species based on similarity in behavioral, morphological, physiological, or resource use as it relates more strongly to ecosystem function. Moreover, an increase in species richness in the gut microbiome can allow more resilient bacteria to flourish and outcompete other beneficial bacteria regardless of pathogenic potential. For instance, glyphosate kills bacterial species beneficial to humans and incorporated in probiotics, yet allows harmful bacteria to persist, leading to resistance. Similarly, glyphosateexposed soils contain a greater abundance of genes associated with antibiotic resistance and a higher number of inter-species transferable genetic material.

Antibiotic resistance can trigger longer-lasting infections, higher medical expenses, the need for more expensive or hazardous medications, and the inability to treat life-threatening illnesses. Nevertheless, studies show an organic diet lowers individual exposure to pesticides, demonstrating a significant reduction in bodily pesticide concentration. Organic can also protect human gut microbe health by reducing the number of toxic chemicals within the body.

The report concludes, "We found that individuals who are regularly consuming organic products had higher healthy eating index values, but that other lifestyle choices are, in all likelihood, also contributing factors. We provide the first evidence of an association between pesticide excretion and changes in gut microbiome metabolism at environmental levels of exposure in the UK population. Our findings highlight the need for future dietary interventional studies to understand the impact of pesticide exposure on gut microbiome composition and function and its health implications."

What to do: To improve and sustain microbial communities, and thus human, animal, and environmental health, toxic pesticide use must stop. Beyond Pesticides challenges the registration of toxic chemicals due to their impacts on soil, air, water, and our health. Beyond Pesticides holds that safer alternatives are available, and organic practices can protect public health and the environment. In addition to positive impacts on the human microbiome, organically grown food (i.e., milk, meat, strawberries, tomatoes, and a range of other foods) contain a much more diverse bacterial community than their conventional counterparts.

SOURCES: Mesnage, R., Bowyer, R.C.E., El Balkhi, S. *et al.* Impacts of dietary exposure to pesticides on faecal microbiome metabolism in adult twins. *Environ Health* **21**, 46 (2022). https://doi.org/10.1186/s12940-022-00860-0.

PARKINSON'S DISEASE | MAY 26, 2022 Neurotoxic Pesticides Disrupt Gut Function Linked to Parkinson's Disease Development

study published in The International Journal of Biochemistry & Cell Biology finds environmental exposure to neurotoxic pesticides increases Parkinson's Disease (PD) risk through gastrointestinal (GI) disruption. Research finds exposure to chemical toxicants, like pesticides, can cause neurotoxic effects or exacerbate preexisting chemical damage to the nervous system. Although the mechanism by which pesticides induce disease development remains unclear, this study suggests environmental pesticide exposure disrupts GI cells responsible for supporting the autonomic nervous system, enteric glial cells (EGCs). These cells are GI cells that play a critical role in the functional

changes that accompany GI dysfunction, as this dysfunction is one of the earliest symptoms indicating the onset of PD.

Parkinson's disease is the second most common neurodegenerative disease, with at least one million Americans living with PD and about 50,000 new diagnoses each year. The disease affects 50% more men than women, and individuals with PD have a variety of symptoms, including loss of muscle control and trembling, anxiety and depression, constipation and urinary difficulties, dementia, and sleep disturbances. Identifying early biomarkers of PD, such as pesticide-mediated toxicity on GI cells, is crucially important as symptoms intensify over time, with no current cure for this fatal disease. While only 10 to 15 percent of PD incidents are genetic, PD is quickly becoming the fastest-growing brain disease due to nongenetic factors. Therefore, research like this highlights the need to examine alternate risk factors for disease development, especially if disease triggers are overwhelmingly nonhereditary. The study notes, "Overall, our study demonstrates that mitochondrial dysfunction in EGCs can induce autophagic dysregulation and a proinflammatory response, thereby affecting gut motility."

The researchers investigated how EGCs respond to environmental pesticide exposure using cellular and animal



models to understand the mechanisms driving gastrointestinal abnormalities. The pesticides implicated in the study include rotenone and tebufenpyrad. Both pesticides induce cell death via mitochondrial dysfunction among neurotransmitters that release, activate, or involve dopamine, also known as dopaminergic cell damage. Mitochondrial stress impairs molecular gradient function in EGCs, increasing inflammation of these cells consistent with GI cellular inflammation from neurotoxic pesticide exposure. Pesticide-induced mitochondrial dysfunction adversely affects smooth muscle motion and kinetic energy of the enteric nervous system (ENS) in the GI tract.

The gut, also known as the "second brain," share similar structural and chemical parallels to the brain. The microbiota in the gut plays a crucial role in lifelong digestion, immune and central nervous system regulation, as well as other bodily functions. Through the gut biome, pesticide exposure can enhance or exacerbate the adverse effects of additional environmental toxicants on the body. Since the gut microbiome shapes metabolism, it can mediate some toxic effects of environParkinson's disease is the second most common neurodegenerative disease, with at least one million Americans living with PD and about 50,000 new diagnoses each year.

mental chemicals. However, with prolonged exposure to various environmental contaminants, critical chemicalinduced changes may occur in the gut microbes, influencing adverse health outcomes. The impacts of pesticides on the human gut microbiome represent another pesticide assault on human health. Because the biome harbors between 10 and 100 trillion symbiotic microbes, pesticide exposure has effects on some of those bacteria. The human gastrointestinal tract and its digestive processes (aka, the "gut") mediate the function of several systems. Dysfunction of the gut microbiome is associated with a host of diseases, including cardiovascular disease, some cancers, multiple sclerosis, diabetes, asthma, Crohn's

disease, Parkinson's disease, and inflammatory bowel disease, as well as allergies, autism, depression, obesity, and other disorders or syndromes.

Parkinson's disease occurs when there is damage to the dopamineraic nerve cells (i.e., those activated by or sensitive to dopamine) in the brain responsible for dopamine production, one of the primary neurotransmitters mediating motor function. Although the cause of dopaminergic cell damage remains unknown, evidence suggests that pesticide exposure, especially chronic exposure, may be the culprit. Several studies identify various pesticides involved in the pathology of PD, including insecticides, rotenone and chlorpyrifos, and herbicides 2,4-D, glyphosate, and paraguat. The scientific literature comprehensively documents the neurotoxic properties of paraquat and rotenone as laboratory experiments reproduce features of Parkinson's in the brain of animals. A Washington State University study determined that residents living near areas treated with glyphosate-the most widely used herbicides in the U.S. - are one-third more likely to die prematurely from Parkinson's disease. In the Louisiana State University

study, exposure to 2,4-D, chlorpyrifos, and paraquat from pasture land, forestry, or woodland operations are prominent risk factors for PD, with the highest risk in areas where chemicals quickly percolate into drinking water sources. Overall, research finds exposure to pesticides increases the risk of developing PD from 33 percent to 80 percent, with some pesticides prompting a higher risk than others. Another study finds a 2.5-fold increase in PD risk among users of each chemical compared to non-users.

Occupational pesticide exposure poses a unique risk through direct handling and application. A 2017 study finds that occupational use of pesticides (i.e., fungicides, herbicides, or insecticides) increases PD risk by 110 to 211 percent. Even more concerning is that some personal protection equipment (PPE) may not adequately protect workers from chemical exposure during application. However, indirect nonoccupational exposure to pesticides can also increase the risk of PD. For instance, 90 percent of Americans have at least one pesticide compound in their body, primarily stemming from dietary exposure, like food and drinking water. These compounds have a global distribution, with evaporation and precipitation facilitating long-range atmospheric transport, deposition, and bioaccumulation of hazardous chemicals in the environment. Thus, exposure to these toxicants can cause several adverse environmental and biological health effects. With the increasing ubiquity of pesticides, current measures safeguarding against pesticide use must adequately detect and assess total chemical contaminants.

This study is the first to demonstrate that exposure to environmental neurotoxic pesticides impairs mitochondrial transformation of energy in living organisms, causing inflammation in EGCs. The mitochondrial dysfunction and inflammatory events induce gut dysfunction. Mitochondrial dysfunction is a significant aspect of PD pathology. Research demonstrates acute and chronic exposure to pesticides, like rotenone, organophosphates, and organochlorines, can inhibit the mitochondrial brain function responsible for cell regeneration and induce oxidative stress. Although many countries, including Europe and Canada, ban the use of chemicals like rotenone and organochlorines due to concerns about links to Parkinson's, among other illnesses, the U.S. merely restricts use as the U.S. Environmental Protection Agency (EPA) permits the use of rotenone to kill invasive fish species. Considering research demonstrates that a multitude of pesticides presenting a risk of developing PD belong to various pesticide classes and have a differing mode of action, advocates say that government officials must evaluate all health effects related to chemical exposure equally regardless of chemical composition. The study concludes, "Our findings have major implications in understanding the GI-related pathogenesis and progression of environmentally linked PD."

"Our findings have major implications in understanding the GI-related pathogenesis and progression of environmentally linked PD"... implicating pesticide's involvment in Parkinson's disease development.

This study adds to the large body of scientific studies strongly implicating pesticide's involvement in Parkinson's disease development. However, indirect health effects from pesticide exposure are not a new phenomenon as pesticide exposure can cause severe human health (i.e., endocrine disruption, cancer, reproductive/birth problems, neurotoxicity, loss of biodiversity, etc.) and wildlife and biodiversity issues, even at low residue levels. Although the exact cause of PD remains unknown, studies continuously identify exposure to pesticides and specific gene-pesticide interactions as significant adverse risk factors. Environmental triggers like occupational

exposure to pesticides can prompt PD in individuals with or without the genetic precursor. PD can develop regardless of whether an individual is a carrier of the PD gene mutation. Pesticides themselves can possess the ability to disrupt neurological function. Therefore, the impacts of pesticides on the nervous system, including the brain, are hazardous, especially for chronically exposed individuals (e.g., farmworkers) or during critical windows of vulnerability and development (e.g., childhood, pregnancy). Considering that health officials expect Parkinson's disease diagnosis to double over the next 20 years, it is essential to mitigate preventable exposure to disease-inducing pesticides. For more information on the effects of pesticide exposure on neurological health, see Beyond Pesticides' Pesticide-Induced Diseases Database pages on Parkinson's disease, dementia-like diseases, such as Alzheimer's, and other impacts on cognitive function.

What to do: Parkinson's disease may have no cure, but prevention practices like organics can eliminate exposure to toxic PD-inducing pesticides. Organic agriculture represents a safer, healthier approach to crop production that does not necessitate toxic pesticide use. Beyond Pesticides encourages farmers to embrace regenerative, organic practices. Those impacted by pesticide drift can refer to Beyond Pesticides' What To Do in a Pesticide Emergency. Furthermore, see Beyond Pesticides' Parkinson's Disease article from the Spring 2008 issue of Pesticides and You.

Source: Bharathi N. Palanisamy, Souvarish Sarkar, Emir Malovic, Manikandan Samidurai, Adhithiya Charli, Gary Zenitsky, Huajun Jin, Vellareddy Anantharam, Arthi Kanthasamy, Anumantha G. Kanthasamy, Environmental neurotoxic pesticide exposure induces gut inflammation and enteric neuronal degeneration by impairing enteric glial mitochondrial function in pesticide models of Parkinson's disease: Potential relevance to gut-brain axis inflammation in Parkinson's disease pathogenesis, The International Journal of Biochemistry & Cell Biology, Volume 147, 2022, 106225, ISSN 1357-2725, https://doi.org/10.1016/ j.biocel.2022.106225.



FARM EXPOSURE AND EFFECTS | FEBRUARY 10, 2022 Higher Disease Prevalence Among Farmers Highlights Need for Organic Practices and Compatible Materials

National Institute of Environmental Health Sciences (NIEHS)-funded study finds that patterns of pesticide exposure among farmers have geographical and temporal significance. Specific use of and exposure to organophosphate and carbamate chemicals decrease enzyme activity within the body, resulting in greater health anomalies among farmers, especially during agricultural seasons. The use of xenobiotic (foreign chemical compounds) substances like pesticides and fertilizers in agriculture are increasing. Thus, those working with and around these toxicants must have protection. Considering that agricultural workers often experience pesticide exposure at higher rates due to occupation, longterm research must identify potential health concerns surrounding common pesticides. The study author, Dana Barr, Ph.D., states, "The majority of farmers in this study reported that they had at least one health symptom associated with

pesticide intoxication. This investigation can be used to promote safer use of pesticides among farmers and mitigate exposure among residents living near a rice field. The findings will be critical for establishing and launching several preventive programs in the future."

Researchers evaluated the health effects of pesticide exposure among

The agricultural industry has a long-standing history of synthetic chemical use, which disproportionally affects farmworkers' health. Farmworkers and persons exposed to high levels of pesticides have an increased risk of developing brain tumors and over 45 different cancers. a cohort of farmers in Thailand during inactive and active rice farming periods. Using geographic information system (GIS) mapping, researchers compared acetyl- and butyryl-cholinesterase (AChE and BuChE) activities (a family of enzymes responsible for neurotransmission) among farmers across regions within the Ratchasima Province of Thailand. Scientists also collected data on the location of rice paddy fields. The results demonstrate that farmers exhibit higher adverse health symptoms from pesticide exposure during active farming periods. The main pesticides of concern are organophosphates and carbamates, due to the effects on enzyme function, as both AChE and BuChE activity decrease during active farming. Moreover, GIS mapping data shows enzyme inhibition within and adjacent to farms, indicating spatial and temporal changes in health.

The agricultural industry has a longstanding history of synthetic chemical

use, which disproportionally affects farmworkers' health. The journal Occupational and Environmental Medicine indicates that farmworkers and persons exposed to high levels of pesticides have an increased risk of developing brain tumors and over 45 different cancers. Farmworkers are at the highest risk of pesticide-induced diseases, and their average life expectancy bears this out. According to the National Farm Worker Ministry, farmworkers have an average life span of 49 years, a 29 year difference from the general U.S. population. Moreover, a recent study finds increased COPD for other pesticideintensive occupations like landscapers (e.g., gardeners/landscapers). Although pesticide exposure through the skin or inhalation is most prevalent among individuals working around these toxic chemicals, pesticide exposure is ubiquitous and not only confined to a field. The general population can encounter toxic chemicals through residues in food and water or through chemical drift.

Over 300 environmental contaminants and their byproducts-from chemicals in plastics to cosmetic/personal care products-are commonly found in water bodies, food commodities, and human blood/urine samples. These toxicants can alter hormone metabolism, producing endocrine-disrupting effects that put the health of animals, humans, and the environment at risk. Synthetic chemicals in pesticides can accumulate in bodies, causing an amalgamation of health effects. These effects can range from heightened risks of various cancers (i.e., prostate, hepatic, liver, etc.) and endocrine disruption to mental health problems (i.e., depression), respiratory illnesses (asthma), and many other pesticide-induced diseases. Therefore, understanding how pesticide exposure influences disease risk is essential in protecting the future of human, animal, and ecological health.

This study adds to the growing body of research demonstrating occupational exposure to pesticides contributes to Over 300 environmental contaminants and their byproducts—from chemicals in plastics to cosmetic/personal care products—are commonly found in water bodies, food commodities, and human blood/urine samples. These toxicants can alter hormone metabolism, producing endocrine-disrupting effects that put the health of animals, humans, and the environment at risk.

higher disease prevalence among individuals working with and around these toxic compounds. Like this study, other research demonstrates that exposure to organophosphate insecticides, like chlorpyrifos, has endocrine disruption properties that induce neurotoxicity via acetylcholinesterase (AChE) inhibition in the nervous tissue. Inhibition of AChE can cause a buildup of acetylcholine (a chemical neurotransmitter responsible for brain and muscle function). This chemical buildup can lead to acute impacts, such as uncontrolled, rapid twitching muscles, paralyzed breathing, convulsions, and, in extreme cases, death. However, the inhibition of AChE is non-specific, making the dispersal of pesticides with this biological activity a severe threat to wildlife and public health.

Although resistance to banning pesticides is tied to crop yields, studies as recent as 2022 show a ban on even the most extensively used pesticides have no adverse impacts on yield. Although this study takes place in Thailand, the results apply to chemical-intensive farmers across the globe. Adverse health effects related to pesticide exposure can occur regardless of geographical location and agricultural practices. For instance, cancer incidents are consistent among women and men agricultural workers, regardless of location, suggesting an underlying common risk factor (i.e., pesticides). Although farmers in the study use personal protective equipment (PPE), the equipment does not always protect against dermal exposure and inhalation after application (i.e., residues on clothing, shoes, hair, etc.). Moreover, current legislation fails to encompass the full impacts of pesticides on farmworkers, especially underrepresented individuals who disproportionately experience more severe health issues.

The study concludes, "[F]armers should be made aware of the safety practices of pesticide handling and application and the proper use of PPE through effective education and training programs. Importantly, the government should consider changing the current policy to allow effective restrictions of pesticide importation, production, and application. In addition, GIS can assist the assessment of agricultural pesticide exposure in the general population and can enable the location verification and pattern visualization of the OP and carbamate poisoning cases. Our work can be used to assist the establishment of a pesticide application free zone to minimize pesticide exposures in the residential areas."

What to do: One way to reduce human and environmental contamination from pesticides is to buy, grow, and support organic. See Beyond Pesticides' webpage, Health Benefits of Organic Agriculture. Learn more about farmworker protection by visiting Beyond Pesticides' Agricultural Justice page.

SOURCE: Sombatsawat E, Barr DB, Panuwet P, Robson MG, Siriwong W. Pesticide toxicity assessment and geographic information system (GIS) application in small-scale rice farming operations, Thailand. Sci Rep. 2022 Jan 11;12(1):499. doi: 10.1038/s41598-021-04523-x.



EPA Overlooks Glyphosate and Roundup Ingredients' Cancer, DNA Damage, and Multigenerational Effects

Given the study published in the study publis

Glyphosate is the most commonly used active ingredient worldwide, appearing in many herbicide formulas, not just Bayer's (formerly Monsanto) Roundup[®]. The use of this chemical has been increasing since the inception of crops genetically modified to tolerate glyphosate over two decades ago. The toxic herbicide readily contaminates the ecosystem with residues pervasive in food and water commodities. In addition to this study, literature proves time and time again that glyphosate has an association with cancer development, as well as human, biotic, and ecosystem harm.

Study lead author Michael Antoniou, Ph.D., cautions, "Our results are the first to simultaneously show glyphosate and Roundup toxicity in a whole mammalian animal model system and provide a mechanism-oxidative stress-by which DNA damage has been observed in other systems, such as mammalian tissue culture cells. These findings show that glyphosate and Roundup score positive in various tests of carcinogenicitytranscriptome/epigenome/miRNA changes, oxidative stress, protein misfolding, and DNA damage-in a living animal (rat) that is accepted as a surrogate for human health effects. In my view, this strengthens the argument that exposure to Roundup herbicides can lead to the type of cancer suffered by

Glyphosate is the most commonly used active ingredient worldwide, appearing in many herbicide formulas, not just Bayer's (formerly Monsanto) Roundup[®]. The use of this chemical has been increasing since the inception of crops genetically modified to tolerate glyphosate over two decades ago.

the plaintiffs in many of the court cases —non-Hodgkin lymphoma."

This study represents a follow-up that builds on the finding of a previous one by the same authors. The previous study compared the effects of MON 5227 (an active ingredient in Roundup) and glyphosate alone in rats and found both ingredients to cause gut microbiome disruption and oxidative stress related to possible liver damage. Thus, the present study intends to determine damage in the liver by analyzing tissue samples. Following standard regulatory testing for pesticide approval, researchers investigated biochemical changes in the blood of the kidneys and liver after exposure to glyphosate and four active ingredients in Roundup formulas: MON 52276 (European Union), MON 76473 (United Kingdom), and MON 76207 (United States). Additionally, researchers performed tests not carried out by standard testing, including observation on molecular changes in the biological function of gene expression and epigenetics (e.g., DNA methylation that changes the activity but not the sequence of a DNA segment) in the kidneys and liver. To highlight changes in biological function linked to cancer, researchers used genetically engineered (GE) cell lines and tested them for direct DNA damage.

The results confirm that liver damage occurs from exposure to glyphosate and Roundup, leading to alterations of gene expression and miRNA (small RNA) in the liver. Specifically, glyphosate and MON 52276 alter nine gene expressions in the liver and kidneys responsible for oxidative stress and DNA damage, prompting cancer development. Researchers suggest changes in miRNA can disrupt the regular function of cell growth regulator genes, like p53, resulting in cancer. The changes in gene expression of p53 strongly indicate a possible pathway for DNA damage and thus a major cancer development risk factor. Furthermore, various research, including this one, demonstrates increases in small RNA, like miR-10 from GBH exposure, have an association with blood cancer development, particularly leukemia and non-Hodgkin lymphoma. Dr. Antoniou notes, "The new data showing changes in miRNA patterns add yet more evidence to the cancercausing potential of glyphosate and Roundup. What is more, our results show that it is not just Roundup, which is a mixture of glyphosate with various

additives, that has carcinogenic potential, but also glyphosate alone."

EPA's not carcinogenic classification of glyphosate perpetuates environmental injustice among individuals disproportionately exposed to chemicals like farmworkers, especially in marginalized communities. Chemical companies knowingly failed and continue to fail to warn farmers adequately about the dangers of the pesticide, and EPA has failed to warn the public that the manufacturer's (Bayer/Monsanto) and agency's chemical review conclusions have been widely disputed.

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The territory for research on pesticides' potential carcinogenicity, and other impacts on human health, is ridiculously complicated. Yet, there is some convergence across research that exposure to certain pesticides increases the risk of developing some cancers. The association that has been in the blinding spotlight for the past few years is between exposures to glyphosate and glyphosate-based herbicides and the risk of developing cancer, particularly non-Hodgkin Lymphoma (NHL). Beyond Pesticides has covered the mounting evidence of the dangers of glyphosate, including a meta-study that suggests a compelling link between exposures to alyphosate-based herbicides and increased risk of NHL. In addition, it has written extensively on developments in the science and regulatory arena, including:

 the International Agency for Research on Cancer (IARC) 2015 landmark designation of glyphosate as potentially carcinogenic

- evidence that the Environmental Protection Agency colluded with Monsanto (maker of Roundup, the most widely used glyphosate-based herbicide) to advantage industry and that Monsanto had ghostwritten research that countered scientific conclusions on the cancer associations of the compound
- and California's 2017 listing of glyphosate under Proposition 65 as a probable carcinogen and a 2018 Appellate Court affirmation of its ability to do so.

Glyphosate has been the subject of a great deal of public advocacy and regulatory attention, as well as the target of thousands of lawsuits. Beyond Pesticides has covered the glyphosate tragedy extensively; see its litigation archives for multiple articles on glyphosate lawsuits. In June 2020, facing approximately 125,000 suits for Roundup's role in cancer outcomes, Bayer announced a \$10 billion settlement to resolve roughly 75% of current and potential future litigation. However, roughly 30,000 complainants ultimately did not sign on to the settlement, so the queue of potential lawsuits is still potentially enormous. Although Bayer tried for a second settlement (~\$2 billion) to handle future claims, a U.S. District Court judge for the Northern District of California rejected Bayer's 2021 settlement proposal. The judge stated that the settlement was inadequate for future victims diagnosed with cancer after using the herbicide. Bayer has never acknowledged any harm caused by glyphosate, maintaining the chemical is safe for use. However, in July 2021, Bayer announced its plan to end sales of its glyphosate-based herbicides (including its flagship product, Roundup) in the domestic U.S. residential lawn and garden market in 2023.

For the first time, this study demonstrates epigenetic changes in DNA, proteins, and small RNA profiles in the liver of organisms exposed to glyphosate and Roundup formula MON 52276.

Researchers observed activation of DNA repair mechanisms in response to DNA damage from glyphosate. Moreover, oxidative stress and the unfolding of proteins occurred at lower concentrations of Roundup, in which the same concentration of glyphosate produced no effect. The researchers recommend regulators rely on methods to detect metabolic changes that conventional biochemical and tissue analyses overlook. Glyphosate acts on the shikimate pathway, present in plants, fungi, bacteria, archaea, and protozoa. Thus, many taxonomic groups of microorganisms are sensitive to glyphosate. Moreover, chronic exposures to the herbicide could lead to the dominance of resistant strains in bacterial communities. Some alyphosate-vulnerable bacterial strains can become resistant to glyphosate (glyphosate-tolerant class II EPSPS). For instance, glyphosate-resistant bacterial strains like E. coli and Pseudomonas alter gene function to enhance the outflow of glyphosate from the bacterial cell. Thus, this resistance mechanism encourages cross-resistance against antibiotics for pathogenic bacterial species like E. coli and Salmonella, altering the microbiome.

Overall, the researchers determined oxidative stress, an imbalance between reactive oxygen species (ROS) and biological mechanisms to detoxify ROS, likely causes liver damage. This liver damage, in turn, leads to inflammation that can damage DNA and prompt carcinogenicity. Similar to this study, others suggest that glyphosate may impact other metabolic pathways beyond the known shikimate. A report by the University of Turku, Finland states, "Even in glyphosate-resistant species, the interference of the herbicide on mitochondrial metabolism may induce oxidative stress and lead to toxic effects."

Although Bayer announced the end of glyphosate sales in 2023, sales of Roundup may continue with different active ingredients. It is essential to note that the study also demonstrates ingredients in Roundup are even more toxic than glyphosate itself. Therefore, new formulations without glyphosate do **Although Bayer announced** the end of glyphosate sales in 2023, sales of Roundup may continue with different active ingredients. It is essential to note that the study also demonstrates ingredients in Roundup are even more toxic than glyphosate itself. Therefore, new formulations without glyphosate do little to mitigate the problem, especially regarding synergistic (combined) impacts of so-called "inert" ingredients in glyphosate formulations.

little to mitigate the problem, especially regarding synergistic (combined) impacts of so-called "inert" ingredients in glyphosate formulations.

Considering pesticide exposure does not affect just one part of the body, but multiple organs, more studies need to assess what other organs or biological mechanisms glyphosate targets, triggering cancer development. These results could strengthen the legal cases of cancer patients in the U.S. who are suing Bayer/Monsanto because they have evidence that their exposure to Roundup caused their disease. The authors conclude, "[A]doption by regulatory agencies of multiomics analyses would result in more accurate evaluation of a chemical's toxicity and therefore better protection measures being enacted with major public health benefits."

Cancer is one of the leading causes of death worldwide, with over eight million people succumbing to the disease every year. Notably, IARC predicts an increase in new cancer cases from 19.3 million to 30.2 million per year by 2040. Therefore, studies related to pesticides and cancer will aid in understanding the underlying mechanisms that cause the disease. Beyond Pesticides challenges the registration of chemicals like glyphosate in court due to their impacts on soil, air, water, and our health. While legal battles press on, government officials must eliminate the use of toxic synthetic herbicides to avoid the adverse effects of chemical exposure and contamination.

What to do: Emphasis on converting to regenerative-organic systems and using least-toxic pest control to mitigate harmful exposure to pesticides, restore soil health, and reduce carbon emissions, should be the main focus moving forward. Public policy must advance a shift to organic rather than allow unnecessary reliance on pesticides. Considering glyphosate levels in the human body decrease by 70% through a one-week switch to an organic diet, purchasing organic food whenever possible-which never allows glyphosate use-can help curb exposure and resulting adverse health effects. For more information on the adverse effects of pesticides on human health, see Pesticide-Induced Diseases Database (PIDD) pages on cancer (including lymphoma) and other diseases. Moreover, Beyond Pesticides provides tools, information, and support to take local action: check out our factsheet on glyphosate/Roundup and our report, Monsanto's Roundup (Glyphosate) Exposed. Contact us for help with local efforts and stay informed of developments through our Daily News Blog and our journal, Pesticides and You. Additionally, check out Carey Gillam's talk on Monsanto's corruption on glyphosate/Roundup at Beyond Pesticides' 36th National Pesticide Forum.

SOURCE: Robin Mesnage, Mariam Ibragim, Daniele Mandrioli, Laura Falcioni, Eva Tibaldi, Fiorella Belpoggi, Inger Brandsma, Emma Bourne, Emanuel Savage, Charles A Mein, Michael N Antoniou, Comparative Toxicogenomics of Glyphosate and Roundup Herbicides by Mammalian Stem Cell-Based Genotoxicity Assays and Molecular Profiling in Sprague-Dawley Rats, *Toxicological Sciences*, Volume 186, Issue 1, March 2022, Pages 83– 101, https://doi.org/10.1093/toxsci/ kfab143 GM Watch



ENVIRONMENTAL INJUSTICE: DISPROPORTIONATE EXPOSURE AND IMPACTS | APRIL 22, 2022 Black, Indigenous, and People of Color Community at Disproportionate Risk from Pesticides, Study Finds

study published on April 18 finds that people in U.S. BIPOC (Black, Indigenous and People of Color) communities, as well as those living in low-income communities, endure a very disproportionate rate of exposure to pesticides, and of subsequent risks of harm. It finds that such disparities exist in both urban and rural communities, and at all points in the pesticide "life cycle," from manufacture to application. A section of Beyond Pesticides' Retrospective 2021 issue of Pesticides and You, "Retrospective 2021: A Call to Urgent Action," is devoted to such inequities. Section IV, "Disproportionate Pesticide Harm Is Racial Injustice: Documenting Victimization: Structural Racism," reprises Beyond Pesticides' 2021 coverage of environmental injustices. It also calls for urgent action re: federal and state "evaluations that go into toxic chemical regulation . . . to reform and replace the current

regulatory decision-making process, which is empirically racist, with one that acknowledges and cares for those with the highest real-world vulnerabilities and exposure[s]."

The first comprehensive assessment of disparities in pesticide protections and oversight in the U.S., the study paper appeared in the journal BMC Public Health. The authors set out the broad history of how humanity moved from "Traditional Ecological Knowledge" approaches to pests, practiced by indigenous populations the world overthrough use of "the largest and most effective pest controller," nature itselfto the current era of massive deployment of chemical pesticides. They also provide the overlay of the dynamic intersection of institutional racism and class discrimination in the U.S. with the current, chemically intensive, paradigm. "This structural racism and classism, defined here as a system brought about

by historical, institutional, cultural, or behavioral societal actions that routinely disadvantage, harm, and cumulatively oppress BIPOC and/or people of lowincome or wealth, has led to significant disparities in exposure to many pollutants that can lead to premature death or chronic disease."

The acute and chronic health impacts of pesticide exposure are myriad. Beyond Pesticides identifies specific diseases and other health anomalies linked to exposures to pesticides, and points readers to research papers that provide evidence of such links, in its Pesticide-Induced Diseases Database. Through its Gateway on Pesticide Hazards and Safe Pest Management, the public can find details on roughly 400 pesticides, including fact sheets, uses, health and environmental effects, and alternatives.

The disproportionate exposures and impacts of pesticide use for BIPOC and low-income community members tend

to occur through occupational activities, largely in agriculture, and/or via places of residence, which may be near to agricultural storage and application sites or pesticide manufactories, or in substandard, overcrowded, and usually urban housing that is typically subject to the use of pesticides as a short-term fix for chronic pest problems. Of course, these inequities are layered over the typical exposure routes to which nearly everyone in the U.S. is vulnerable: through food, contaminated drinking water and air, and/or pesticides used on public and private landscapes and in all kinds of buildings.

The peer-reviewed study was conducted by researchers from environmental/conservation, farmworker, and racial justice organizations, as well as from HBCUs (Historically Black Colleges and Universities). The researchers' objective was "to identify and discuss not only the historical injustices that have led to these disparities, but also the current laws, policies and regulatory practices that perpetuate them to this day with the ultimate goal of proposing achievable solutions." The team asserts that the disparities identified continue via current regulations and statutes that (1) inadequately protect workers, (2) operate with a pesticide safety "double standard," and (3) permit the export of toxic pesticides to "developing" countries, as detailed in these specific findings:

- disproportionate exposures to harmful pesticides: biomarkers for 12 dangerous pesticides, tracked over the past 20 years, were found in the blood and urine of Mexican-American and Black people at average levels up to five times those in white people.
- weaker protections for agricultural workers: although 10,000–20,000 largely Latinx—farmworkers are sickened annually from pesticide exposure, such workers are not covered by the same regulatory pesticide protections provided to the general public.
- unequal risks: people of color comprise 38% of the aggregate population of California, Georgia, Arkansas,

Tennessee, Missouri, South Carolina, and Louisiana, but that 38% represents 63% of those living nearby to 31 pesticide manufacturing facilities that are in violation of environmental laws (such as the *Clean Air Act* and the *Clean Water Act*).

- poor enforcement: based on available data for a recent five-year period, approximately 1% of agricultural operations that use pesticides had any annual inspections for violations of worker protections—despite violations found at nearly half of inspected facilities; further, enforcement actions proceeded against only 19% of the violators.
- toxic housing: 80% of low-income housing sites in New York State, for example, regularly apply pesticides indoors; a home air quality monitoring study found that 30% of pregnant African American and Dominican women in New York City had at least eight pesticides in their bodies, and 83% had at least one pesticide in umbilical cord samples.
- export of harm: pesticides banned in the U.S. are nevertheless allowed to be produced here and exported; the study notes that organophosphate and carbamate pesticides banned domestically were sold to 42 countries between 2015 and 2019, and 78% of importing countries report more than 30% of their workforce members are poisoned by pesticides annually.

On the matter of the weaker protections for farmworkers and others exposed occupationally to pesticides, the authors explain: "For the general population, exposed mainly to pesticides through their diet, water and residential use, EPA takes a risk-only approachapproving a pesticide only if the agency determines that it will not result in significant harm. Yet for farmworkers and those exposed to pesticides mainly through their work, EPA takes a costbenefit approach whereby harm to workers is allowed as long as the purported benefit of the pesticide, presumably to the grower, sufficiently offsets

those harms." Such unequal treatment is dangerous, unethical, and functionally racist.

In addition, the paper asserts that racial, ethnic, and income disparities persist in part because of policies and regulatory practices that fail to:

- implement Executive Orders (EOs) on EJ (environmental justice) matters, such as the U.S. Environmental Protection Agency's (EPA's) failure to implement EO 12898, "Federal Action to Address Environmental Justice in Minority Populations and Low-income Populations"—in the 25 years since its 1994 issue.
- account for off-label pesticide use and provide the training and support that could reduce such uses; examples of the problems include these, from the research: 14-65% of surveyed farmworkers across multiple states reported receiving no pesticide safety instruction by their employer; and although EPA touts the refrain, "the label is the law," it nevertheless does not require that pesticide manufacturers provide pesticide labels in any language other than Englishdespite the facts that 83% of U.S. farmworkers are Latinx or Hispanic, and only 28% of farmworkers report that they can read English well.
- monitor and follow-up effectively with vulnerable communities once a pesticide has been approved; new pesticide products are often approved with minimal toxicity assessments, making an effective monitoring system (for health and environmental impacts) critical; but periodic review of registered pesticides is compromised by a lack of both epidemiological data and follow-up data on people with the greatest exposures; the paper asserts, "An underfunded surveillance system that relies exclusively on a dataset that extensively underrepresents harm to BIPOC and lower-income com-munities is designed to fail."
- implement important protections for children, who are uniquely vulnerable to developmental toxicants; the 1996 Food Quality Protection Act (FQPA)

required an extra margin of safety for children—a "safety factor" that would reduce the amount of pesticide considered "safe" for children by tenfold; but the researchers note that "implementation of the . . . safety factor has been dismal from the outset. . . . A recent in-depth analysis of 47 non-organophosphate pesticides found that only 13% of acute food exposures and 12% of chronic food exposures incorporated any FQPA children's safety factor whatsoever."

The research paper states the "meta" issue clearly: "This is not simply a pesticides issue, but a broader public health and civil rights issue. The true fix is to shift the [U.S.] to a more just system based on the Precautionary Principle to prevent harmful pollution exposure to everyone, regardless of skin tone or income. However, there are actions that can be taken within our existing framework in the short term to make our unjust regulatory system work better for everyone."

The solutions proposed by the researchers include regulatory actions that could reduce the disparate impacts of pesticides on BIPOC communities by:

- eliminating (or reducing the magnitude of) the pesticide safety double standard
- implementing a system to adequately monitor and account for harms to environmental justice communities
- strengthening worker protections
- reducing unintended pesticide harms
- adequately protecting children, who are the most vulnerable to pesticide harms
- prohibiting export of unregistered pesticides to other countries
- assessing and rectifying regulatory capture within the EPA Office of Pesticide Programs

Beyond Pesticides has long pointed to the Precautionary Principle as an optimal approach to the registration and use of all pesticides. In 2019, for example, we argued for precaution as a fundamental and important platform for pesticide reform, given the regulatory inefficacy and negligence of EPA. We have also called attention to the "regulatory capture" of federal agencies, including the USDA's (U.S. Department of Agriculture's) National Organic Standards Board, and EPA—particularly, the Office of Pesticide Programs, as detailed here, here, and here.

The study makes abundantly clear the importance of the work of environ-

"Pesticides are more likely to harm people of color because of firmly entrenched policies and laws that stack the deck against them. This research identifies concrete steps the Biden administration can take to begin righting these wrongs." Beyond Pesticides will continue to monitor progress on inequities related to pesticides, agriculture, farmworker well-being, and health of BIPOC communities in the U.S.

mental justice, and other health and environmental, organizations, which have welcomed the publication of this research. Jeannie Economos of the Farmworker Association of Florida commented, "The people doing some of the most important work in our country harvesting the food that feeds the nation

— bear a disproportionate burden of the toxic pesticide exposure that risks their and their family's health and lives. This report makes this unequivocally clear, so we ask our political leaders committed to environmental justice, 'What are you going to do about it?'"

Amy K. Liebman of the Migrant Clinicians Network added, "Our regulatory systems exclude farmworkers from basic protections. This results in farmworkers and their families being regularly overexposed to pesticides that have acute and chronic health repercussions, and negatively affect the health of agricultural communities. Strong and enforced regulations are needed now." Another response came from Fatemeh Shafiei, director of environmental studies and associate professor of political science at Spelman College: "For too long communities of color have served as literal dumping grounds for many of our nation's most dangerous toxic chemicals, including pesticides. This must change. It's time for state and federal regulators across the U.S. to jumpstart aggressive efforts to put an end to this deeply troubling form of environmental racism."

Finally, Nathan Donley, PhD, lead author on the research and environmental health science director for the Center for Biological Diversity, commented, "Pesticides are more likely to harm people of color because of firmly entrenched policies and laws that stack the deck against them. This research identifies concrete steps the Biden administration can take to begin righting these wrongs." Beyond Pesticides will continue to monitor progress on inequities related to pesticides, agriculture, farmworker well-being, and health of BIPOC communities in the U.S.

What to do: For current reporting on matters related to environmental justice, see Beyond Pesticides' Daily News Blog EJ archives. We also recommend that readers check out Section IV, "Disproportionate Pesticide Harm Is Racial Injustice: Documenting Victimization: Structural Racism" in our Retrospective 2021: A Call to Urgent Action" issue of *Pesticides and You*.

SOURCES: Donley, N., Bullard, R.D., Economos, J. *et al.* Pesticides and environmental injustice in the USA: root causes, current regulatory reinforcement and a path forward. *BMC Public Health* 22, 708 (2022). https://doi.org/10.1186/s12889-022-13057-4.



POST-HURRICANE WATER CONTAMINATION | JULY 20, 2022 Post-Hurricane Flood Cleanup in Houston Exposed Residents to Range of Pesticides and Industrial Chemicals

lood cleanup in Houston after Hurricane Harvey increased resident exposure to a range of pesticides and other industrial chemical compounds, according to a study published recently in the International Journal of Environmental Research and Public Health by scientists at Oregon State University (OSU). The findings are particularly concerning for a community already subject to some of the highest rates of environmental contamination in the country. "Houston is one of our most industrialized cities," said study coauthor Kim Anderson, PhD, of OSU. "When we look a year after the storm, we see that several neighborhoods that are closer to industrial zones-socioeconomically disadvantaged neighborhoods-had higher concentrations of chemicals right from the get-go, and that was only exacerbated when the hurricane came in."

Hurricane Harvey made landfall in Southern Texas as a category 4 hurricane in 2017. Widespread flooding resulted in damage to chemical plants and oil refineries throughout the city, including 13 of the astounding 41 Superfund sites present in the city of Houston. Cleanup and remediation efforts brought concern among residents that chemicals from these industrial sites were being mixed with floodwaters, exposing individuals to a range of hazardous compounds.

To better understand what chemicals individuals were exposed to and their level of exposure, scientists utilized silicone wristbands originally developed by Dr. Anderson. The wristbands passively sample chemicals the wearer is exposed to in the environment. Scientists were able to get approval for their study within a week, and subsequently began distributing silicone wristbands within three weeks, timing their use as cleanup efforts were still underway. "At that point, flooding was still occurring. I think that's a huge strength of this study," said coauthor Diana Rohlman, PhD, associate professor at OSU. "From the public health perspective, that's the data people want: 'I'm actively flooded, actively cleaning my house; what am I being exposed to right now?'"

Research participants wore the silicone wristbands for seven days. Researchers then took the wristbands back to the lab, where over 1,500 potential chemicals, including pesticides, polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), personal care products, flame retardants, phthalates, pharmaceuticals, and other industrial compounds were screened.

To compare the results recorded posthurricane clean up to a baseline level of exposure for Houston residents, researchers followed up with a certain subset of study participants one year later. Overall, 172 individuals participated in the initial testing, and 238 in the follow-up testing. Within those groups, 99 Houston residents participated in both the initial screening and the follow-up.

Post hurricane cleanup resulted in Houston residents being exposed to 162 different chemicals. Of these, 41 were pesticides, 25 PAHs, 14 flame retardants, 36 personal care products, 10 phthalates, four PCBs, two phar maceuticals, and 30 other industrial compounds. During the next year's follow-up, researchers still found Houston residents exposed to 137 different chemicals. Within these two groups 101 chemical compounds overlapped. However, most concerning is that for 75% of the compounds detected at both times, including personal care products, pesticides, flame retardants, pharmaceuticals, and industrial compounds, levels of these chemicals were significantly higher during flood clean up.

Scientists note that it is difficult to specify health risks based on the sampling, as many of the chemicals detected do not have health guidelines or as much toxicological research behind them. As a result, they recommend in an OSU press release that those cleaning up after floods wear personal protective equipment when working in questionable standing waters.

The pesticides detected, including the insecticide chlorpyrifos, mosquito larvicide methoprene, synergist piperonyl butoxide and a range of synthetic pyrethroids, all present hazards to human health. Yet, beyond individual chemical toxicity, there is concern regarding the potential synergistic effect of multiple simultaneous chemicals.

While the range of contaminants detected after Hurricane Harvey is particularly concerning within highly industrialized Houston, it is possible that similar levels of contamination would be seen in every highly industrialized urban city area subject to flooding. A 2019 study looking at urban runoff from heavy rains in 17 states found most samples containing over 73 different chemicals per site, with pesticides accounting for the most frequently detected chemicals.

While hurricanes are often associated with widespread damage to buildings and other infrastructure, the public health toll from this exposure will continue as climate change increases the size and intensity of hurricanes hitting the U.S.

What to do: For more information on the risk pesticides pose to waterways and action, see Beyond Pesticides Threatened Waters program page.

SOURCE: Samon, S.M.; Rohlman, D.; Tidwell, L.G.; Hoffman, P.D.; Oluyomi, A.O.; Anderson, K.A. Associating Increased Chemical Exposure to Hurricane Harvey in a Longitudinal Panel Using Silicone Wristbands. *Int. J. Environ. Res. Public Health* 2022, *19*, 6670. https:// doi.org/10.3390/ijerph19116670; Oregon State University press release

GLOBAL PESTICIDE HAZARD FOOTPRINT | DECEMBER 7, 2022 Developed Countries with 18% of World Population Responsible for 49% of Pesticide Hazard Footprint

recent study from Australian researchers has investigated pesticide use through an unusual lens—by quantifying the environmental footprints of pesticide use in 82 countries and territories (and eight regions), and then concluding that international trade drives significant pesticide use. The researchers identify the U.S., Brazil, and Spain as the biggest exporters of the "pesticide hazard load" associated with those environmental footprints, and China, the United Kingdom, and Germany as the top three importers. They lay responsibility for this hazard load at the feet of the unsustainable intensification of chemical-intensive agriculture (via synthetic pesticide and fertilizer use during the past 50 years) and ratcheting consumer demand for

goods and services. Indeed, they conclude that the latter, in "developed" countries, is responsible for a substantial portion of the pesticide pollution in *other* countries.

The study authors note that previous "efforts to quantify the environmental footprints of global production and consumption have covered a wide range of indicators, including greenhouse gas emissions, water scarcity, biodiversity, nitrogen pollution, acidification, land use, and others, but they have largely missed . . . represent[ing] the environmental pressures exerted by pesticide use." The researchers set themselves the task of quantifying the "footprints" of pesticide use, from producers to final consumers, in order to map how international trade drives pesticide use, and identify potential repercussions if/ when a nation's policy were to shift from domestic production toward increased importation. They note that prior research has evidenced impacts of specific products and processes, but has not accounted for the role of globalization and international trade.

The researchers remind readers that the intensity of chemical-dependent agriculture (which uses copious amounts of synthetic pesticides and fertilizers) is unsustainable; these practices degrade both terrestrial and aquatic ecosystems, deplete water resources, and contribute to the climate crisis, among other impacts. Beyond Pesticides has spent its tenure demonstrating that pesticide use has huge impacts on the functions of ecosystems, biodiversity (and insect and



pollinator loss, especially), natural resources, and human health.

The study employs an unusual metric in its investigation; it defines pesticide footprints as the "hazard load" of pesticides used for crop production to satisfy consumer demand for food (for humans and animals), textiles, and services that utilize either. They define hazard load (HL) as the measurement of the total body weight of nontarget organisms that would be required to absorb pesticides accumulating in the environment. The higher the HL, the greater the environmental pressure related to consumption. (The study analyzes only the use of insecticides, herbicides, and fungicides on croplands, did not account for pesticide impacts on human health or for acute exposure impacts, and used data from 2015.)

The researchers' analyses account for roughly 79% of global pesticide use, and 70%, 70%, and 63%, respectively, of use in Brazil, the U.S., and China, the world's top three pesticide consumers. Insecticides, according to the researchers, contribute 80% of the global insecticide footprint, and herbicides, 10%. The study's methodology included estimating residual pesticides—the amounts remaining in the environment after application. Of the 3.24 tonnes (or 3.57 U.S. tons) of pesticides analyzed, the study finds that roughly 9.3% accumulated as residues in the environment.

The study employs an unusual metric in its investigation; it defines pesticide footprints as the "hazard load" (HL) of pesticides used for crop production to satisfy consumer demand for food (for humans and animals), textiles, and services that utilize either. They define HL as the measurement of the total body weight of nontarget organisms that would be required to absorb pesticides accumulating in the environment. That amount of residue translates to a hazard load of about two gigatonnes (2,204,622,622 U.S. tons) of organismic body weight (see last paragraph), 34% of which the team attributes to consumption by developed countries (which house 18% of global population), and 66% to consumption in developing countries, which represent most of the world's people. Try, for a moment, to imagine how many organisms that HL would require; it is a stupefying quantity that would be required to absorb the environmental residue from that 79% of global pesticide deployment.

The world's pesticide footprint is distributed across sectors, with plantbased foods comprising the largest portion at 59%; the orchard fruit and grapes sector accounts for a whopping 17% of the global figure. Animal-based foods contribute roughly 11%. Strikingly, the study finds that "17% of the pesticide footprints in developed countries is attributed to the consumption of empty calorie food products such as soft drinks, alcoholic drinks, chocolates, ice-creams, and sugars. In contrast, these food items contribute only 9% of the footprints in developing countries." Clothing and other textile sectors comprise 4% of the global pesticide footprint; consumption of food and textile products in the service and industrial sectors are responsible for another 13%.

The well-known outsized environmental footprint of the developed economies/countries in other regards (climate, water consumption, energy use, et al.) is borne out in the pesticide footprints, as well. The study authors assert that approximately "49% of pesticide footprints caused by the consumption in developed countries [-which harbor only 18% of global population—is] embodied in international trade (i.e., the pesticide hazard loads were occurring abroad), while the consumption of imported goods contributes only 23% of the pesticide footprints in developing countries."

Roughly 32% of global pesticide footprints are traded internationally (i.e., 32% of global pesticide hazard loads occurred outside of the country of final consumption). More than 90% of pesticide footprints imported by some European countries were caused by active pesticide substances/ingredients that were banned for use in those importing countries. (See Beyond Pesticides coverage of the direct export of banned pesticides here and here.)

The study finds that China is the biggest net importer of goods with embodied HLs from insecticides and herbicides, followed by Germany, the UK (United Kingdom), Japan, and India. ("A net importer exerts more environmental pressures (i.e., more pesticide hazard loads) abroad due to their consumption than locally for exports, and vice versa for net exporters.") The U.S. is the largest net exporter of goods with insecticide- and herbicide-embodied HLs, followed by Brazil; 34% of the U.S. HL exports head to China. Roughly 61% of pesticide footprints carried in Brazil's exports is caused by consumption in developed countries, especially the U.S., Germany, and the UK.

The study traces the flows of such embodied pesticide footprints along international trade supply lines, and The study traces the flows of such embodied pesticide footprints along international trade supply lines, and finds that the biggest flow moves from the U.S. to China, mostly due to soybeans and other grain/legume commodities. **Orchard fruits and grapes yield** the highest footprints (per unit mass and calories), and wheat the lowest. Soybeans show the lowest footprint among protein-rich crops; meat registers a slightly higher footprint per unit.

finds that the biggest flow moves from the U.S. to China, mostly due to soybeans and other grain/legume commodities. As for impacts of human food crops, orchard fruits, and grapes yield the highest footprints (per unit mass and calories), and wheat the lowest. Soybeans show the lowest footprint among protein-rich crops; meat registers a slightly higher footprint per unit.

Having tracked and quantified the pesticide footprints of commodities as they are exported and imported around the world, the authors conclude: "A reciprocal pesticide regulation may need to be implemented for imports to discourage the consumption of imported commodities produced using the substances banned in the importing country. Countries importing pesticide footprint should also contribute a fair share in the effort to develop technology for sustainable pest management and the implementation of remediation projects to reduce pesticide contamination in exporting countries. To reduce environmental impacts from global food production, our study suggests that, in addition to sustainable pest management strategies that reduce pesticide use, the strategy of shifting human diet

towards plant-based foods should be accompanied by the promotion of awareness to minimize food waste and food loss, reduction of overconsumption, and a decrease in the consumption of empty-calorie foods."

The authors make valuable points about the responsibility of countries not to export banned pesticides, about the importance of reducing waste and overconsumption, about the pesticide footprint of nutritionally empty food items, and the advisement of shifting to more plant-based foods in the diets of, especially, developed nations. Yet, as with so much research on which Beyond Pesticides reports, conclusions that argue for "reduction" of pesticide use, "sustainable" pesticide use, integrated pest management (IPM), and the like -though well-intentioned-seem to miss the fundamental point. No incremental "reductions," or IPM, will halt the ubiquitous number and variety of downstream impacts of pesticide use, never mind deal with what has already been deployed. Right now, pesticides aredamaging pollinator populations, adding to the human chemical body burden, catalyzing disease processes, launching trophic cascades, degrading agricultural soils, and so much more.

What to do: Only agricultural and other land management practices that eliminate petrochemical pesticides and fertilizers-what in the U.S. is called organic production-would stop the toxic flow of pesticides, many of which have never undergone adequate risk evaluations. Advocate for the transition to organic regenerative agriculture, and other benign land management approaches. You can join/contribute, take up the issue in your local community, organize with others for state-level action, and more; contact Beyond Pesticides for help: info@BeyondPesticides. org or 202.543.5450.

SOURCE: Tang, F.H.M., Malik, A., Li, M. et al. International demand for food and services drives environmental footprints of pesticide use. Commun Earth Environ 3, 272 (2022). https://doi.org/10.1038/s43247-022-00601-8.



MILITARY EXPOSURE HAZARD: GULF WAR ILLNESS | AMY 24, 2022 Breakthrough Study Shows Organophosphate Nerve Gas Caused Gulf War Illness

esearch is providing strong causal evidence that Gulf War Illness (GWI) is the result of exposure to sarin gas, an organophosphate nerve agent used by Saddam Hussein as a chemical weapon during the Gulf War. The findings, published in Environmental Health Perspectives, have important implications for the hundreds of thousands of American service members suffering from a constellation of chronic symptoms without a true understanding of how they became sick. "Quite simply, our findings prove that Gulf War illness was caused by sarin, which was released when we bombed Iragi chemical weapons storage and production facilities," said Robert Haley, MD, lead author of the study and epidemiologist at University of Texas Southwestern. "There are still more than 100,000 Gulf War veterans who are not getting help for this illness and our hope is that these findings will accelerate the search for better treatment."

Sarin was first synthesized in the late 1930s by Nazi chemists working for IG Farben (a consortium that included Bayer) in an attempt to create stronger and more powerful insecticides. Sarin is a G-series organophosphate (named after the scientists that created them), characterized by high acute toxicity and quick evaporation after release. Exposure to

During the Gulf War, the U.S. military bombed Saddam Hussein's stockpiles of sarin gas. Satellite imagery from the time show that debris plumes from these bombed sites drifted over to American troop positions. Nerve agent alarms were set off at American encampments during the course of the war. sarin can quickly result in death, though lower levels of exposure have been linked to long-term brain and nervous system impairment. The chemical was identified as a potential chemical weapon, but not used per se during World War II. It was subsequently produced by both the U.S. and USSR during the 1950s. Production ceased near the end of that decade, though stockpiles remained in the U.S. until the 1970s. In the late 1980s, Saddam Hussein used chemical weapons against both Kurdish civilians and Iranian soldiers. Production and stockpiling of sarin was banned under the United Nations Chemical Weapons Convention of 1993.

During the Gulf War, the U.S. military bombed Saddam Hussein's stockpiles of sarin gas. Satellite imagery from the time show that debris plumes from these bombed sites drifted over to American troop positions. Nerve agent alarms were set off at certain American encampments during the course of the war. Veterans dealing with Gulf War Illness have described a range of ongoing symptoms, from fever to fatigue, headaches, night sweats and insomnia, difficulty finding words, issues with concentration and retaining information, sexual dysfunction, respiratory problems, dizziness, skin rashes, joint and body pain and diarrhea and indigestion. The U.S. Department of Veterans Affairs (VA) refers to the illness as a "chronic multisymptom illness."

GWI has been investigated and associated with a range of environmental exposures over the years, including depleted uranium, smoke from oil wells, and other chemicals exposures like carbamates, DEET, and permethrin, used extensively to address pest problems among the deployed. Firm epidemiological data showing causation has been elusive due to scientific scrutiny over recall bias from self-reported exposures, selection bias of studied cohorts, and other potential confounding exposures.

"What makes this new study a game-changer is that it links GWI with a very strong gene-environment interaction that cannot be explained away by errors in recalling the environmental exposure or other biases in the data," Dr. Haley said.

To make their determination, researchers enrolled 1,016 randomly selected veterans deployed during the Gulf War out of over 8,000 that completed a U.S. Military Health Survey. Half of whom developed GWI and half did not. Researchers collected blood and DNA samples from all those enrolled, and completed a questionnaire specifically asking whether—and if so, how often, nerve agent alarms sounded where they were living or working while in Iraq (alarm frequency was used as a measure to gauge exposure amounts).

The enrolled veterans' DNA—in particular, a gene known as paraoxonase-1 (PON1), were analyzed by researchers. Previous research has found PON1 to be a genetic determinant to human susceptibility to organophosphate poisoning. There are two versions of the gene—a "Q" version that produces a blood enzyme that breaks down sarin and an "R" version that can break down other chemicals but does not do well at neutralizing sarin. Individuals may have QQ, QR, or RR genotypes.

Members who put their lives on the line deserve answers regarding how they became sick and meaningful action to treat their illnesses.

Gulf Veteran's PON1 genes tied very closely to risk of GWI. Among service members who heard nerve agent alarms during their deployment, QQ genotypes had a 3.75 fold increase risk of GWI, QR a 4.4 fold increased risk, and RR were 8.9 times likely to develop GWI. These results, adequately addressing a range of confounders while showing a strong 'gold standard' gene-environment interaction, provide a high degree of confidence of causality, according to the researchers. "Your risk is going up step by step depending on your genotype, because those genes are mediating how well your body inactivates sarin," said Dr. Haley. "It doesn't mean you can't get Gulf War illness if you have the QQ genotype, because even the highest-level genetic protection can be overwhelmed by higher intensity exposure. There's no other risk factor coming anywhere close to having this level of causal evidence for Gulf War illness."

Front line service members who put their lives on the line deserve answers regarding how they became sick and meaningful action to treat their illnesses. Far too many veterans of the Vietnam war are still suffering with illnesses caused by exposure to dioxin present in the notorious herbicide Agent Orange. But after fighting in war, sickened service members have found that they must fight a different sort of fight at home for their own health care. Veterans of the Gulf War are likewise still fighting for care. A 2017 Government Accountability Office report found that 80% of Gulf War veteran disability claims are denied by the VA. GWI claims are approved at a rate roughly three times lower than all other potential claimed disabilities. With strong data now on the cause, the VA must move rapidly to ensure American veterans get the treatment they have earned.

As the National Capital Poison Control Center notes, pesticides and nerve agents are similar poisons with similar symptoms. Numerous individuals across the country-many of whom reach out to Beyond Pesticides for assistanceare suffering from a debilitating range of environmentally induced chronic symptoms that affect their ability to function in day-to-day life. This constellation of conditions is often referred to as Multiple Chemical Sensitivity, Idiopathic Environmental Illness, or Toxicant Induced Loss of Tolerance. A recent review by a national team of researchers incorporates GWI into its review of chemical sensitivity conditions, with important findings for wider public health.

What to do: More investment is needed in both epidemiologic approaches to determine the cause of environmental illnesses among service members and the general public, and treatments to address the myriad of chronic conditions one may experience after a triggering exposure. For more information on chemical sensitivities, read a Doris Rapp, MD talk in *Pesticides and You*, and visit the University of Texas, San Antonio website on the Hoffman TILT program.

SOURCE: Robert W. Haley, Gerald Kramer, Junhui Xiao, Jill A. Dever, and John F. Teiber 2022. Evaluation of a Gene–Environment Interaction of *PON1* and Low-Level Nerve Agent Exposure with Gulf War Illness: A Prevalence Case–Control Study Drawn from the U.S. Military Health Survey's National Population Sample. Environmental Health Perspectives 130:5 CID: 057001. https://doi.org/10.1289/ EHP9009; University of Texas Southwestern Medical Center press release, Environmental Health Perspectives, (Also See Environmental Health Perspectives editorial on the study).



MALE INFERTILITY | AUGUST 3, 2022 Scientific Literature Review Again Connects Pesticides and Male Fertility Problems

systematic review of scientific studies on pesticides and fertility finds exposure associated with lower semen quality, DNA fragmentation, and chromosomal abnormalities. Published in the journal Andrology, the review is yet another warning from a long string of researchers sounding the alarm over the connection between alobal fertility and toxic chemical exposure. With data from the U.S. Centers for Disease Control and Prevention (CDC) indicating roughly one in five couples are unable to conceive after a year of trying, and trends continuing to slope downwards, it is critical that contributing factors be identified so that protective changes can be made.

After screening over 1,300 studies, researchers narrowed their review down to 64 papers assessing semen parameters and DNA integrity after pesticide exposure. Each study is analyzed for its design, the pesticide investigated, the population studied, controls, and reproductive effects determined.

Pesticides are evaluated for their impacts to sperm quality and DNA integrity based on their chemical class. Organochlorine insecticides, which are generally banned but still persistent in soil, air, water, and food in the United States, include a range of impacts to sperm quality. Higher levels of DDT or its breakdown metabolite DDE are associated with lower semen count. and motility and morphology below normal threshold values established by the World Health Organization (WHO). (Under WHO threshold values, a subfertile condition is defined by values lower than the fifth percentile of the general population.) Several studies find that as organochlorine concentrations increase in individual males, sperm parameters also fall. In addition to sperm quality, organochlorines are associated with chromosomal aberrations in several studies, including effects such as sperm disomy, where sperm

have extra or missing chromosomes. This can result in viable offspring, but those offspring are at greater risk of abnormalities.

Organophosphate, the class of insecticides that replaced the organochlorines as they were generally phased out, also present a range of deleterious impacts. These chemicals include pesticides like malathion, still widely used, and chlorpyrifos, which is only now being phased out of agricultural use. Effects on sperm parameters are particularly pronounced for individuals in farming regions or with a history of occupational pesticide work. However, studies on the general population also show cause for concern, finding total sperm count and concentrations inversely related to urinary metabolites of organophosphate insecticides. Apart from sperm quality, the literature reveals studies showing organophosphate exposure resulting in missing or extra chromosomes in sperm, with particular attention

paid to diethyl phosphate, a nonspecific organophosphate metabolite.

Synthetic pyrethroids are also singled out in the scientific literature for their links to sperm damage. These are the insecticides that are replacing the organophosphates, as they are being phased out for their myriad health hazards. Unfortunately, the game of whacka-mole played by the pesticide industry, with EPA's permission, has not resulted in chemicals that are safer for long-term human fertility. Like organophosphates, occupationally exposed individuals are particularly affected, with pyrethroid factory workers showing higher rates of sperm abnormalities and lower motility than nonexposed individuals. Factory workers are also more likely to exhibit DNA fragmentation in their sperm. Another concentration-dependent relationship is found, with individuals reporting higher levels of urinary 3-phenoxybenzoic acid (3-PBA), a nonspecific pyrethroid metabolite, having a lower sperm count, disomy, and a greater chance of exhibiting sperm morphology below WHO thresholds.

Beyond these three classes, scientists did find evidence of negative associations

with carbamate class insecticides, fungicides, and herbicides, but the low number of studies does not allow for extensive analysis. Mixtures of various pesticides are cited as having similar effects to the three main pesticide classes investigated though firm results were difficult to specify due to lack of complete information. In general, occupationally exposed workers are most at risk, with chronic exposure being associated with greater sperm defects.

The results of the study are concerning in light of steadily declining sperm counts. A 2017 study found that sperm counts since 1973 have fallen by nearly 60%. One author of that study, Shanna Swan, PhD, captured public attention regarding sperm declines through her book Countdown, which goes into great depth regarding the impact of environmental chemicals on human fertility. Watch Dr. Swan's talk, Modern Life and the Threat to the Future, at Beyond Pesticides' 2021 National Forum, *Cultivating Healthy Communities*.

Researchers have been sounding the alarm on the impact of pesticides on fertility for decades. In 2013, a previous literature review evaluating pesticide impacts on fertility found pesticides strongly associated with declines in sperm count. As she recounted at the 2021 Forum, Dr. Swan's own work is borne out of efforts to try to disprove a paper published in 1992 by Carlsen et al., which highlights significant declines in sperm quality since the late 1930s.

What to do: As the human civilization grapples with a range of cascading crises, from climate change to the insect apocalypse and global biodiversity crisis, we may be missing the chance to address one of the most critical aspects to the continuation of humanity as we now know it. For more information on the fertility crisis, see Dr. Swan's presentation to the National Pesticide Forum on Beyond Pesticides' Youtube page. Share the presentation with your community to advance organic land management of parks and playing fields.

SOURCE: Giulioni, C, Maurizi, V, Castellani, D, et al. The environmental and occupational influence of pesticides on male fertility: A systematic review of human studies. *Andrology*. 2022; 10: 1250–1271. https://doi.org/10.1111/andr.13228.

ALZHEIMER'S/NEURODEGENERATIVE DISEASE | AUGUST 4, 2022 Glyphosate Weed Killer Crosses Blood-Brain Barrier, Linked to Alzheimer's and Other Neurodegenerative Diseases

n Arizona State University (ASU) study, published in the Journal of Neuroinflammation, shows that the popular herbicide glyphosate can infiltrate the brain through the blood (blood-brain barrier), increasing neurological disease risk. The bloodbrain barrier filters various molecules entering the brain from the circulatory system. However, the permeation of glyphosate molecules elevates the expression of TNF α and the accumulation of soluble beta-amyloid (A β) proteins in the brain and has associations with immune, inflammatory, and neurode-

generative diseases, like Alzheimer's disease (AD).

More than six million people in the U.S. are living with Alzheimer's, and cases are expected to double by 2050. Although Alzheimer's research has focused heavily on finding genetic causes of the disease, fewer than half of cases are genetic. Thus, researchers are now evaluating how environmental contaminants may increase disease risk. Over 300 environmental contaminants and their byproducts, including pesticides, are chemicals commonly present in human blood and urine samples and can increase neurotoxicity risk when crossing the brain barrier. Therefore, studies like this highlight the importance of understanding how chemical accumulation in the body can impact long-term health and disease prognosis. The study notes, "Brain glyphosate correlates with increased TNFα levels, suggesting that exposure to this herbicide may trigger neuroinflammation in the brain, which may induce changes that are seen in neurodegenerative disorders. [...] Collectively, given that a large subset of the population may be exposed to this chemical agent, these results raise



awareness of the detrimental effects glyphosate exposure may have on the brain and human health."

Several studies demonstrate that glyphosate is detectable in the brain tissue of animals. However, this research investigates if persistent exposure to glyphosate leads to detectability in brain tissue and how the chemical's presence affects $TNF\alpha$ levels in the brain. Using urine, plasma, and brain samples from mice in the study, researchers examined gene expression associated with dose-dependent exposure to glyphosate. Moreover, the study employs a novel one-step glyphosate extraction method using liquid chromatography-mass spectrometry (LC-MS)based quantification to measure the level of glyphosate and its breakdown product aminomethylphosphonic acid (AMPA) in brain tissues. The results confirm that glyphosate infiltrates brain tissue, elevating TNFa levels and soluble Aβ, causing cell death among exposed cortical neurons. The novel one-step glyphosate extraction method provides the first evidence of dose-dependent glyphosate accumulation in the brain. Moreover, the extraction method finds a small amount of AMPA in brain tissue,

indicating glyphosate is also breaking down in the body. Therefore, glyphosate exposure has implications for neurodegenerative diseases like AD, resulting from elevated protein levels and expression.

The nervous system is an integral part of the human body and includes the brain, spinal cord, and a vast network of nerves and neurons, all of which are responsible for many bodily functions-from sensation to movement. However, exposure to chemical toxicants, like pesticides, can cause neurotoxic effects or exacerbate preexisting chemical damage to the nervous system. The impacts of pesticides on the nervous system, including the brain, are hazardous, especially for chronically exposed individuals (e.g., farmworkers) or during critical windows of vulnerability and development (e.g., childhood, pregnancy). Mounting evidence over the past years shows that chronic exposure to sublethal (low) levels of pesticides adversely affects the central nervous system (CNS) and neural receptors, such as connections between nerves, the brain, enzymes, and DNA. Specifically, researchers identify agricultural chemical exposure as a cause of many

adverse CNS impacts and neurological diseases, including Alzheimer's, amyotrophic lateral sclerosis (ALS), and Parkinson's disease. Therefore, advocates say it is essential to avoid toxic chemical exposure to lessen potential acute and chronic health risks.

The study highlights that glyphosate crosses the blood-brain barrier in vitro (in an artificial environment outside the body), but this study verifies this in vivo (in a living organism). Glyphosate exposure increases inflammatory cytokine proteins in the blood, especially TNFa. The overexpression of the TNFa protein has associations with cancer, rheumatoid arthritis, psoriasis, multiple sclerosis, and other diseases. Although this study adds to the growing body of research on pesticide neurotoxicity, it is the first to demonstrate that glyphosate successfully crosses the blood-brain barrier, accumulating in the brain in a dose-dependent manner.

However, this is not the first time that toxic compounds have been shown to transfer from the blood to other organs and vice versa. Several studies find pesticide compounds in a mother's blood can transfer to the fetus via the umbilical cord. Furthermore, a 2021 study finds that pregnant women already have over 100 detectable chemicals in blood and umbilical cord samples, including banned persistent organic pollutants (POPs). However, 89 percent of these chemical contaminants are from unidentified sources, lack adequate information, or were not previously detectable in humans.

Pesticides, themselves mixtures of chemicals such as Agent Orange or dioxins, and therapeutic hormones or pharmaceutical products, possess the ability to disrupt neurological function. These chemicals can pass through the skin (dermal) and mucosal membranes, including the lungs (inhalation) and gut (ingestion), and into blood circulation. For instance, studies suggest pesticide formulants (adjuvants), such as POEA (polyoxyethylene tallow amine), have neurotoxic activity. POEA is present in some glyphosate-based herbicides like Roundup and contributes to nervous system toxicity with the active ingredient (glyphosate).

The study concludes, "While there are many correlations between glyphosate and various illnesses, our goal is to shed light on the correlation between glyphosate application and AD [Alzheimer's diseases]. Future work will focus on uncovering the molecular overlap between glyphosate exposure and AD pathology. Specifically, we will focus on determining if glyphosate exposure is capable of exacerbating amyloid [Aβ] pathology and inducing cell death, in vivo in mouse models of AD."

There is a lack of complete understanding of the etiology of pesticideinduced diseases, including predictable lag time between chemical exposure, health impacts, and epidemiological data. Pesticides themselves can possess the ability to disrupt neurological function. Pesticides' impact on the nervous system, including the brain, are hazardous, especially for chronically exposed individuals or during critical windows of vulnerability and development. Therefore, studies related to pesticides and neurological disorders can help scientists understand the underlying mechanisms that cause neurodegenerative diseases. Although occupational and environmental factors, like pesticides, adversely affect human health, regulatory reviews are plagued by numerous limitations in defining real-world poisoning, as captured by epidemiologic studies in Beyond Pesticides' Pesticide-Induced Diseases Database (PIDD) and Daily News Blog. The adverse health effects of pesticides, exposure, and the aggregate risk of pesticides showcase a need for more precise research surrounding occupational and

residential pesticide exposure in order to make complete determinations and fully recognize uncertainty in regulatory decisions that are precautionary.

What to do: Existing information, including this study, supports the clear need for a strategic shift away from pesticide dependency. For more information on the effects of pesticide exposure on neurological health, see Beyond Pesticides' PIDD pages on brain and nervous system disorders, including dementia-like diseases, such as Alzheimer's, and other impacts on cognitive function. Alzheimer's disease has no cure, but preventive practices like organics can eliminate exposure to toxic AD-inducing pesticides. Organic agriculture represents a safer, healthier approach to crop production that does not necessitate pesticide use. Beyond Pesticides encourages farmers to embrace regenerative, organic practices. A complement to buying organic is contacting various organic farming organizations to learn more about what you can do.

SOURCE: Winstone, J.K., Pathak, K.V., Winslow, W. *et al.* Glyphosate infiltrates the brain and increases pro-inflammatory cytokine TNFα: implications for neurodegenerative disorders. *J Neuroinflammation* 19, 193 (2022). https://doi.org/10.1186/s12974-022-02544-5 Arizona State University.

As Thyroid Cancer | August 26, 2022 As Thyroid Cancer Cases Rise, Study Finds Pesticide Link

Research from a team in California finds one-third of pesticides it reviewed—including glyphosate, paraquat dichloride, and oxyfluorfen—to be associated with the development of thyroid cancer. Researchers investigated the links between exposure to pesticides—including 29 that cause DNA cell damage—and the risk of this cancer. The researchers also find that in all the single-pollutant models they employed, paraquat dichloride—a widely used herbicide—is linked to this cancer. In 2021, Beyond Pesticides covered

research by the U.S. National Institutes of Health (NIH) that demonstrated that exposures to lindane and metalaxyl also cause heightened risk of thyroid cancer. These study findings add to the already considerable concern about pervasive pesticide exposure—not only among farmers and applicators, but also in the general population.

It is worth noting that, in addition to elevated thyroid cancer risks, multiple pesticides can cause other health damage. Paraquat is also acutely toxic, and can cause longer-term reproductive, renal, and hepatic damage to humans; it is toxic to birds, fish, and other aquatic organisms, and slightly so to honeybees. Glyphosate, as Beyond Pesticides has written frequently, is carcinogenic, and is associated with human, biotic, and ecosystem harm. Oxyfluorfen exposures deliver risk of reproductive, renal, hepatic, and developmental damage to humans, and toxicity to fish and other aquatic creatures.

The research team, from the University of California (UC) Los Angeles Health Sciences, published its study in *The*



Journal of Clinical Endocrinology & Metabolism. The authors say it "provides the first evidence supporting the hypothesis that residential pesticide exposure from agricultural use is associated with an increased risk of thyroid cancer" [emphasis by Beyond Pesticides].

Thyroid cancer is one of the few cancers whose incidence has risen in recent decades—by 3% since 1992, according to *Science Daily's* reporting on the California research. The American Thyroid Association also notes the dramatic increase in incidence, and says thyroid cancer is now the fastest-growing cancer in women, with most of that increase representing papillary thyroid cancer (the most common and slowest-growing of the subtypes).

Some of the increased incidence is likely attributable to better detection methods and increased use of imaging in health care. While genetics certainly play a role in vulnerability to thyroid disease generally, widespread exposures to certain pesticides—whether through residues in the food supply, occupational exposures, or as in the subject study, residence in an agricultural production area—appear to pose a real risk for the development of thyroid cancers. While genetics certainly play a role in vulnerability to thyroid disease generally, widespread exposures to certain pesticides —whether through residues in the food supply, occupational exposures, or as in the subject study, residence in an agricultural production area—appear to pose a real risk for the development of thyroid cancers.

A Scientific American article notes that 20 years ago, a study published in the American Journal of Epidemiology found that "Iowa and North Carolina women married to men using such pesticides as aldrin, DDT and lindane were at much higher risk of developing thyroid disease than women in non-agricultural areas" — at an incidence rate of 12.5%, compared to a 1–8% rate in the general population. [Note: the organochlorine pesticides aldrin and DDT were banned by the U.S. Environmental Protection Agency in 1974 and 1972, respectively.]

Beyond Pesticides was quoted in that study article: "It's not just farm women who should worry. Trace amounts of chemical pesticides and fertilizers most certainly end up in some of the food we eat. The nonprofit group Beyond Pesticides warns that some 60 percent of pesticides used today have been shown to affect the thyroid gland's production of T3 and T4 hormones. Commercially available insecticides and fungicides have also been implicated."

The UC researchers did not need to stray far for their study; they focused on roughly 25% of all pesticides deployed in the U.S. (The state has been experiencing an uptick in advanced thyroid cancer diagnoses.)

The team used data from the California Cancer Registry (for 1999–2012) to examine residential exposure to 29 agricultural pesticides that cause DNA damage or endocrine disruption (ED) and used GIS (geographic information system) data to identify reasonable exposure estimates for each participant. The study sample comprised 2,067 thyroid cancer cases and 1,003 control participants. All study participants were at least 35 years old, had a thyroid cancer diagnosis, and lived in the study's target geographic area at the time of diagnosis. Control subjects were also at least 35, lived in that same geographic area, and had been living in California for at least five years before the research interview.

Principal investigator Avital Harari, M.D., pointed to the increased incidence of thyroid cancer and implications of the study's findings. She said, "[T]he risk of advanced thyroid cancers, which can increase risk of mortality and cancer recurrence, has been found to be higher in the state of California as compared to other states. Therefore, it is essential to elucidate risk factors for getting thyroid cancer and understand potentially alterable causes of this disease in order to decrease risks for future generations. . . . Our research suggests several novel associations between pesticide exposure and increased risk of thyroid cancer. Specifically, exposure to the pesticide paraquat is positively associated with thyroid cancer risk." She cites additional findings: that exposures to other pesticides, in combination with those to paraguat (in multi-pollutant models) also suggest increased thyroid cancer risk, and that exposures (over a 20-year period) to a larger number of unique pesticides proportionately increase the cancer risk.

Most previous research has focused on the role of endocrine-disrupting pesticides in the development of thyroid cancer, or disease development among those exposed occupationally (e.g., in this research, this, and this). The pesticides metalaxyl and lindane, both established endocrine disruptors, have been implicated in heightened thyroid cancer risk across multiple studies, including the NIH study mentioned above. See more, older research on Beyond Pesticides' Pesticide-Induced Diseases Database webpage, in the section on thyroid cancer. The Science Daily coverage of the UC study explains further that "certain pesticides are established mutagens or have been shown to induce tumor growth and chromosomal abnormalities in vitro. These include glyphosate the active ingredient in widely used herbicides—and pesticides that induce

Threats to public health—in the subject study, from pesticides associated with development of thyroid cancer, but from toxic pesticides and chemicals far more broadly—are not being adequately mitigated by governments at federal, state, or local levels. And those threats are certainly not front and center in the business models of the agrochemical companies that manufacture pesticide products.

DNA cell damage in vitro. Pesticides also can alter thyroid hormone production, which has been associated with thyroid cancer risk."

The relevant methods of action of pesticides re: thyroid cancer are the mutagenic or the (less direct) endocrine disrupting. The actions of endocrine disruptors were laid out by Beyond Pesticides in 2021: "'The ingredients in many pesticides (and in many consumer products) act as endocrine disruptors in humans and other animals in several ways. They may: (1) mimic actions of hormones the body produces (e.g., estrogen or testosterone), causing reactions similar to those generated by the naturally produced hormones; (2) block hormone receptor cells, thereby preventing the actions of natural hormones; or (3) affect the synthesis, transport, metabolism, and/or excretion of hormones, thus altering the concentrations of natural hormones in tissues or at receptor sites.' Pesticides acting as EDs can . . . distort hormone levels in the body."

Threats to public health—in the subject study, from pesticides associated with development of thyroid cancer, but from toxic pesticides and chemicals far more broadly—are not being adequately mitigated by governments at federal, state, or local levels. And those threats are certainly not front and center in the business models of the agrochemical companies that manufacture pesticide products. Thus, the onus for changing the U.S. system of allowing toxic chemical use without adequate, precautionary, and protective review falls on the public and its organizational health, environment, climate (and other) advocatessuch as Beyond Pesticides and many, many others.

What to do: Our involvement, whether as professionals, laypeople, elected officials, or concerned advocates, is critical to enhancing public understanding of the science that underlies the current health, biodiversity, and climate crises, and to motivating action on the local, state, and national levels. These crises arise from a confluence of issues, and are harming all life and every environment on the planet. The need for carefully defined sustainable land management, building and household practices, and consumer and industrial products is urgent. The 2022 National Forum Series launched Beyond Pesticides' campaign to eliminate fossil fuel-based pesticide use within the next decadeputting a stop to toxic emissions, exposure, and residues, while embracing an organic systems approach that is holistic and respectful of life.

SOURCE: Negar Omidakhsh, Julia E Heck, Myles Cockburn, Chenxiao Ling, Jerome M Hershman, Avital Harari. Thyroid Cancer and Pesticide Use in a Central California Agricultural Area: A Case Control Study. *The Journal of Clinical Endocrinology & Metabolism*, 2022 107 (9): e3574 DOI: 10.1210/clinem/dgac413; Science Daily



Hormone Mimicking Properties of Glyphosate Weed Killer and Related Compounds Increase Breast Cancer Risk

study published in *Chemosphere* adds to the growing body of research that demonstrates the role that endocrine (hormone) disrupting effects of glyphosate play in breast cancer development. Exposure to the herbicide glyphosate and other glyphosate-based herbicides (GBHs) at high concentrations mimics the estrogen-like cellular effects of 17β -estradiol (E2), altering binding activity to estrogen receptor α (ER α) sites, thus causing fundamental changes in breast cancer cell proliferation (abundance).

Glyphosate is the most commonly used active ingredient worldwide, appearing in many herbicide formulas, not just Bayer's (formerly Monsanto) Roundup[®]. The use of this chemical has been increasing since the inception of crops genetically modified to tolerate glyphosate over two decades ago. The toxic herbicide readily contaminates the ecosystem with residues pervasive in food and water commodities. In addition to this study, the scientific literature shows time and time again that glyphosate has an association with cancer development, as well as human, biotic, and ecosystem harm. Therefore, advocates point to the need for national policies to reassess hazards associated with disease development and diagnosis upon exposure to chemical pollutants. The researchers note, "The results obtained in this study are of toxicological relevance since they indicate that glyphosate could be a potential endocrine disruptor in the mammalian system. Additionally, these findings suggest that glyphosate at high concentrations may have strong significance in tamoxifen [breast cancer drug] resistance and breast cancer progression. [F]urther studies in animal models must confirm these effects on organ systems."

The study evaluates the cytotoxic (toxic to cells) effect of analytical grade glyphosate and GBHs to evaluate its estrogenic activity. The literature shows that significant exposure to these GBHs can cause cell death from the active ingredient glyphosate, as well as other ingredients in the formulations. These ingredients can have detergent-like properties (e.g., adjuvants) that can amplify the cytotoxic effects of glyphosate. The researchers aim to clarify the molecular mechanism involved in glyphosate-induced estrogen production and breast cancer cells. The Chilean researchers in the study find exposure to glyphosate at high concentrations induces estrogen-like effects through binding to estrogen receptor α (ER α) sites, mimicking the cell effects of 17β estradiol (E2), attaching a phosphate group to the zinc (Zn) II ion (phosphorylation), thus causing fundamental changes to estrogen in breast cancer cells. Like past studies, this study demonstrates that glyphosate mimics the effect of E2 through Erα phosphorylation.

Breast cancer is the most common cancer among women, causing the second most cancer-related deaths in the U.S. Past studies suggest that genetic inheritance factors influence breast cancer occurrence. However, genetic factors only play a minor role in breast cancer incidents, while exposure to external environmental factors (i.e., chemical exposure) may play a more

Advocates argue that global leaders must fully understand the cause of pesticide-induced diseases before the chemicals enter the environment. Policy reform and practices that eliminate toxic pesticide use can end the uncertainty surrounding potential harm.

notable role. According to the Centers for Disease Control and Prevention (CDC), breast cancer is a disease that causes breast cells to grow out of control, with the type of breast cancer depending on the cells themselves. Most common forms of breast cancer have receptors on the cell surface that can increase cancer growth when activated by estrogen, progesterone, or too much of the protein called HER2. Hormones generated by the endocrine system greatly influence hormone cancer incidents among humans (e.g., breast, prostate, and thyroid cancers). Several studies and reports, including U.S. Environmental Protection Agency (EPA) data, identify hundreds of chemicals as influential factors associated with breast cancer risk. One in ten women will receive a breast cancer diagnosis, and genetics can only account for five to ten percent of cases. There are grave concerns over exposure to endocrine (hormone) disrupting chemicals and

pollutants that produce adverse health effects. Considering not only glyphosate but over 296 chemicals in consumer products can increase breast cancer risk through endocrine disruption, it is essential to understand how chemical exposure impacts chronic disease occurrence.

Glyphosate has been the subject of a great deal of public advocacy and regulatory attention and is the target of thousands of lawsuits. Beyond Pesticides has covered the glyphosate tragedy extensively; see its litigation archives for multiple articles on glyphosate lawsuits.

Several studies link pesticide use and residue to various cancers, from more prevalent forms like breast cancer to rare ones like kidney cancer nephroblastoma (Wilms' tumor). Although the connection between pesticides and associated cancer risks is nothing new, past studies suggest glyphosate and GBHs act as endocrine disruptors, affecting the development and regulation of estrogen hormones that promote breast cancer. However, this study is one of the few to evaluate the molecular mechanisms involved in toxicological changes initiating breast cancer events. Phosphorylation with a Zn (II) ion stabilized the bond between the estrogenimitating activity of glyphosate and GBHs to the $Er\alpha$. Therefore, the bond promotes the overexpression of estrogensensitive genes, increasing consequences on breast cancer cell activity. The study concludes, "The results obtained in this study are of toxicological relevance since they indicate that glyphosate could be a potential endocrine disruptor in the mammalian system."

Cancer is a leading cause of death worldwide. Much pesticide use and exposure are associated with cancer effects. Studies concerning pesticides and cancer help future epidemiologic research understand the underlying mechanisms that cause cancer. Although the link between agricultural practices and pesticide-related illnesses is stark, over 63 percent of commonly used lawn pesticides and 70 percent of commonly used school pesticides have links to cancer. Advocates argue that global leaders must fully understand the cause of pesticide-induced diseases before the chemicals enter the environment. Policy reform and practices that eliminate toxic pesticide use can end the uncertainty surrounding potential harm. For more information on the harms of pesticides, see Beyond Pesticides' Pesticide-Induced Diseases Database pages on breast cancer, endocrine disruption, and other diseases. This database supports the need for strategic action to shift away from pesticide dependency.

What to do: Prevention of the causes of breast cancer, not just awareness, is critical to solving this disease. In 1985, Imperial Chemical Industries and the American Cancer Society declared October "Breast Cancer Awareness Month" as part of a campaign to promote mammograms for the early detection of breast cancer. Unfortunately, most people are all too aware of breast cancer. Detection and treatment of cancers do not prevent the problem. EPA should evaluate and ban endocrinedisrupting pesticides and make organic food production and land management the standard that legally establishes toxic pesticide use as "unreasonable."

Moreover, proper prevention practices, like buying, growing, and supporting organics, can eliminate exposure to toxic pesticides. Organic agriculture has many health and environmental benefits that curtail the need for chemical-intensive agricultural practices. Regenerative organic agriculture nurtures soil health through organic carbon sequestration while preventing pests and generating a higher return than chemical-intensive agriculture. For more information on how organic is the right choice, see the Beyond Pesticides webpage, Health Benefits of Organic Agriculture.

SOURCE: Juan P. Muñoz, Rocío Araya-Osorio, Raúl Mera-Adasme, Gloria M. Calaf, Glyphosate mimics 17β-estradiol effects promoting estrogen receptor alpha activity in breast cancer cells, Chemosphere, Volume 313, 2023, 137201, ISSN 0045-6535, https://doi. org/10.1016/j.chemosphere.2022.137201.

HAZARDOUS INERT INGREDIENTS UNDERREGULATED | AUGUST 9, 2022 "Inert" Pesticide Ingredients and Failure to Regulate Raise Dangers for All U.S. Residents

he most widely used pesticide chemicals in the United States are not listed on product labels, yet pose widespread environmental and public health hazards, according to commentary published this month in Environmental Health Perspectives by two veteran researchers. At issue are adjuvants and so-called "inert" (or "other") ingredients, chemicals that are added to formulated pesticide products, but do not undergo the same safety reviews as the active ingredient in pesticide products. This donut hole of regulation has permitted, as the commentary shows, millions of pounds of chemicals to be applied in California and throughout the country without proper scientific evaluation of their human health or ecological impact.

Researchers first draw a distinction between adjuvant products and inert ingredients in pesticide products. Adjuvants are materials specifically designed to improve the performance of a pesticide Pesticide manufacturers can use any inert ingredient in EPA's inert ingredient database without disclosing that material on the pesticide product label. There are no reporting requirements for inert ingredients in any state.

spray and are sold separately from formulated pesticide products. Adjuvants are "tank mixed" with a pesticide prior to its application. Inert ingredients are any ingredient within a formulated pesticide product that is not designed to prevent, destroy, or repel a pest. Adjuvants and inert ingredients can be the same material—the difference lies in when they are added to a formulated pesticide product and the claimed purpose of their use. This distinction is important because researchers utilize data from California's pesticide reporting system for their review. In California, pesticide adjuvants are required to be registered as pesticides, and their use reported to the state on a monthly basis. The U.S. Environmental Protection Agency (EPA) does not require this, nor does any other state than California. In California and throughout the country, inert ingredients are minimally reviewed by EPA and added to an inert ingredient database. Pesticide manufacturers can use any inert ingredient in EPA's inert ingredient database without disclosing that material on the pesticide product label. There are no reporting requirements for inert ingredients in any state.

An evaluation of California's pesticide reports finds that among all pesticides and adjuvants registered, 37 of the 100 most widely used pesticides in California are adjuvants. Researchers subsequently zeroed in on the most

used material, the adjuvant α -(p-nonylphenyl)-ω-hydroxypoly(oxyethylene) (APNOHO). Over 10 million acres of agricultural land in California is sprayed with APNOHO each year. The chemical is a nonionic surfactant, used to increase the penetration of an active ingredient in attempts to improve a pesticide's performance. In addition to its registration as an adjuvant in over 150 adjuvant products in California, a freedom of information act request to EPA uncovered it being used as an inert ingredient in over 650 federally registered fully formulated pesticides (including insecticides, herbicides, and fungicides).

With no oversight of this chemical, APNOHO use in California has more than doubled over the past 20 years, from just over one million pounds per year in 2000 to 2.2 million pounds in 2019. APNOHO and other chemicals in its class are applied to nearly 12 million acres of farmland in California each year. Between its use as an adjuvant and inert ingredient in other states, there is no telling how much of this chemical U.S. residents are being exposed to each year.

The widespread use of this material raises a range of health and environmental worries. APNOHO is considered an endocrine (hormone) disrupting chemical by the European Union, yet despite a recent damning report from the EPA Office of Inspector, the U.S. lags far behind in its safety evaluations of these concerning impacts. Out of over 1,300 chemicals that require testing, EPA has issued orders for a scant 52. An analysis in the commentary finds that the little data EPA has produced on APNOHO indicates its hormone disrupting activity is more potent than the active pesticide ingredients and known endocrine disruptors methoxychlor and vinclozolin.

Endocrine disruptors pose a growing risk to the American public; one that is increasing due to a lack of regulation by EPA. These materials function by: (i) mimicking the action of a naturallyproduced hormone, such as estrogen or testosterone, thereby setting off similar chemical reactions in the body; (ii) blocking hormone receptors in cells, thereby preventing the action of normal hormones; or (iii) affecting the synthesis, transport, metabolism and excretion of hormones, thus altering the concentrations of natural hormones. Endocrine disruptors have been linked to attention deficit hyperactivity disorder (ADHD), Parkinson's and Alzheimer's diseases, diabetes, cardiovascular disease, obesity, early puberty, infertility and other reproductive disorders, childhood and adult cancers, and other metabolic disorders.

Regulators and policymakers are urged to consider health and environmental effects that result from combinations of pesticides, adjuvants, and inert ingredients. It is further recommended that officials in states other than California require registration of pesticide adjuvants.

In addition to effects on the body's hormonal system, APNOHO is associated with increased risk of birth defects in laboratory and epidemiological studies, including one paper that shows a doubled risk for the birth defect craniosynostosis. The chemical likewise poses significant environmental hazards, with data showing harm to aquatic life greater than that caused by the neonicotinoid insecticide imidacloprid. Researchers note that APNOHO is considered hazardous within other U.S. laws, including the Toxic Release Inventory and *Clean Air Act*.

To better understand the implications of the widespread use of APNOHO and other inerts and adjuvants, the commentary suggests recommendations both for other researchers and policymakers. For researchers, it is suggested that adjuvants and inerts be included in epidemiological studies, chemical abstract service (CAS) numbers be included for all ingredients in all pesticide products studied (if unable to discern up front, analytical techniques should be employed to find and identify all ingredients to the greatest extent possible), and all pesticides, inert ingredients, and adjuvants should be evaluated for endocrine-disrupting activity.

Regulators and policymakers are urged to consider health and environmental effects that result from combinations of pesticides, adjuvants, and inert ingredients. It is further recommended that officials in states other than California require registration of pesticide adjuvants. Lastly, the authors note that it has been 25 years since the American Medical Association recommended that pesticide products contain all ingredients on their labels and safety data sheets, making these steps long overdue.

"In the past, improving public access to data about emissions of toxic chemicals has prompted important health and safety improvements," the authors note, referencing the impact of Toxic Release Inventory data in prompting updates to the *Clean Air Act*.

What to do: Beyond Pesticides is strongly in favor and has been consistently active in efforts to push EPA to fulfill its statutory obligations to review endocrine-disrupting pesticides and increase public health transparency by disclosing all ingredients in pesticide formulations. Take action today to tell EPA to regulate hormone disruption chemicals, and Congress to pass the *Protect America's Children from Toxic Pesticides Act* (PACTPA), which would require label disclosure of all inert ingredients in a pesticide.

SOURCE: Caroline Cox and Michael Zeiss. 2022. Health, Pesticide Adjuvants, and Inert Ingredients: California Case Study Illustrates Need for Data Access. Environmental Health Perspectives 130:8 CID: 085001 https:/ doi.org/10.1289/EHP10634; EHP Invited Commentary)

COVID: ELEVATED DISINFECTANT HAZARDS | FEBRUARY 1, 2022 Increased Accumulation of Disinfectant Chemicals in the Body During the Pandemic Threatens Health, Despite Available Alternatives

study published in Environmental Science and Technology finds that concentrations of quaternary ammonium compounds (QUATs or QACs) in the human body have increased during the Covid-19 pandemic, raising health and safety concerns. QACs include a variety of chemicals in personal care, pharmaceutical, and medical products used as disinfectants, sanitizers, antimicrobials. However, over the past 70 years, large-scale production and use of these compounds led to accumulation in the environment, including surface water, sediment, and soil.

Previously, researchers thought most QACs lack the potential to bioaccumulate, as the chemicals are highly water soluble, while dermal and oral absorption rates are low. However, emerging evidence demonstrates that specific QACs bioaccumulate in blood and other body tissues and can cause a range of toxic effects. Therefore, studies like this highlight the significance of monitoring chemical exposure for adverse health effects. The researchers note, "Further efforts are needed to explore the relationship between the use of QACcontaining products and the levels of QACs in human blood or of their metabolites in urine. Considering the increased use of some QACs as a result of the Covid-19 pandemic, our findings

The World Health Organization (WHO) and other infectious disease specialists condemn indiscriminate and vast amounts of disinfectant spraying in public areas, deeming it ineffective and a health hazard on contact or when combined with other disinfectants. warrant further exposure and epidemiological research focused on QACs."

Amidst the outbreak of SARS-CoV-2 (Covid-19), the global demand for disinfectants and sanitizers has increased substantially as a means of preventing illness in residential and nonresidential settings. Initially, public health officials considered disinfecting highly trafficked areas as the most effective way to combat Covid-19. This notion has led to dangerous disinfecting practices in many countries where trucks, drones, or robots disperse massive amounts of disinfectants into public areas. Furthermore, the Centers for Disease Control and Prevention (CDC) has reported a sharp increase in calls to Poison Control Centers regarding illnesses resulting from the use or misuse of toxic disinfectants during the pandemic. The World Health Organization (WHO) and other infectious disease specialists condemn indiscriminate and vast amounts of disinfectant spraying in public areas,

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deeming it ineffective and a health hazard on contact or when combined with other disinfectants.

The researchers performed an in vitro-in vivo extrapolation (IVIVE) model to determine the bioaccumulation potential of 18 QACs in blood samples from the liver before (2019) and during (2020) the Covid-19 pandemic. The model determines the clearance rate in vivo (in the body), in which a slower clearance rate means higher bioaccumulation potential. The results show 15 out of the 18 QACs are detectable in blood samples, with QAC concentrations significantly higher during the pandemic than prior to it. The main routes of exposure include diet, inhalation, ingestion, or the skin.

More than a third of U.S. residents participate in high-risk Covid-19 practices, misusing toxic disinfectant cleaners and disinfectants to prevent infection. Quaternary ammonium compounds are among some of the most harmful disinfectants, as their "long-lasting" properties have adverse impacts on human health, which has extensive documentation in the scientific literature. Effects include mutations, lower fertility, and increased antibiotic resistance. The overuse of QAC disinfectants in U.S. Immigration and Custom Enforcement (ICE) detainment centers causes nose bleeds and other adverse health effects.

Furthermore, Beyond Pesticides receives questions from concerned teachers asking for less harmful disinfectants to use in the classroom, especially as many are experiencing adverse impacts of disinfectant use (e.g., chemical skin burns, respiratory issues). Since QACs are in most disinfectant products, it remains ubiquitous in the environment as misuse continues.

Although disinfectants, like QACs, kill viruses, bacteria, and other microbes via cell wall and protein destruction, they can also negatively affect the immune system, thus reducing resistance to disease. People who have a preexisting condition or are of advanced age, who may have a weakened immune or respiratory system, are more vulnerable to the effects of the virus. When managing viral and bacterial infections, chemicals that exacerbate the risk to vulnerable individuals are of serious concern.

QACs are harmful to the respiratory system and have a long list of adverse effects, from cancer and genetic mutations to lower fertility and increased antibiotic resistance. Most recently, the QAC antimicrobial cetylpyridinium chloride (CPC) has raised concerns. The compound is present in mouthwashes, lozenges, toothpaste, and nasal sprays and is thus commonly encountered orally. A recent study finds CPCs have associations with adverse respiratory effects (e.g., lung inflammation). Moreover, acute oral inhalation can be fatal. Although CPC also has uses as an "inert" or undisclosed ingredient in pesticide products, recent findings demonstrate CPC has more biological potential. The respiratory system is essential to human survival, regulating gas exchange (oxygen-carbon dioxide) in the body to balance acid and base tissue cells for normal function. Considering Covid-19 is a systemic (general) disease that overwhelmingly impacts the respiratory system of many patients, exposure to CPCs present a heightened risk of co-occurring symptoms. Damage to the respiratory system can also trigger the development of extra-respiratory systemic manifestations like rheumatoid arthritis, and cardiovascular disease.

While EPA has certified several disinfectants as effective against Covid-19 (List N), many of these chemicals are hazardous. These chemicals include QACs and other toxic compounds documented on Beyond Pesticides' list of "Disinfectants to Avoid." Although disinfection can kill pathogens, one must consider guidelines associated with proper selection and use of products. Conveniently, several safer disinfectants on EPA's list are effective against the virus, including citric acid, ethanol, isopropanol, L-lactic acid, hydrogen peroxide, sodium bisulfate, dodecylbenzene sulfonic acid, and thymol. These chemicals are present on Beyond Pesticides' "good" list of "Disinfectants to Look for," as natural-based substances

tend to be safer while still effective at eliminating the virus on surfaces. Beyond Pesticides has said, "It is important during public health emergencies involving infectious diseases to scrutinize practices and products very carefully so that hazards presented by the crisis are not elevated because of the unnecessary threat introduced with toxic chemical use.... There is tremendous pressure to use toxic disinfectants, despite the availability of safer products. In fact, while [CDC] is recommending 70% alcohol for surface disinfection, [EPA's] Office of Pesticide Programs is advising the use of unnecessarily toxic substances, and reducing standards that govern their allowance on the market."

This study is the first to comprehensively assess the bioaccumulation of QACs in blood via biomonitoring, demonstrating a difference in chemical concentrations before and during the pandemic. The study notes that frequent detection of QACs in blood reveals widespread exposure among the general population. The major QAC groups include benzylalkyldimethylammonium compounds (BACs), dialkyldimethylammonium compounds (DDACs), and alkyltrimethylammonium compounds (ATMACs). The results show that, of the three groups, ATMACs are most abundant in blood samples. The authors conclude, "[T]he higher QAC concentrations in blood collected during the pandemic suggest increased exposure during this period, possibly due to the

As the U.S. Covid-19 cases continue to rise, there is an urgent need to evaluate the effect pesticide exposure and uses have on health. Although some practices and products can prevent coronavirus infections, the continued use of toxic pesticides in the surrounding environment increases disease risk factors. increased disinfection of the indoor and outdoor environment."

As the U.S. Covid-19 cases continue to rise, there is an urgent need to evaluate the effect pesticide exposure and uses have on health. Although some practices and products can prevent coronavirus infections, the continued use of toxic pesticides in the surrounding environment increases disease risk factors. When managing viral and bacterial infections, advocates say that we must not exacerbate the risk to animals and humans, while avoiding or controlling the threat. In the case of Covid-19, there exists measures of protectionboth practices and products-that can prevent infection without using toxic products that increase risk factors. Advocates maintain that individuals and aovernment officials alike should assess all risks associated with pesticide use, including the mode of action. However, EPA's failure to respond to current science is a significant shortcoming of its risk assessment process, especially regarding disease implications.

What to do: Individuals and government officials should observe all chemical ingredients on the disinfectant and sanitizer product labels and look at the use instructions to ensure that the method of use is safe for you. Beyond Pesticides tracks the most recent health studies related to pesticide exposure through our Pesticide-Induced Diseases Database (PIDD). This database supports the clear need for strategic action to shift away from pesticide dependency. For more information on harms associated with pesticide exposure, see PIDD pages on asthma/respiratory effects and other diseases. Additionally, learn how to protect yourself from Covid-19 safely by visiting Beyond Pesticides' webpage on Disinfectants and Sanitizers for more information.

SOURCE: Zheng G, Webster TF, Salamova A. Quaternary Ammonium Compounds: Bioaccumulation Potentials in Humans and Levels in Blood before and during the Covid-19 Pandemic. Environ Sci Technol. 2021 Nov 2;55(21):14689-14698 doi: 10.1021/acs.