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LYN PATRICK, ND

Deep Dive into Pesticides: Health Impacts, Testing and Case Studies

Infographics/References Credits

TOXDetect PROFILE

Pesticide Atlas 2023 U.S. Edition

- All data is referenced therein
- Crinnion W, Pizzorno J. Clinical

Environmental Medicine:
Elsevier Press 2019

Abbreviations:

GSH – glutathione

GST – glutathione-s-transferase

GPx – glutathione peroxidase

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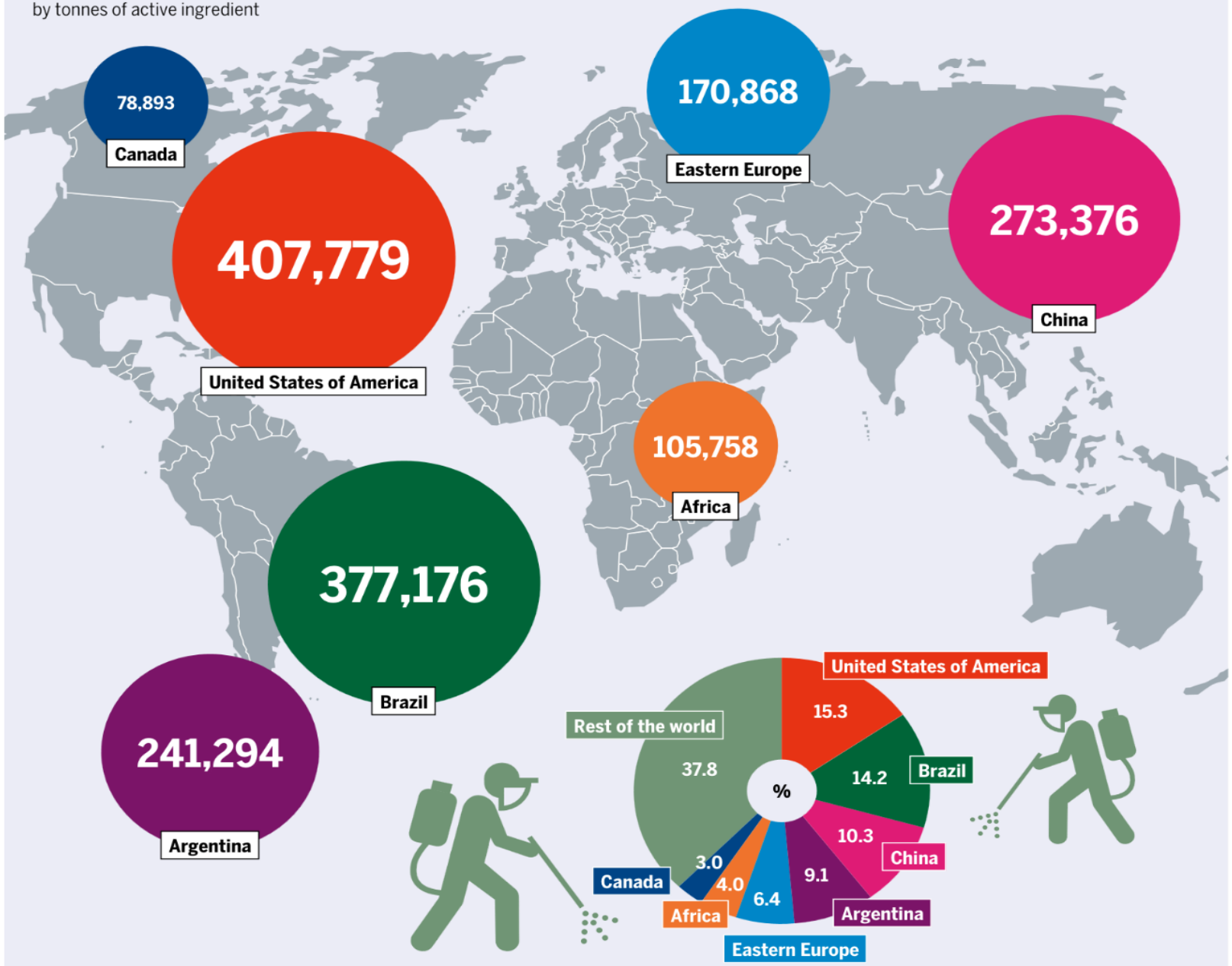
THE U.S. IS NUMBER ONE

Pesticide use in 2020 in key regions/countries, by tonnes of active ingredient



Use estimates are based on sales data; Source: UN Food and Agriculture Organization.

Pesticides are Everywhere: Air, Rain

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- Atrazine, metolachlor, and propanil were detected in ≥50% of the air and rain samples in both 1995 and 2007.

- Glyphosate and its degradation product, aminomethyl-phosphonic acid (AMPA), were detected in ≥75% of air and rain samples in 2007 but not detectable only 10 years prior.

PMID: 24549493

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Drinking Water Contamination

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- US Department of Agriculture estimates that **50 million people** in the United States obtain their drinking water from groundwater that is potentially contaminated by pesticides and other agricultural chemicals.
- Only 13 pesticides are regulated with maximum contaminant levels (MCLs) under the Safe Drinking Water Act: glyphosate, atrazine, simazine, and 2,4-D.
- Not included are about **900 other pesticides** registered for use in the U.S. in parks, golf courses, and on agricultural crops.

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How are our patients exposed?

- Indoor/outdoor animals (dogs playing in parks)
- Animals chemically treated for fleas etc.
- Well water
- City water
- Regularly go out to eat in restaurants
- Regularly eat non-organic animal products including dairy, eggs, farmed fish, and meat

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How are our patients exposed?

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- Large fish: croaker, sea bass, mackerel, perch, sablefish, marlin, grouper, bluefish
- Eat fish from lakes or rivers
- Regularly eat farmed fish (Atlantic salmon, catfish, all carp, tilapia, rainbow trout)
- Use antibacterial soap or personal care products with triclosan or triclocarban, Microban sportswear, products with Microban

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USA: Ground Zero for Pesticide Use

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- The United States uses more pesticides than any other country or region followed by Brazil, China, and Argentina.
- According to the USDA, a total of about **400** different agricultural pesticides totaling **>1 billion lbs.** were used in the United States in 2017, the latest year data is available.
- The greatest use on corn(163 million pounds), soybean(115 million pounds), cotton (17 million pounds), and rice (4 million pounds).
- The state of California produces over 1/3 of the country's vegetables and 2/3 of the country's fruits and nuts and uses over 200 million pounds per year of pesticide active ingredient.
- The pesticide application rate on California cropland is about 4.5 times the national average, with the **top crops** for pesticide use including **almonds, grapes, tomatoes, strawberries, and oranges**.

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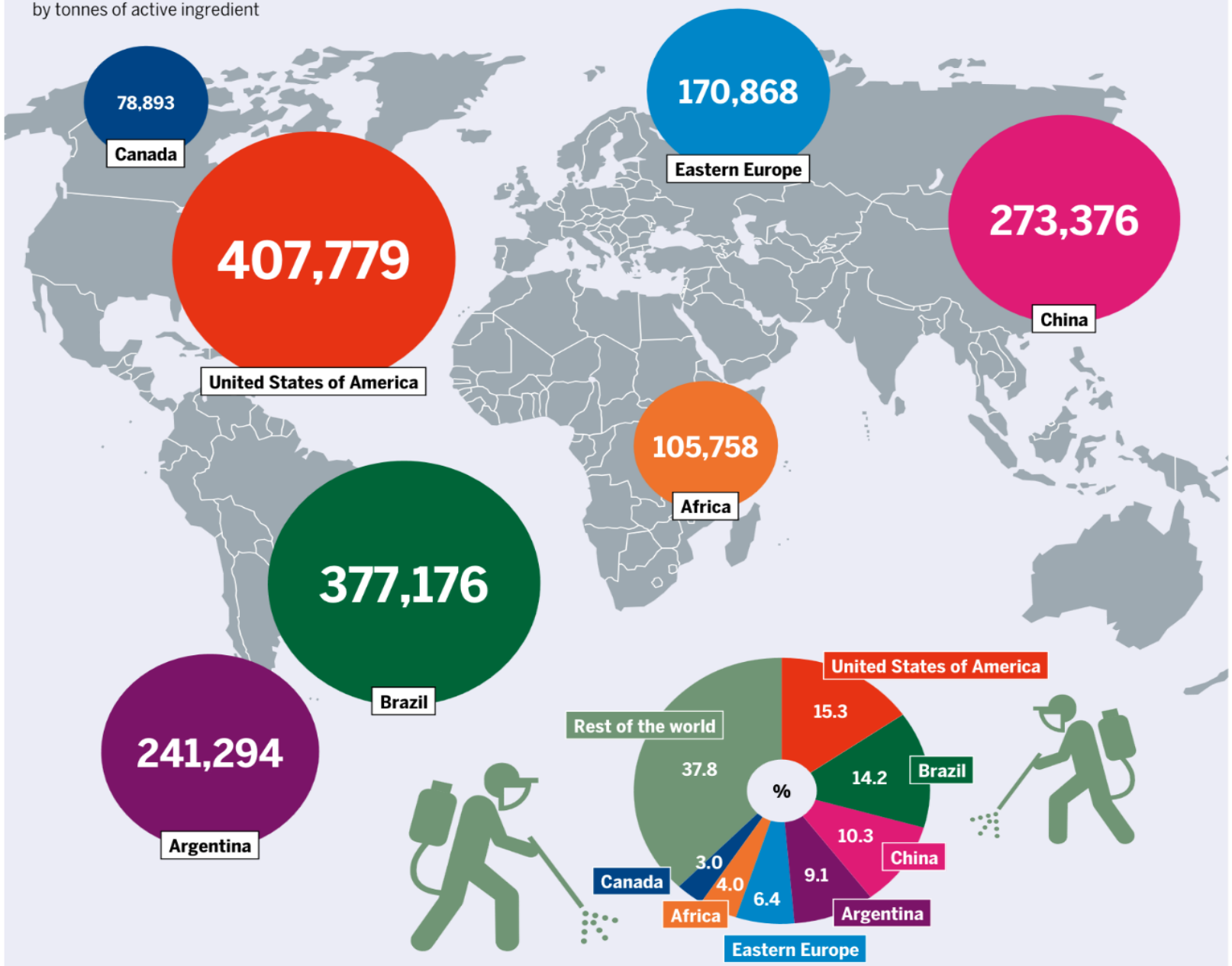
THE U.S. IS NUMBER ONE

Pesticide use in 2020 in key regions/countries, by tonnes of active ingredient



Use estimates are based on sales data; Source: UN Food and Agriculture Organization.

Pesticides: an American Experiment

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- **60%** (> 645 million lbs.) were considered **hazardous to human health**, according to the WHO's data.
- **85** pesticides that are banned in more than **30 countries** were still used in the United States in 2023
- **Phorate**, the most used "extremely hazardous" insecticide in the U.S. in 2017, is **banned in 38 countries**, including China, Brazil and India.
- None of the "extremely hazardous" pesticides can be used in the 27 nations of the European Union.

https://water.usgs.gov/nawqa/pnsp/usage/maps/county-level/
https://www.who.int/publications/i/item/9789240005662

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USA: Ground Zero for Pesticide Use

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- In 2019, 1 out of every 4 pounds of pesticides used in the U.S. are of ingredients that had been banned in the European Union.
- For some of these banned pesticides, the EPA has actually facilitated their use in the U.S. by removing restrictions meant to protect people and the environment.
- **Aldicarb**, for instance- a pesticide banned in 125 countries and one of only 36 pesticides classified as "extremely hazardous" by the World Health Organization- gained legal use on oranges in the U.S. in 2021.

Pesticide Atlas 2023

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The Invisible Residues

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frontiers in Public Health

REVIEW
published: 22 January 2018
doi: 10.3389/fpubh.2017.00361

Check for updates

Ignoring Adjuvant Toxicity Falsifies the Safety Profile of Commercial Pesticides

Robin Mesnage and Michael N. Antoniou*

Gene Expression and Therapy Group, Department of Medical and Molecular Genetics, School of Basic & Medical Biosciences, King's College London, Guy's Hospital, London, United Kingdom

We tested the toxicity of 9 pesticides: 3 major herbicides, 3 insecticides, and 3 fungicides, comparing active principles and their formulations, on three human cell lines (HepG2, HEK293, and JEG3)

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BOTTOM LINE

- **Roundup** was found in this experiment to be 125 times more toxic than glyphosate.
- **Fungicides** were the most toxic from concentrations 300–600 times lower than currently applied agricultural dilutions, followed by herbicides and then insecticides
- 8 formulations out of 9 were up to **1000 TIMES** more toxic than their active principle ingredients. **WHY?????**

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Pesticide industry's dirty little secret: "inert ingredients"

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- ***Surveys disclosed that almost three quarters of the pesticide products contained at least 95% "inerts" by weight.***
- EPA uses a limited set of criteria to assign "inert" ingredients to these lists.
- EPA considers carcinogenicity, adverse reproductive effects, neurotoxicity/chronic effects, developmental toxicity, documented ecological effects and the potential for bioaccumulation.
- EPA does not consider such effects as endocrine disruption, allergenic effects and chemical sensitization.
- **"Nevertheless, the descriptive titles for these groups reveal a simple truth: pesticide products contain a variety of ingredients that either are known to be toxic or have not been adequately tested for toxicity, and the public is denied knowledge of their presence."**

Attorney General of New York State / Environmental Protection Bureau May 2000
www.oag.state.ny.us

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Where are the “Inert” Formulants?

SPEED ZONE BROADLEAF HERBICIDE

NOTIFICATION

JAN 15 2015

EPA Reg. No. 2217-833

ACTIVE INGREDIENT:	
2,4-D, 2-ethylhexyl ester	28.57%
Mecoprop-p, acid	5.88%
Dicamba, acid	1.71%
Carfentrazone-ethyl	0.62%
OTHER INGREDIENTS:	63.22%
TOTAL	100.00%

THIS PRODUCT CONTAINS:

1.53 lb 2,4-dichlorophenoxyacetic acid equivalent per gallon or 18.95%.
0.48 lb (+)-R-2-(2-methyl-4-chlorophenoxy)propionic acid equivalent per gallon or 5.88%.
0.14 lb 3,6-dichloro-o-anisic acid equivalent per gallon or 1.71%.
0.05 lb Ethyl α,2-dichloro-5-[4(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropanoate per gallon or 0.62%

Isomer Specific by AOAC Methods.
Contains petroleum distillates
TRIMEC® is a registered trademark of PBI/Gordon Corporation.

KEEP OUT OF REACH OF CHILDREN

This is the product sprayed in my town park to kill weeks like dandelion, no signage was being used post-spray (as in “stay off the grass”) until neighbors advocated for safer park for children

Pesticides Contain Metals

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Toxicology Reports 5 (2018) 156–163

Contents lists available at ScienceDirect

Toxicology Reports

journal homepage: www.elsevier.com/locate/toxrep

Toxicity of formulants and heavy metals in glyphosate-based herbicides and other pesticides

N. Defarge[a], J. Spiroux de Vendômois[b], G.E. Séralini[a,*]

[a] University of Caen Normandy, Department of Biology and Network on Risks, Quality and Sustainable Environment MRSH, Esplanade de la Paix, 14032 Caen Cedex, France

[b] CRIIGEN, 81 Rue Monceau, 75008 Paris, France

Pesticides were found to contain **arsenic, chromium, cobalt, lead** and **nickel**, which are known to be toxic and endocrine disruptors- in 22 pesticides, including 11 glyphosate-based pesticides.

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Pesticides Contain Solvents

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- **Benzene**
- **Toluene**
- Chloroform
- carbon tetrachloride
- 1,2-dichloroethane
- 1,4-dioxane
- 2-nitropropane
- Exposure to such solvents could partly explain some of the reported excesses of leukemia and non-Hodgkin's lymphoma among farmers.

PMID: 8465174

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Classes of Pesticides

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- **Organochlorine** pesticides: ex. DDT
- **Organophosphate** pesticides: cholinesterase inhibitors ex. Malathion, glyphosate-containing herbicides **but not glyphosate itself**
- **Carbamates:** "weaker" cholinesterase inhibitors ex. Carbofuran
- **Pyrethroids:** while related to naturally occurring pyrethrins, they are mostly synthetic and very strong sensitizing (allergy-inducing) agents, ex. Cyfluthrin Cypermethrin Deltamethrin Permethrin
- **Fungicides:** commonly used on foods like grapes, strawberries, coffee, ex. chlorothalonil, mancozeb, azoxystrobin (most common contaminant pesticide in food in U.S.)

Classes of Pesticides

TOXDetect PROFILE

- **Chlorophenoxy** herbicides: ex. 2,4-D
- **Triazine** herbicides: ex. Atrazine, Simazine
- **Neonicotinoids:** ex. Imidaclopirid
- **Fumigants:** used in air, soil, and on grains and crops post-harvest to reduce insects- a potential source of exposure to pesticide residues on food. ex. methyl bromide (phased out in 2005 but still produced in US for restrictive use)
- **Phosphanoglycine** herbicides: Glyphosate

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Organochlorine Pesticides- Still In Us

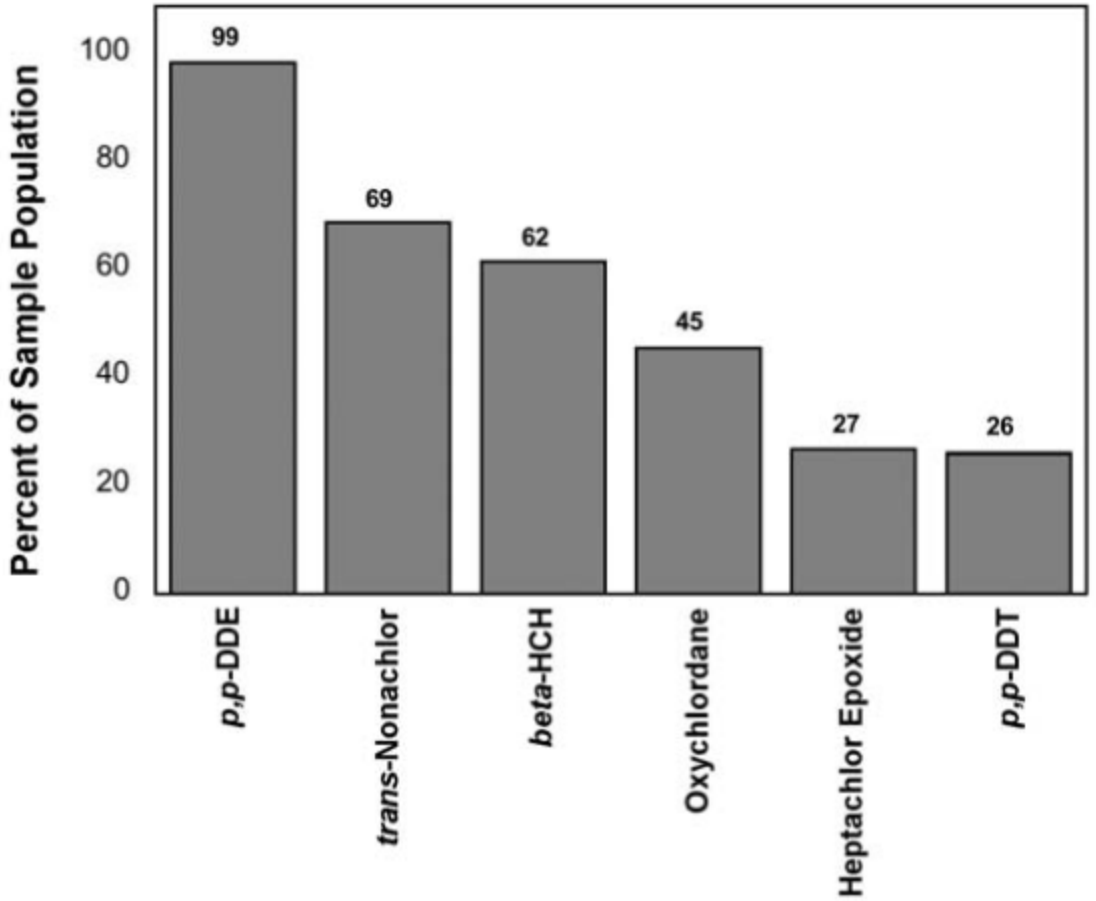

Figure 2. A High Percentage of Those Tested Had Pesticides or Metabolites in Blood. Three of the six organochlorine pesticides found in blood were present in more than 50% of the people whose blood was tested.

Environ Health Perspect, 2004, 112(2): 186-200.

Chlorinated Pesticides

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- Source of Exposure: fat-soluble: found in animal fat (dairy (butter highest), meat, fish) but also found in vegetables w ability to uptake dieldrin (squash, zucchini, cucumber) even if they were grown organically (OC pesticides have long half-lives in soil). Found in homes build before 1988 (Chlordane used in SE US as termiticide) at levels higher than EPA allowable in indoor air.
- Half-lives: Lactation is primary method of reducing body burden in all mammals but absent that source of lowering body burden: 60 days to 10-15 years. Highest body burden found in omental fat.

Clinical Environmental Medicine p. 235-243.

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Chlorinated Pesticides

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- DDE: increased mast cell degranulation, CMI deficiency (increasing risk for herpes zoster), increased risk for pancreatic CA and liver CA (OR 3.2), increased risk for otitis media in children w DDE exposure.
- Conditions: Diabetes, (highest risk w transnonachlor: OR 37.7), obesity, birth defects (cryptorchidism), NHL (OR 5.3 if elevated levels HCB), Parkinsonism, CVD, seminoma, prostate CA, decreased CMI

Fungicides

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- EPOXICONAZOLE used on: wheat, barley, rye, triticale, soybeans, banana, rice, **coffee**, turnips, and red as well as sugar beets. Carcinogen, ovarian cysts, adrenal damage, hypochromic anemia, reproductive toxicant in animals
- TEBUCONAZOLE used on: cherries grapes plums peaches nectarines snap peas, "safe" in US, removed from use in EU due to endocrine disruptor effects
- PROCHLORAZ used on: citrus, stone fruits, grains, almonds banned in US approved for use in S. America, Asia, EU. Known endocrine disruptor

EPA PESTICIDE FACT SHEET: https://www3.epa.gov/pesticides/chem_search/reg_actions/registration/fs_PC-123909_01-Aug-06.pdf

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Organophosphate Pesticides

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- 50% of all insecticide use globally technically does not include glyphosate but may be included as an OP
- Often combined with solvents (causing axonal and myelin degeneration) and arsenic (high ROS generation) and contain metals (predominately arsenic)
- Sources: indoor and outdoor spraying, plasticizers, flame retardants, lubricants, non-organic food (children eating conventional food have **NINE** times higher urinary levels of malathion and chlorpyrifos
- NOT just cholinesterase inhibitors! Evidence for endocrine disruption (obesity, diabetes), lowered IQ, ADHD (chlorpyrifos),PDD, Cancer: NHL, glioma, lung CA.
- Half-life: 2-50 days depending on PON-1 function (low activity linked to increased risk for Parkinsons, lymphoma, glioma, depression, bipolar disorder)

Clinical Environmental Medicine p 247-253.

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OP- Not Just Acetylcholinesterase Deactivation

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OP also deactivate:

- Serine hydrolase
- Carboxylesterase
- The above are enzymes found in serum, liver, brain, lung
- OP cause mitochondrial toxicity leading to neuronal damage and oxidative damage (8-OHdG)
- These mechanisms explain how OPs cause inflammatory changes, oxidative stress and neurodegeneration.

.

Neurotoxicology 2012;33:575-84./Chem Biol Interact 2005;157-158:277-83./Chem Biol Interact 2010;187:344-8./Toxicol Lett 2001;120:343-51./Toxicol Appl Pharmacol 1999;160(1):33-42.

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IMMUNOTOXICITY

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- Greenhouse workers – decreased Th1, elevated IL-22 (cancer initiation)
- Carbamate pesticides – suppression of Th1 cells and the IFN-γ-induced production of NO in macrophages (cancer)
- Carbamates – shift immune response to Th2 through the inhibition of IFN-γ, increase IL-4 and IL-10 production, and reduction of pro-inflammatory cytokine (IL-1β and TNF-α) production by macrophages.
- Chlorpyrifos- decrease in NK cells
- Parathion, chlorpyrifos- increase TNF-α, IL-6 and IL-1β in human hepatocellular carcinoma (HepG2) cells, suppressing paraoxonase 1 (PON1) gene (increased susceptibility to organophosphate toxicity)

PMID: 27600395

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IMMUNOTOXICITY

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- Malathion: Mast cell degranulation
- Agricultural exposure in children: Th2 dominance-asthma
- 4 carbamates and 4 organophosphates: show in vitro ↓IL-2
- Herbicides: ↑odds of asthma 4.5
- Pesticides: ↑odds of asthma 2.39
- Chlorpyrifos: ↑ incidence allergies
- DDE and HCB: ↑IgE levels: eczema, asthma
- Atrazine: ↓Natural Killer cell function

Toxicol Lett 1997;93(1):73-82./Environ Health Perspect. 2006;114(2):1916-1922./Immunopharmacol Immunotoxicol 1993;15(2-3):199-215/Environ Health Perspect 2003;112:760-765./Environ Health Perspect 1999;107:895-899.
Arch Environ Health 2001;56(6): 485-492./Ind Health 2003:41(3):158-166./Chem Biol Interact 2003;145):311-319.

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OPs are Endocrine Disruptors

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- OPs disrupt glucose homeostasis leading to elevated serum glucose levels due to altered signaling in pancreatic B cells.
- Oxidative stress due to OPP exposure can reduce glucose-stimulated insulin secretion resulting in increased serum glucose levels.
- OPPs inhibit thyroid hormone receptor binding
- Methoxychlor alters estradiol metabolism
- Chlorpyrifos inhibits adrenal steroidogenesis

Toxicology (2012), http://dx.doi.org/10.1016/j.tox.2012.09.011

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Organophosphate Endocrine Disruption Most Vulnerable Population: Fetus

Prenatal exposures are associated with:

- reduced birth weight
- head circumference
- gestational length

Prenatal and postnatal exposures have been linked with:

- altered reflexes
- inattention
- behavior problems
- lowered IQ
- developmental disorders in infants and toddlers
- potential associations with pediatric asthma, cancer, and birth defects

Environ Health Perspect 2011;119:1182-8./*Neurotoxicology*. 2013;39: 158–168.
Environ Health Perspect 2010;118:1768-74.

Organophosphate Endocrine Disruption Most Vulnerable Population: Fetus

Prenatal exposure in greenhouse workers:

- Boys- decrease in penile length and reduced testicular volume and lower serum concentrations of testosterone
- Girls- earlier breast development increased androstenedione levels (leading to estradiol via aromatization)

Environ. Health Perspect. 2008;*116*:566-572./ Int J Androl 2012;35(3):265-72. / Int J Androl 2012;35(3):273-82.

Organophosphate Pesticides Toxic Effects

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- Non-Hodgkin's lymphoma (farmers)
- Leukemia (farmers)
- Glioma (applicators)
- Lung Cancer (applicators)
- Cardiotoxicity: prolonged QT interval, ventricular arrhythmia, hypertension, sinus tachycardia or bradycardia (post-acute exposure)
- Pediatric ADHD, lowered IQ, pervasive developmental disorder, impaired social functioning
- Delayed Polyneuropathy (post-acute exposure)

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Adults/OP Toxic Effects

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- Pesticide applicators and their families: increased cancer incidence (lung, pancreatic, colon and rectal, leukemia, non-Hodgkin lymphoma, multiple myeloma, breast, bladder, prostate, brain, melanoma and childhood cancers.
- Higher risk for cognitive decline, dementia and mortality in Hispanic Americans w 5 year prior hx OP exposure (correlated with low adiponectin)
- Occupational exposure: deficits in reaction time, working memory and mental processing, depression, motor steadiness, tension and fatigue.
- Arrythmias, heart disease, congestive heart failure in those with previous acute exposure (N = 7,561 exposed)

Environ Res. 2018;160:132-139./Environ Health Perspect 2006;114:691-6. Environ. Health Perspect. 2010:118, 1117-1125./PLoS ONE 10(9): e0137632. doi:10.1371/journal.pone.0137632/ Toxicol Indust Health 2015;32(8):1527-1536./ Int J Occ Environ Health. 2016;22(1):68-79./ Cancer Causes Control 2001 Aug;12(6):509-17./Cancer Res 1992 May 1;52(9):2447-55./Toxicology2007,229:194-205.

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Adults/OP Toxic Effects

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- Depression (applicators)
- Impaired neurobehavioral function: psychomotor speed, executive function, visuospatial ability, working and visual memory
- Rheumatoid arthritis (applicators)
- Cutaneous melanoma (farmers)
- Hypothyroidism (farmers)
- Atopic asthma
- Allergic and nonallergic respiratory symptoms

OP Exposure

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- Higher risk for cognitive decline, dementia and mortality in Hispanic Americans w 5 year prior hx OP exposure (correlated with low adiponectin)
- Occupational exposure: deficits in reaction time, working memory and mental processing, depression, motor steadiness, tension and fatigue. Delayed Polyneuropathy (post-acute exposure)
- Arrythmias, heart disease, congestive heart failure in those with previous acute exposure (N = 7,561 exposed)
- Children: Pediatric ADHD, lowered IQ, pervasive developmental disorder, impaired social functioning

Environ Res. 2018;160:132-139./Environ Health Perspect 2006;114:691-6. Environ. Health Perspect. 2010:118, 1117-1125./PLoS ONE 10(9): e0137632. doi:10.1371/journal.pone.0137632/ Toxicol Indust Health 2015;32(8):1527-1536./ Int J Occ Environ Health. 2016;22(1):68-79./ Cancer Causes Control 2001 Aug;12(6):509-17./Cancer Res 1992 May 1;52(9):2447-55./Toxicology2007,229:194-205.

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TOXDetect Profile
Pesticide Metabolites

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14) 3-Phenoxybenzoic Acid (3-PBA)

Pyrethoids, Permethrin, Cypermethrin, Cyhalothrins, Fenpropathrin, Deltamethrin, Trihalomethrin

Parent Compound: Pyrethroids

Pyrethroids are widely used in agriculture, household insect control, and veterinary medicine. Pyrethroids work by targeting the nervous system of insects, causing hyperexcitation and paralysis. The most common potential impacts to health include neurobehavioral, neurodevelopmental, and endocrine disruption. Exposure has also been associated with an increased risk of all-cause and cardiovascular disease mortality.

TOXDetect Profile
Pesticide Metabolites

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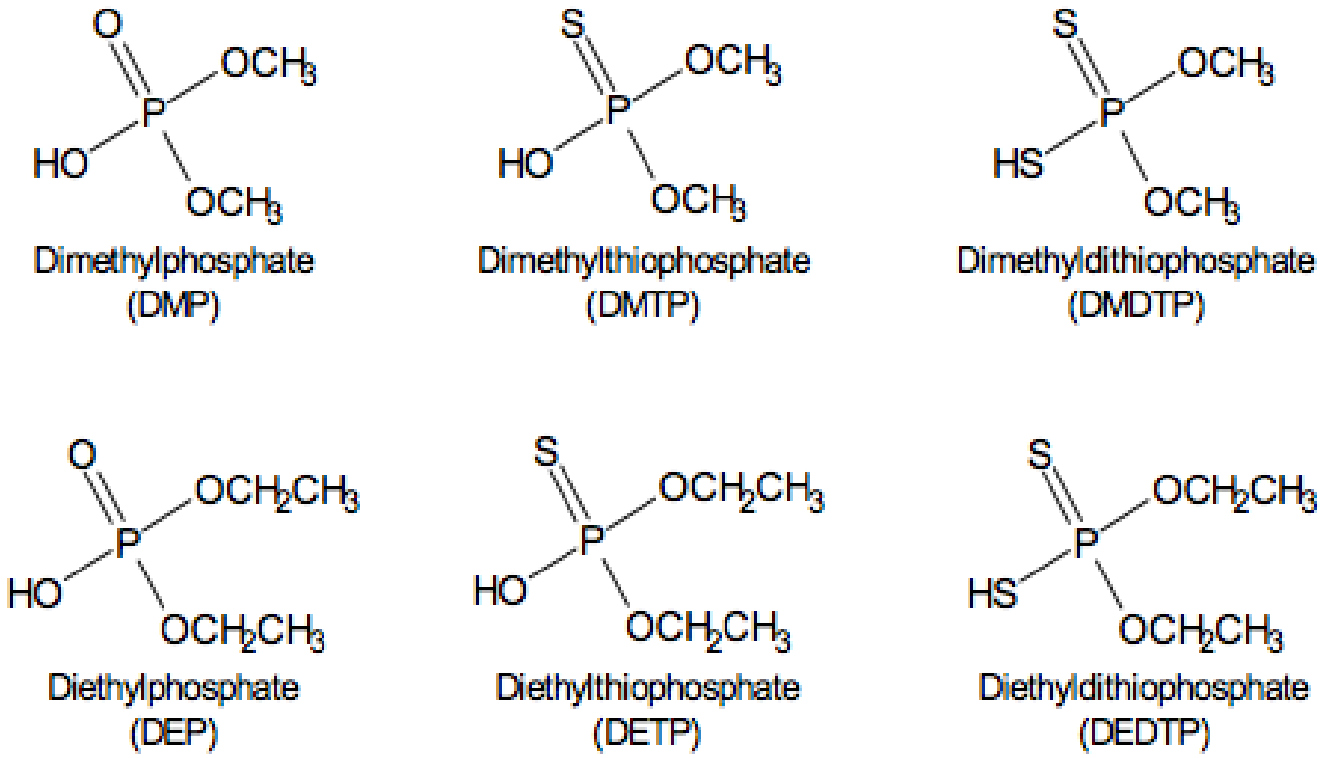
15) **Diethylphosphate (DEP)**
Organophosphates

Parent Compound: Organophosphates
Organophosphate pesticides are widely used in agriculture to control pests, as well as in residential settings to manage insects and rodents. The organophosphate pesticides work by inhibiting the activity of acetylcholinesterase, an enzyme essential for proper nerve function. Exposure to organophosphates has been associated with neurological deficits, neurodegenerative diseases, peripheral nerve effects, and neurodevelopmental issues. Additionally, long-term exposure has been linked to oxidative stress, psychological effects, and liver function abnormalities.

We metabolize all organophosphate pesticides into some combination of either:

1. Diethylphosphate (DEP) OR
2. Dimethylphosphate (DMP) urinary metabolites

Figure 1. Structures of dialkylphosphate metabolites of organophosphorus pesticides.



Int. J. Environ. Res. Public Health 2011, 8, 3063-3098; doi:10.3390/ijerph8083063

TOXDetect Profile
Pesticide Metabolites

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13) **2,4-Dichlorophenoxyacetic Acid (2,4-D)** 2,4-Dichlorophenoxyacetic Acid (2,4-D)

5.10

Parent Compound: 2,4-Dichlorophenoxyacetic Acid (2,4-D)

2,4-Dichlorophenoxyacetic Acid (2,4-D) is one of the most widely used herbicides in the world. It is commonly used in agriculture and landscaping. Chronic exposure to lower levels of 2,4-D has been associated with potential health effects, including endocrine disruption, reproductive effects, developmental effects, and increased risk of non-Hodgkin lymphoma.

2,4-D is one of the most widely used **herbicides** worldwide and the third most widely used herbicide in the USA and Canada: it is the main ingredient in over 600 products available on the market in the U.S and 1500 globally.

PMID: **29203058**

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2,4-D (Dichlorophenoxyacetic acid)

Widely used in agriculture since 1946 for weed control.

Sprayed on:

wheat and small grains, sorghum, corn, rice, sugar cane, soybeans, coffee, rangeland and pasture. It is also used on rights-of-way, roadsides, non-crop areas, **forestry**, **lawn, parks**, **turf, golf courses** and to kill aquatic weeds.

2,4-D + Glyphosate = Enlist Duo

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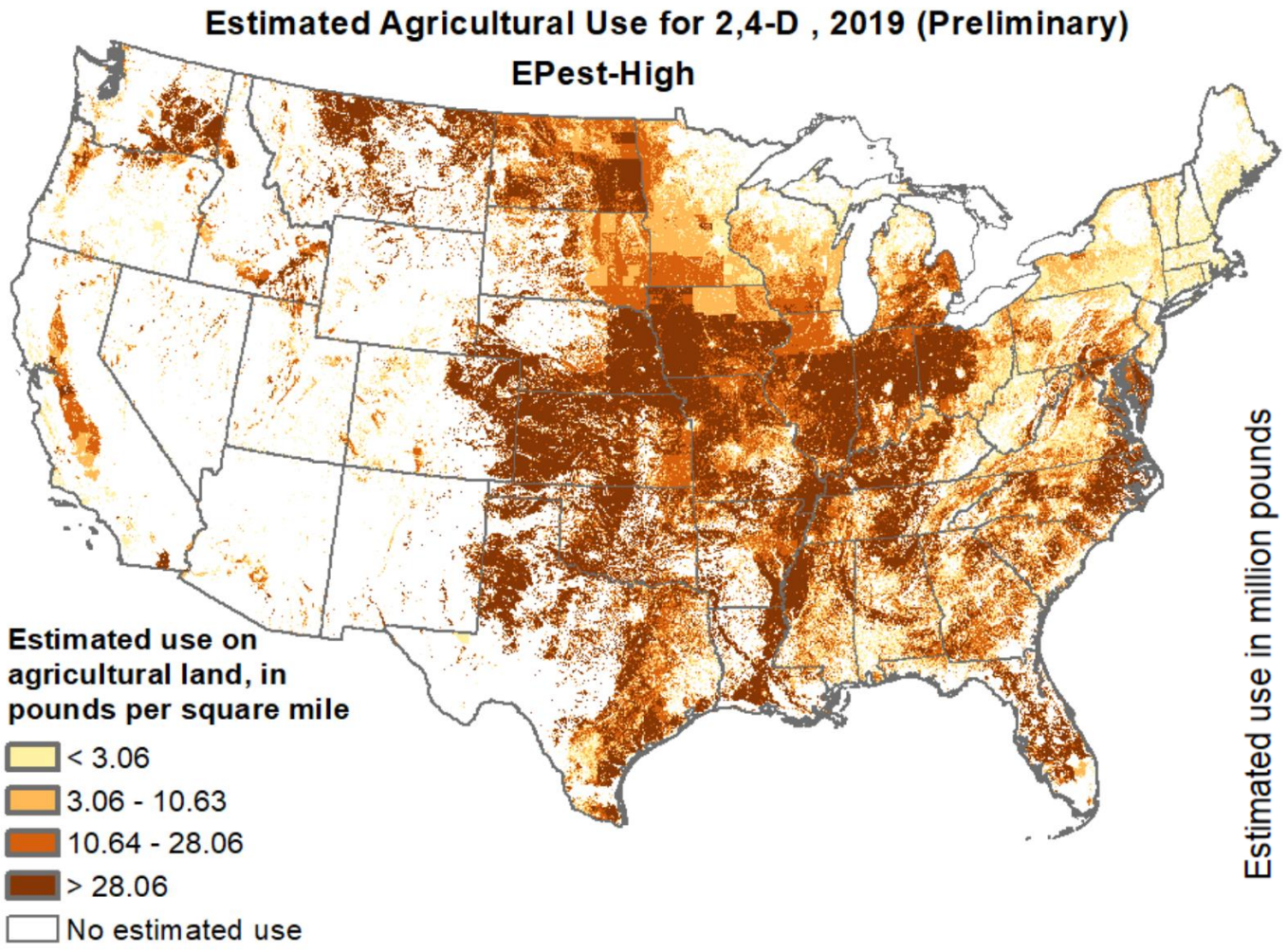

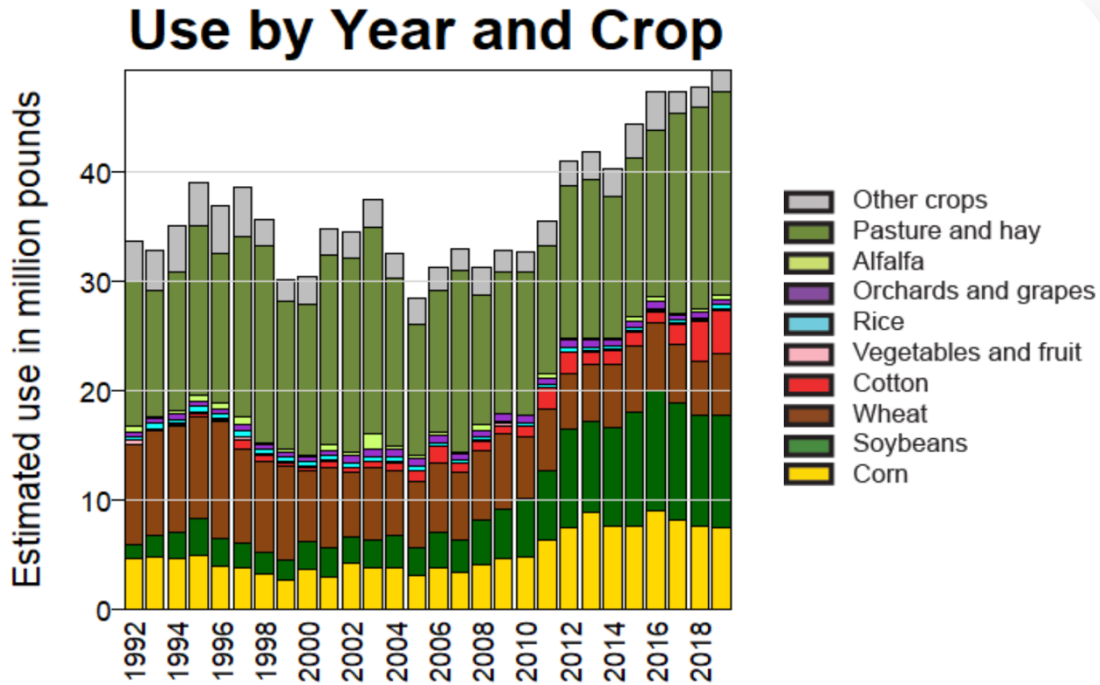

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2,4-D (Dichlorophenoxyacetic acid)

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Demographic Categories	Survey (Years)	Geometric Mean (95% CI)	95th Percentile (95% CI)	Sample Size
Total population	11-12	0.342 (.310-.378)	1.62 (1.35-1.91)	2365
Total population	13-14	0.328 (.299-.361)	1.49 (1.19-1.86)	2669
Total population	15-16	0.359 (.325-.397)	1.60 (1.36-2.09)	3033
Age 3-5 years	15-16	0.893 (.778-1.03)	4.24 (2.67-10.0)	502
Age 6-11 years	11-12	0.541 (.467-.627)	2.92 (1.62-5.02)	385
Age 6-11 years	13-14	0.597 (.448-.794)	4.00 (1.86-11.2)	421
Age 6-11 years	15-16	0.615 (.523-.724)	2.68 (1.53-9.91)	418
Age 12-19 years	11-12	0.255 (.218-.300)	.899 (.784-1.35)	380
Age 12-19 years	13-14	0.286 (.255-.320)	1.09 (.784-1.25)	428
Age 12-19 years	15-16	0.284 (.248-.326)	.909 (.691-1.57)	404
Age 20+ years	11-12	0.34 (.301-.385)	1.62 (1.25-1.93)	1600
Age 20+ years	13-14	0.314 (.288-.342)	1.37 (1.15-1.64)	1820
Age 20+ years	15-16	0.337 (.304-.375)	1.51 (1.23-1.95)	1709

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Toxicity of 2,4-D

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- Animal studies show exposure to 2,4-D during pregnancy or lactation lead to distribution of 2,4-D to the fetus or to milk.
- IARC- possible human carcinogen 2015
- Odds ratio Non-Hodkin's Lymphoma 1.73 PMID: 28476329
- Large B-cell lymphoma PMID: 36207110
- Thyroid, kidney damage in animal studies
- NHANES: Among subjects with low HDL (25 mg/dL), urinary 2,4-D was associated with:
  - increased levels of triglycerides
  - Increased fasting insulin, C-peptide
  - Increased TSH
  - ALL of above more apparent in susceptible subpopulations: HgbA1c > 5.1% or T4 ≤ 8.5 µg/dl
  - subjects with high HDL did not experience adverse 2,4-D-associated effects.

PMID: 20187939

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What Explains this Association?

TOXDetect PROFILE

- 2,4-D interferes with thyroid hormone transport
- Subclinical hypothyroidism = lower HDL, increased total cholesterol
- Low HDL – increases risk for insulin resistance, hypertension, association not causation, what's the cause?
- **OXIDATIVE STRESS**

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2,4-D and Liver Function

TOXDetect PROFILE

Common markers associated with liver inflammation and damage in animal/human studies of 2,4-D exposure:

Decrease in antioxidant capacity:

↓ catalase, superoxide dismutase, GST, GPx and hepatic GST

↑ levels of malondialdehyde.

Exposure also results in impairment in liver energetic function, blood glucose alterations and decrease in hepatic glycogen levels.

PMID: 38250991

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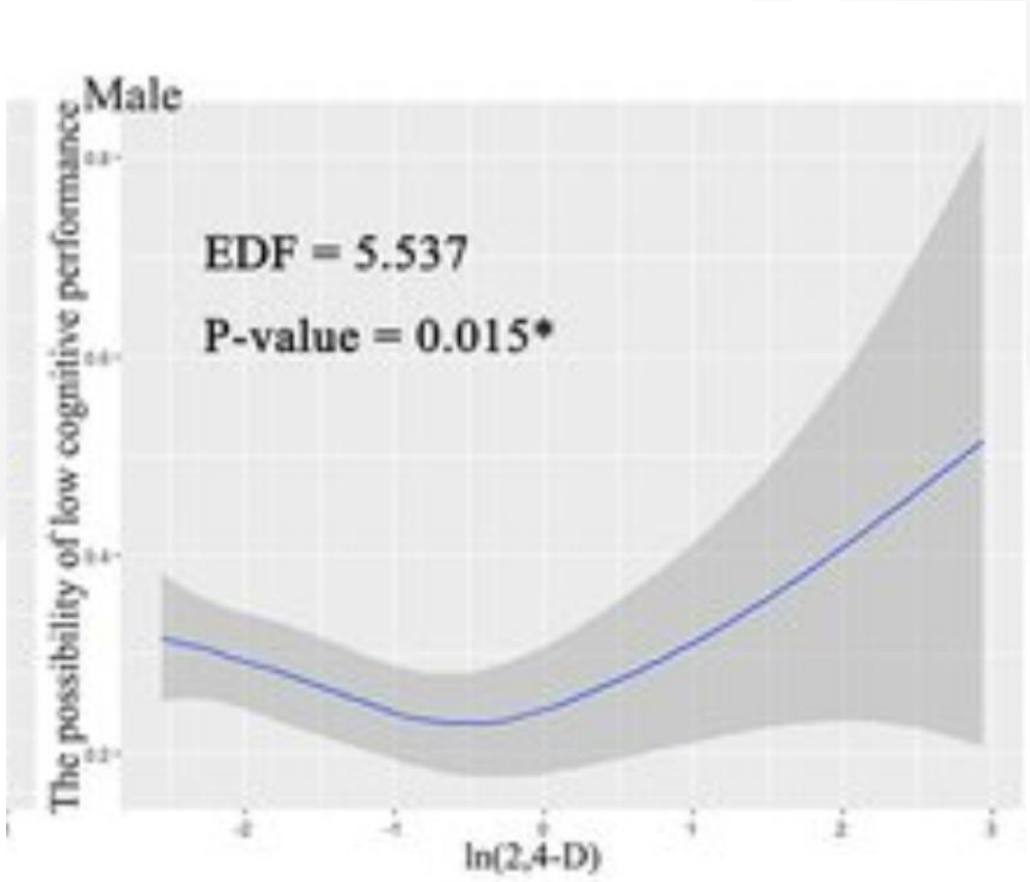
2,4-D and Cognitive Function

TOXDetect PROFILE

- 1364 older U.S. adults (60+ years) and urine levels of 2,4-D
- Conclusion: "There is a U-shaped relationship between human urinary 2,4-D concentrations and cognitive impairment in older U.S. adults, especially in **males**, so controlling 2,4-D exposure within an appropriate range is particularly important for cognitive function."



J Expo Sci Environ Epidemiol **34**, 308–316 (2024)

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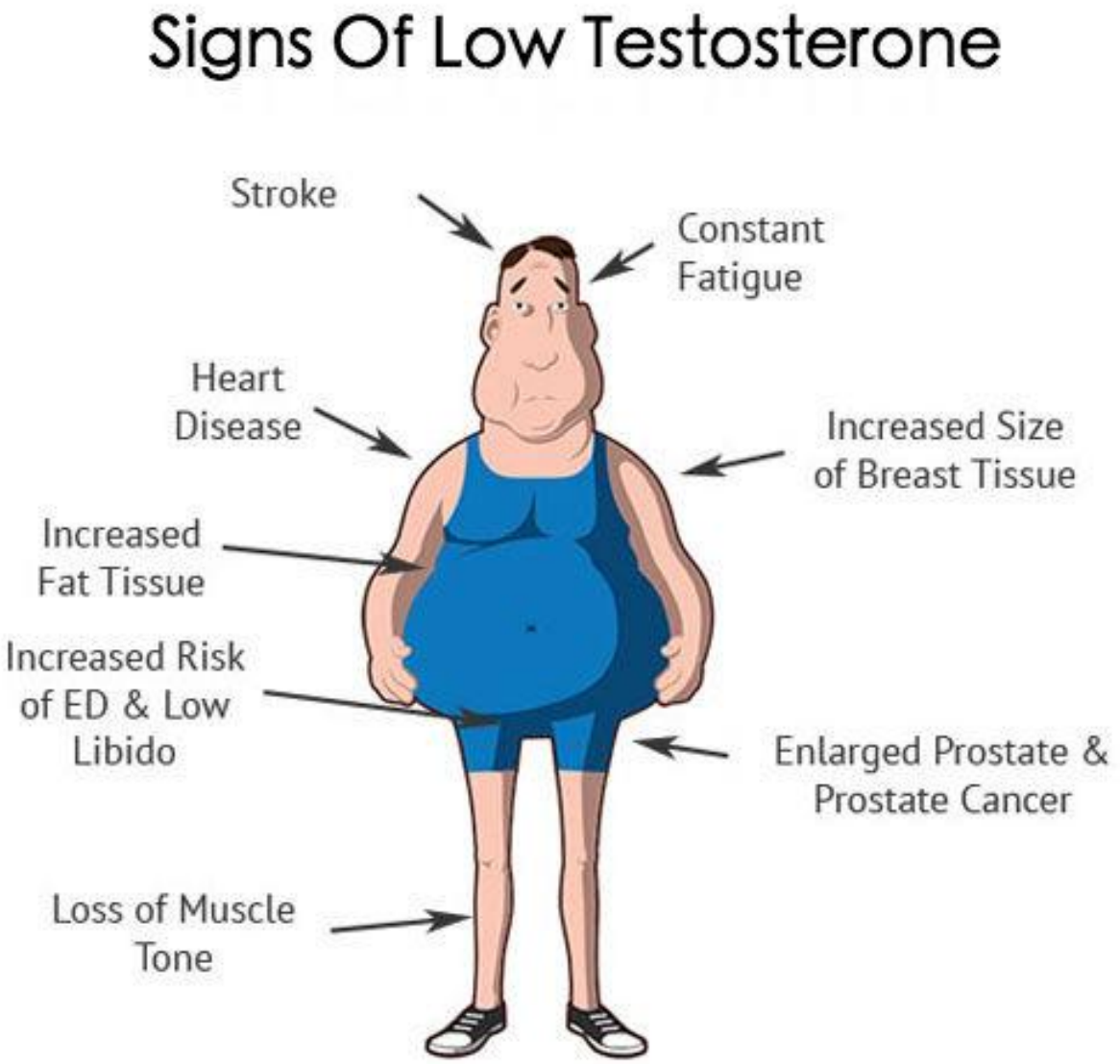
2,4-D and Testosterone

TOXDetect PROFILE



Significant negative association between urinary 2,4-D and mean serum testosterone among 456 U.S. adult males (β = - 11.4 ng/dL, p = 0.02)

PMID: 34985686

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2,4-D Persistent Pesticide-Avoidance is Crucial

- ½ life in water- from 15-300 days
- According to EPA data, 2,4-D contaminates drinking water of **15,811,375** people in the U.S.

https://www.ewg.org/tapwater/chemical-contaminants.php

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2,4-D in Gluten-Free Food

TOXDetect PROFILE

- In one non-published study by GMO Science and Moms Across America trace or quantifiable levels of 2,4-D were found in **54% of 46** gluten-free food samples tested (bread, pasta, crackers, snacks, flour, dessert mixes, and chips).

https://www.momsacrossamerica.com/glutenfree_food_test_results

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Aside: Gluten-Free? Not

In same study by GMO Science and Moms Across America 4 out of 46 foods that were labeled gluten-free:

- **Simple Mills Brownie mix (31.7 ppm gluten),**
- **Made Good Soft Baked Double Chocolate cookies (56.1 ppm gluten)**
- **Trader Joe's Almost Everything Bagels (269.8 ppm gluten),**
- **Simple Mills almond flour crackers (59.4 ppm gluten)**
- Levels above the FDA allowable 20 ppm of gluten should legally be recalled. The Gluten-Free Certification Organization (GFCO) states that gluten-free food should have less than 10 ppm.

Elimination of 2,4-D

TOXDetect PROFILE

- OAT-1 transporter protein in kidneys responsible for elimination of 2,4-D. This is phase III detoxification and controls renal excretion.
- The most abundant 2,4-D conjugates found in animal urine were those with glycine (about 34% of the administered dose at 120 hours) and glucuronide (7%), and were more abundant than the parent compound, 2,4-D.
- There has been little research done on human metabolism of 2,4-D. It appears to be excreted unmetabolized OR conjugated.
- Supporting glucuronidation MAY assist in 2,4-D elimination: glycine, dandelion root, rooibos, cruciferous vegetables, resveratrol, astaxanthin, curcumin

PMID: 26167297

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TOXDetect Profile
Pesticide Metabolites

TOXDetect PROFILE

15) Diethylphosphate (DEP)

Organophosphates

Parent Compound: Organophosphates

Organophosphate pesticides are widely used in agriculture to control pests, as well as in residential settings to manage insects and rodents. The organophosphate pesticides work by inhibiting the activity of acetylcholinesterase, an enzyme essential for proper nerve function. Exposure to organophosphates has been associated with neurological deficits, neurodegenerative diseases, peripheral nerve effects, and neurodevelopmental issues. Additionally, long-term exposure has been linked to oxidative stress, psychological effects, and liver function abnormalities.

About 75% of registered organophosphorus insecticides are metabolized in the body to measurable dialkyl phosphate metabolites.

TOXDetect PROFILE

	DMP	DMTP	DMDTP	DEP	DETP	DEDTP
Pesticide (CAS number)	**Dimethyl-phosphate (813-79-5)**	**Dimethylthio-phosphate (1112-38-5)**	**Dimethyldithio-phosphate (756-80-9)**	**Diethyl-phosphate (598-02-7)**	**Diethylthio-phosphate (2465-65-8)**	**Diethyldithio-phosphate (298-06-6)**
Azinphos methyl	•	•	•			
Chlorethoxyphos				•	•	
Chlorpyrifos				•	•	
Chlorpyrifos methyl	•	•				
Coumaphos				•	•	
Dichlorvos (DDVP)	•					
Diazinon				•	•	
Dicrotophos	•					
Dimethoate	•	•	•			
Disulfoton				•	•	•
Ethion				•	•	•
Fenitrothion	•	•				
Fenthion	•	•				
Isazaphos-methyl	•	•				
Malathion	•	•	•			
Methidathion	•	•	•			
Methyl parathion	•	•				
Naled	•					
Oxydemeton-methyl	•	•				
Parathion				•	•	
Phorate				•	•	•
Phosmet	•	•	•			
Pirimiphos-methyl	•	•				
Sulfotepp				•	•	
Temephos	•	•				
Terbufos				•	•	•
Tetrachlorvinphos	•					

Int J Environ Res Public Health 2011;8:3063-3098.

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TOXDetect PROFILE

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Azinphos methyl	•	•	•			
Chlorethoxyphos				•	•	
Chlorpyrifos				•	•	
Chlorpyrifos methyl	•	•				
Coumaphos				•	•	
Dichlorvos (DDVP)	•					
Diazinon				•	•	
Dicrotophos	•					
Dimethoate	•	•	•			
Disulfoton				•	•	•
Ethion				•	•	•
Fenitrothion	•	•				
Fenthion	•	•				
Isazaphos-methyl	•	•				
Malathion	•	•	•			
Methidathion	•	•	•			
Methyl parathion	•	•				
Naled	•					
Oxydemeton-methyl	•	•				
Parathion				•	•	
Phorate				•	•	•
Phosmet	•	•	•			
Pirimiphos-methyl	•	•				
Sulfotepp				•	•	
Temephos	•	•				
Terbufos				•	•	•
Tetrachlorvinphos	•					

Int J Environ Res Public Health 2011;8:3063-3098.

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Dialkyl Metabolites

TOXDetect PROFILE

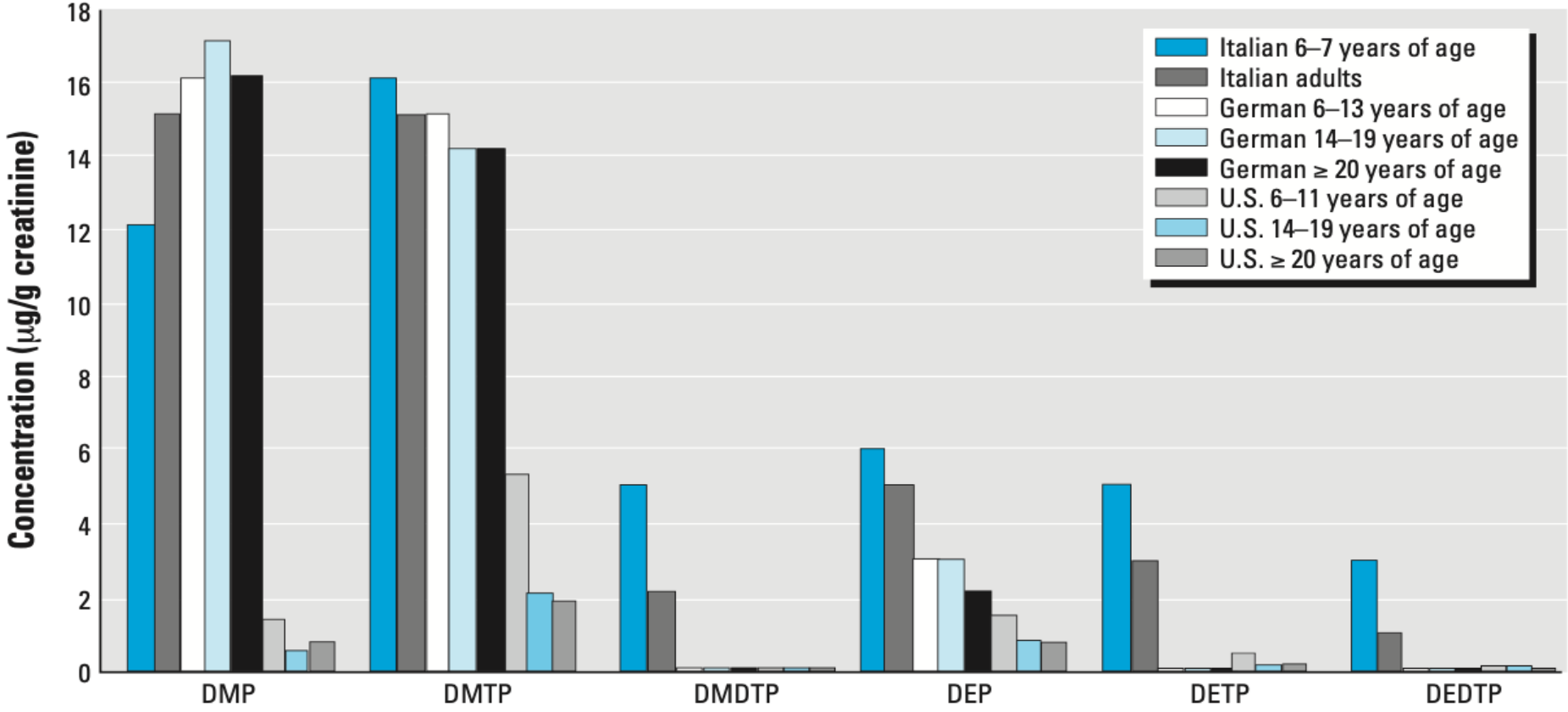

Figure 4. Population-based median DAP concentrations in the United States, Italy (Aprea et al. 1996, 2000), and Germany (Hardt and Angerer 2000; Heudorf and Angerer 2001).

PMID: 14754573

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Organophosphate Pesticides

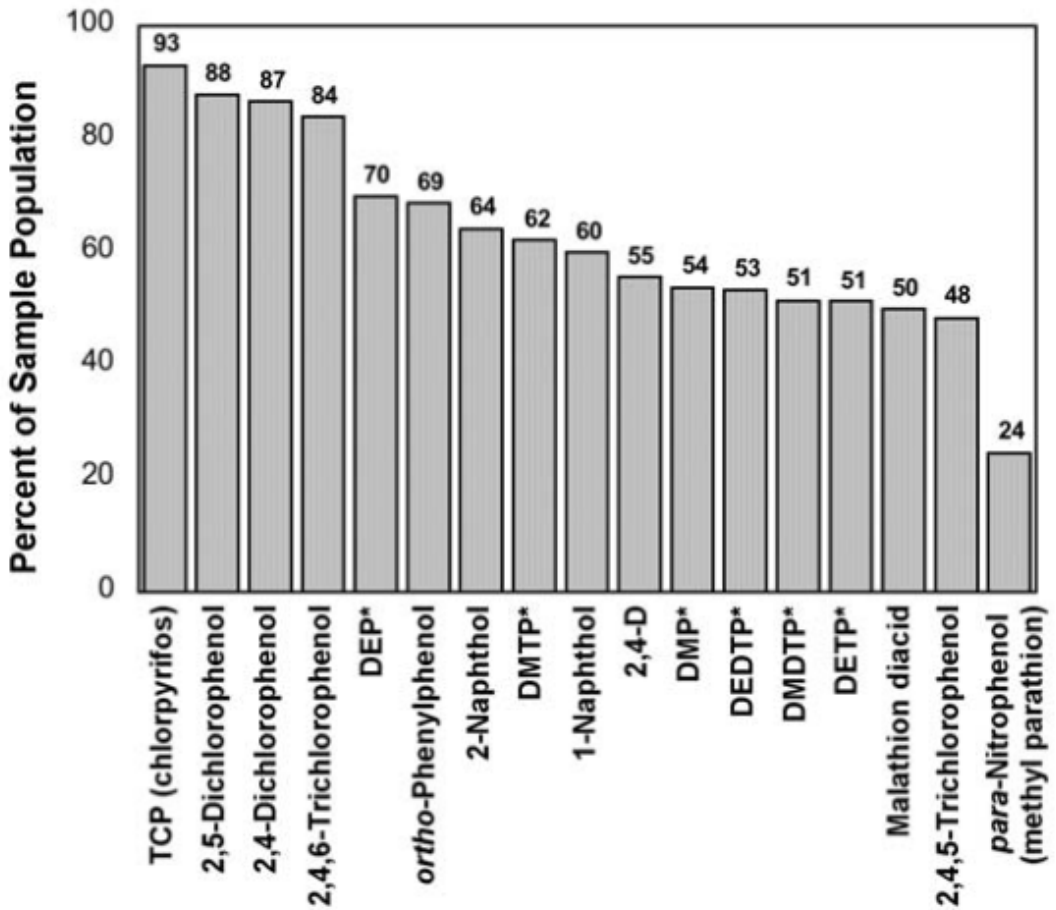

Figure 1. A High Percentage of Those Tested Had Pesticides or Metabolites in Urine. Fifteen of the pesticides or metabolites found in urine were present in 50% or more of people whose urine was tested.

Environ Health Perspect, 2004, 112(2): 186-200.

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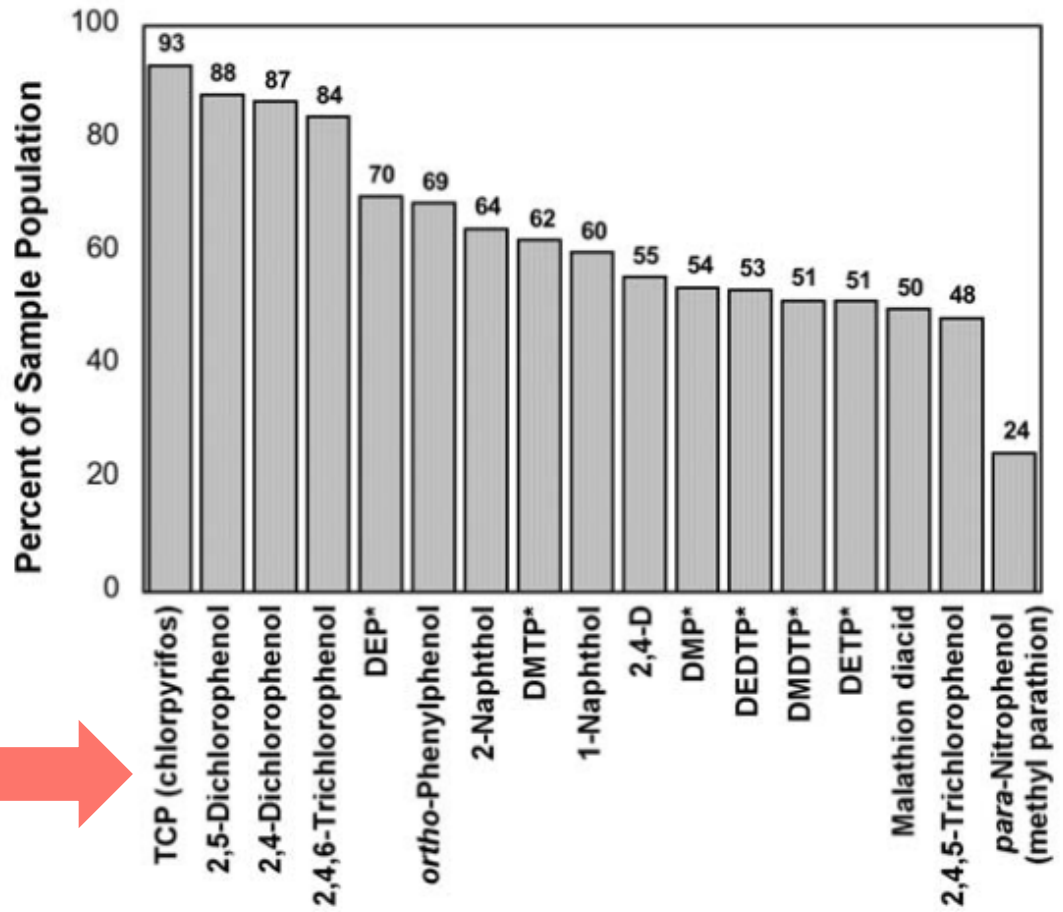
Organophosphate Pesticides



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Children are Vulnerable

TOXDetect PROFILE

- Chlorpyrifos (Dursban, Lorsban, Brodan) detected in over 90% of children's urine
- Pyrethrin metabolite (3-BPA) in 60-100% of children's urine
- Diazinon (Spectracide) 77-100% of children's urine
- Analysis of NHANES subset: 1,139 children age 8-15. Children with higher metabolite levels were significantly more likely to be diagnosed with **ADHD** than children with lower exposure.

Environ Health Perspect 2010;118:1768-74. Pediatrics 2010;125:e1270-7.

Some of the Most Toxic Pesticides = DEP Metabolites

TOXDetect PROFILE

Organophosphate Pesticides that are converted to DEP

Chlorethoxyphos	Ethion
Chlorfenvinphos	Malathion
Chlorpyrifos- methyl	Parathion
Coumaphos	Phorate
Diazinon	Sulfotep
Dioxathion	TEPP
Disulfoton	Terbufos
Dimathoate	Triazophos

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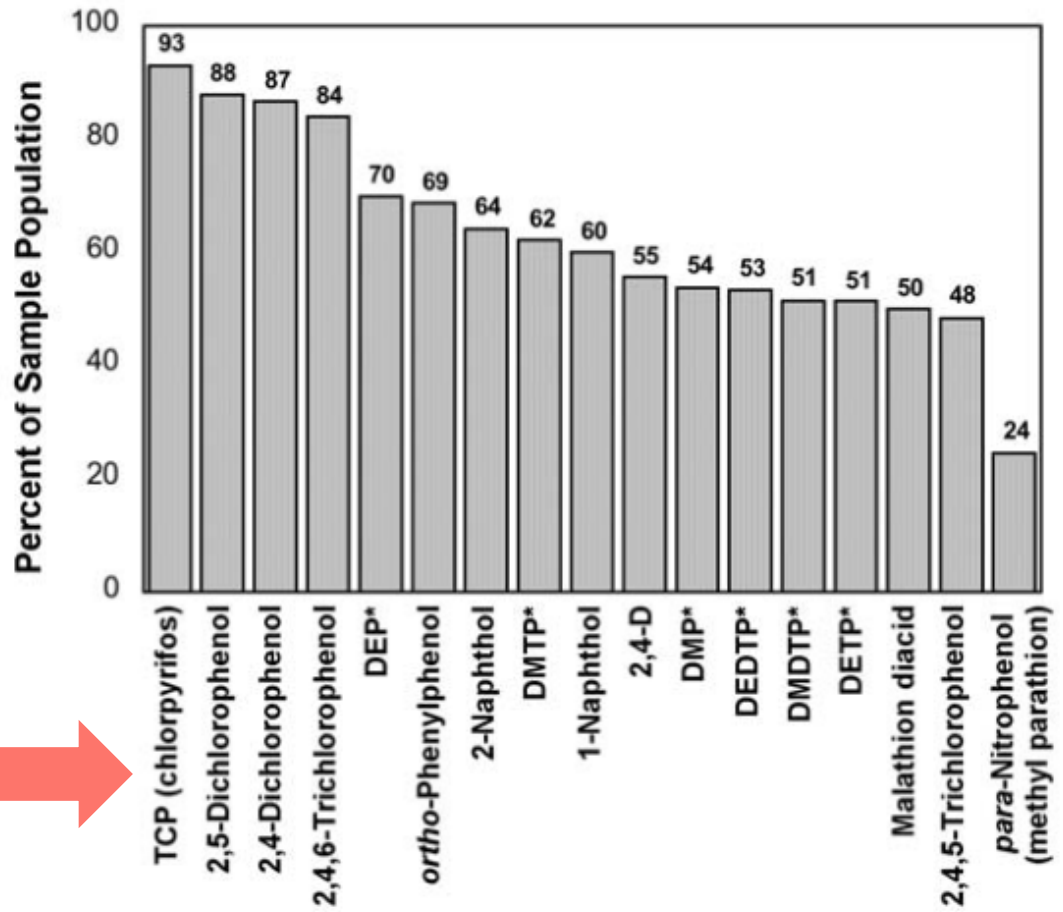
Chlorpyrifos: The DDT of our Time

- **2007:** Pesticide Action Network and the Natural Resources Defense Council file a legal petition against the U.S. EPA calling for a full chlorpyrifos ban, represented by the attorneys at Earthjustice
- In November 2023, the 8th Circuit Court of Appeals reversed the EPA's ban on chlorpyrifos enacted in 2021.
- In rolling back this ruling, the 8th Circuit Court will open the market for chlorpyrifos to be used in food production starting in 2024- which would continue until the EPA reinstates the ban.

Organophosphate Pesticides



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Environ Health Perspect, 2004, 112(2): 186-200.

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Chlorpyrifos: the "Coca-Cola of Pesticides"

TOXDetect PROFILE

- In 2017: 44,000 American farms collectively used between 6-10 million pounds of chlorpyrifos each year on everything from corn, soybeans, asparagus, citrus, peaches, strawberries, broccoli, cauliflower, onions, walnuts, wheat and cranberries.

- Prior to the recent ban in 2021, More than half of all apples and broccoli in the U.S. were sprayed with chlorpyrifos.

- Chlorpyrifos is used on corn: feedstock that is residual in milk, eggs, and meat.

- The most recent USDA/FDA data from 2015 – 2019 shows that chlorpyrifos residues were detected on 37 different foods some above allowable levels.

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EPA: Chlorpyrifos in Drinking Water and Air

TOXDetect PROFILE

In its 2016 Refined Drinking Water Assessment, EPA found that drinking water across the nation is likely contaminated with unsafe levels of chlorpyrifos.

EPA'S high end estimates indicate that in the most contaminated areas, chlorpyrifos contamination may be 12,000 times higher than levels of concern. Reports do not specify locations.

Chlorpyrifos is found at unsafe levels in the air in 2016 at schools, homes, and communities in agricultural areas.

https://www.regulations.gov/document/EPA-HQ-OPP-2015-0653-0437
https://www.epa.gov/pesticides/updated-human-health-risk-analyses-chlorpyrifos

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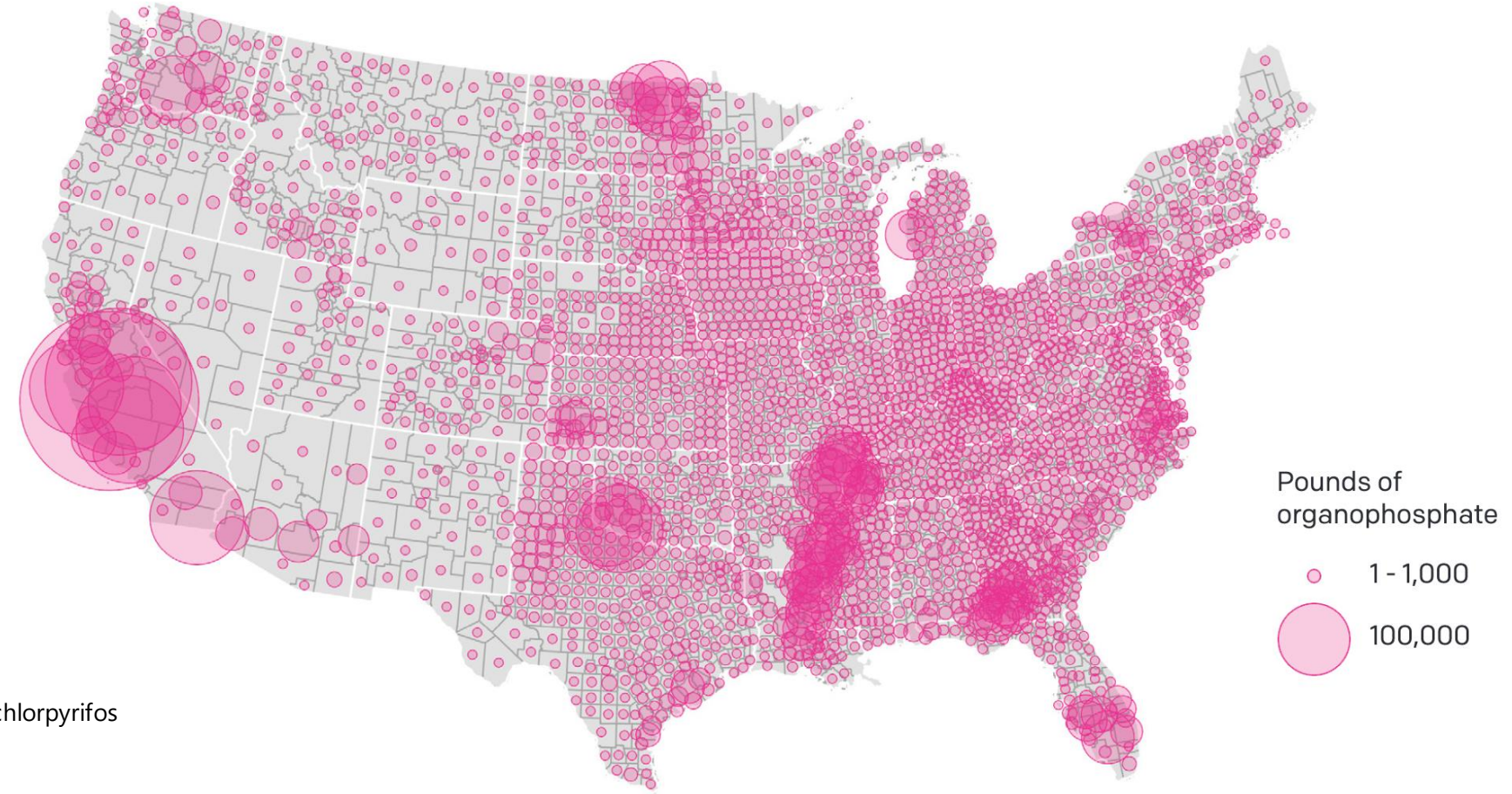
2017 USGS E-pest Low Model (not incl. golf courses)

TOXDetect PROFILE

REPORT FINDINGS

Chlorpyrifos Hot Spots Across the United States



https://earthjustice.org/wp-content/uploads/report_final_chlorpyrifos_aug-2021.pdf

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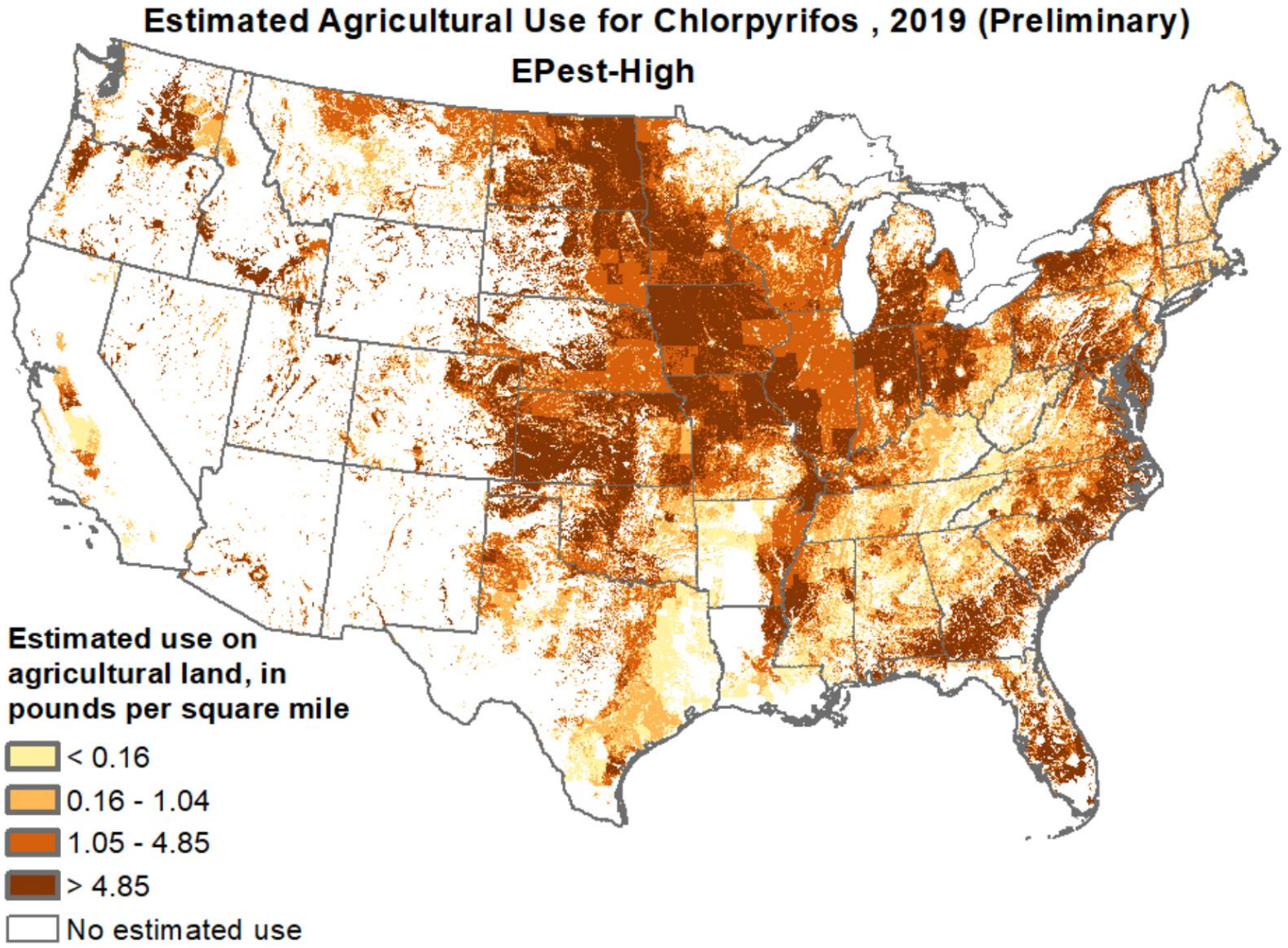
USGS Pesticide Use Map for 2019

TOXDetect PROFILE



https://water.usgs.gov/nawqa/pnsp/usage/maps/

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Ubiquitous Pesticide

TOXDetect PROFILE

- First registered in 1965 **chlor**pyrifos is a chlorinated organophosphate (OP) insecticide. (The chlorinated part of this pesticide makes it unique and fat-soluble)
- Before regulatory action by the EPA to phase out residential use began in 2000, CPF applications were particularly heavy in **urban** areas, where the exposed populations included pregnant women (Berkowitz et al. 2003; Whyatt et al. 2002, 2003).
- In a sample of pregnant women in New York City (Perera et al. 2002) detectable levels of CPF were found in 99.7% of personal air samples, 100% of indoor air samples, and 64–70% of blood samples collected from umbilical cord plasma at delivery (Whyatt et al. 2002).

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Chlorpyrifos-GI toxic

TOXDetect PROFILE

- Chlorpyrifos causes dysbiosis and leaky gut leading to lowered insulin sensitivity and promoting obesity in animal models.
- Exposure to chlorpyrifos in model of human intestine inoculated w human feces induced dysbiosis with proliferation of Bacteroides sp. and decreased levels of Lactobacillus sp. and Bifidobacterium sp.

- **Chlorpyrifos and atrazine together have strong synergistic effect and increase susceptibility to viral infections in amphibians.**

PMID: 19415385/PMID: 30744700/PMID: 27018521

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Liang *et al. Microbiome* (2019) 7:19
https://doi.org/10.1186/s40168-019-0635-4

Microbiome

RESEARCH Open Access

Organophosphorus pesticide chlorpyrifos intake promotes obesity and insulin resistance through impacting gut and gut microbiota

Yiran Liang[1,2†], Jing Zhan[1†], Donghui Liu[1], Mai Luo[1], Jiajun Han[1], Xueke Liu[1], Chang Liu[1], Zheng Cheng[1], Zhiqiang Zhou[1] and Peng Wang[1*]

"Chlorpyrifos caused broken integrity of the gut barrier, leading to increased lipopolysaccharide entry into the body and finally low-grade inflammation, while genetic background and diet pattern have limited influence on the chlorpyrifos-induced results. Moreover, the mice given chlorpyrifos-altered microbiota had gained more fat and lower insulin sensitivity."

Chlorpyrifos: Inflammatory Effects

TOXDetect PROFILE

- 29 patients with documented chlorpyrifos exposure from indoor use, office, classroom or home use, spills, or vehicle (incl. school bus).
- 5 mos. post-application wipes showed CPF levels from <10-2900 ppm.
- Symptoms reported post-exposure:
  - Flu-like illness: fatigue, myalgia, memory loss, HA, dizziness
  - Upper and lower respiratory Sx
  - Joint and muscle pain
  - GI Sx

PMID: 7682805/12507170

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Chlorpyrifos: Immunotoxic

TOXDetect PROFILE

- Patients developed multiple allergies post-exposure
- 4 developed antibiotic sensitivities post-exposure
- 2 developed Lupus and Lupus-like syndrome
- All had evidence of atopy
- Significant evidence for anti-myelin Ab, **anti-parietal cell Ab**, anti-brush border Ab, anti-smooth muscle, anti-microsomal Ab in exposed group vs. controls
- **Anti-parietal cell Ab leads to B12 deficiency**

PMID: 12507170

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How Chlorpyrifos Does It's Damage: Key to Treament

TOXDetect PROFILE

- Like almost all OP pesticides chlorpyrifos blocks cholinesterase enzymes and other crucial enzymes involved in liver/kidney function
- Much of the damage is caused by significant oxidative stress induced by the oxidation of the OP molecule and formation of OP oxons.
- The body has an elegant way of dealing with these destructive molecules by breaking them down through the PON (par**oxon**ase enzyme system)
- SNPs (single nucleotide polymorphisms) in this enzyme can decrease levels in the body making these individuals canaries in the coal mine for chlorpyrifos exposure.

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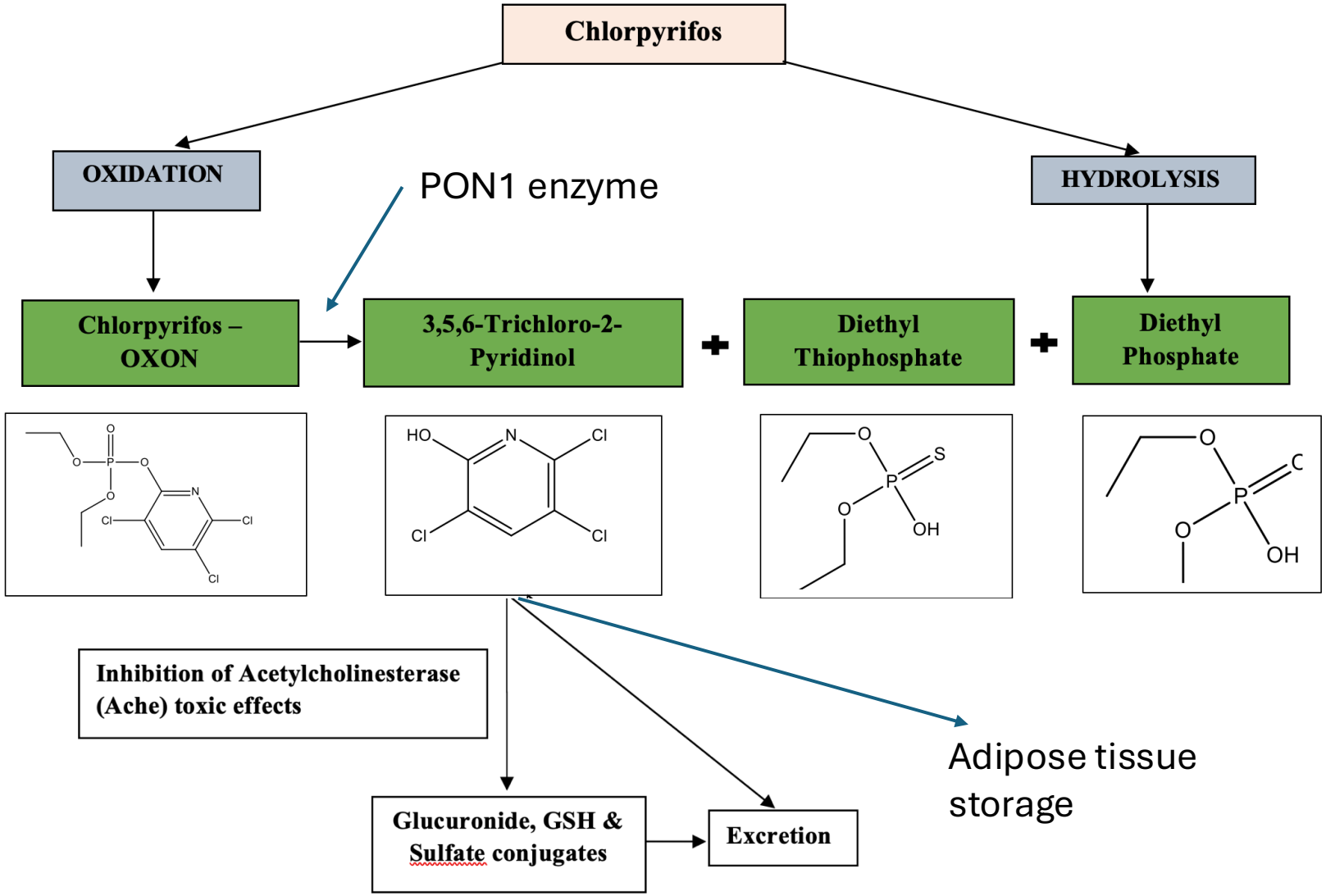
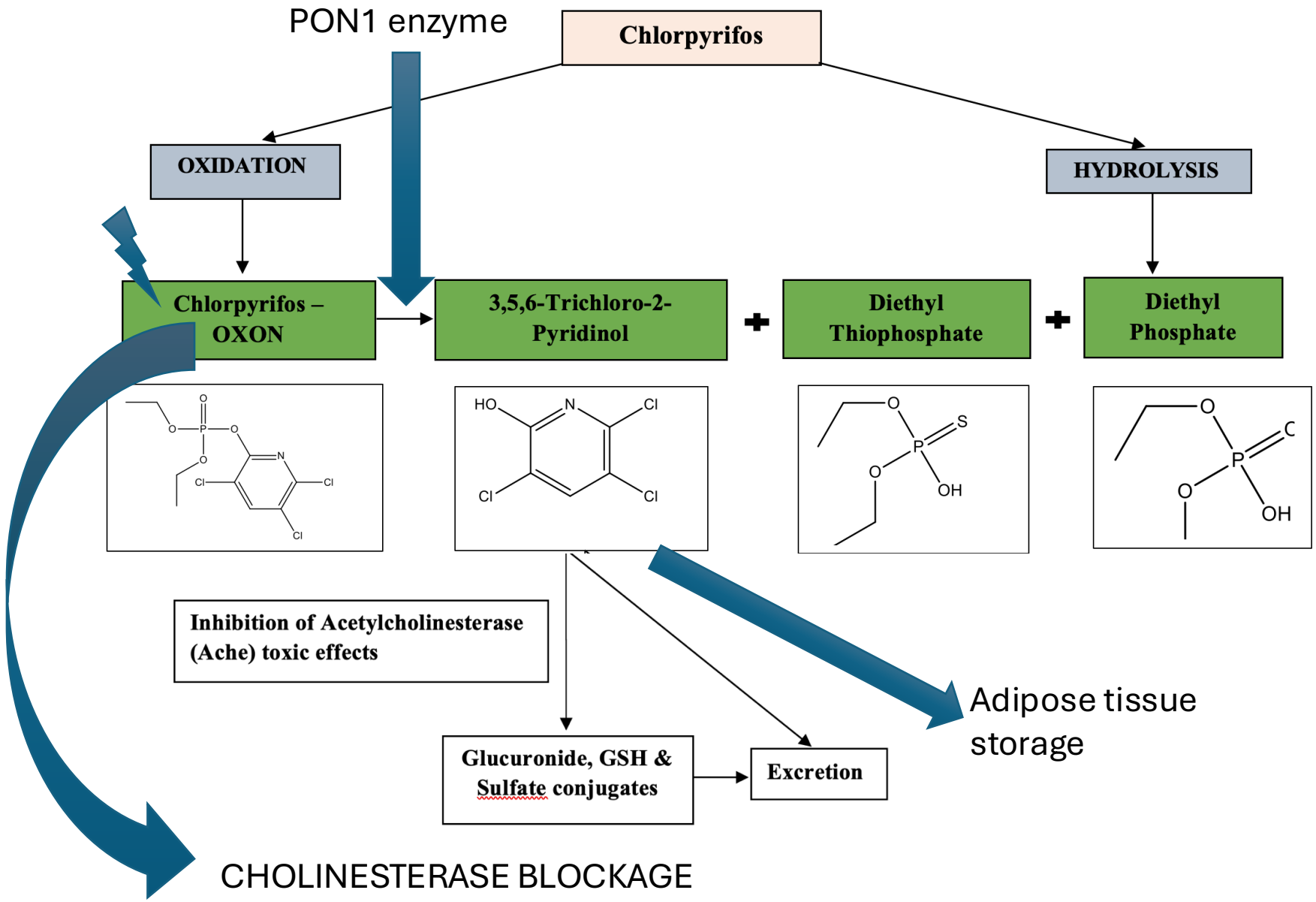

Chlorpyrifos
OXIDATION
PON1 enzyme
HYDROLYSIS
Chlorpyrifos – OXON
3,5,6-Trichloro-2-Pyridinol
Diethyl Thiophosphate
Diethyl Phosphate
Inhibition of Acetylcholinesterase (Ache) toxic effects
Glucuronide, GSH & Sulfate conjugates
Excretion
Adipose tissue storage


PON1 enzyme
Chlorpyrifos
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3,5,6-Trichloro-2-Pyridinol
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Glucuronide, GSH & Sulfate conjugates
Excretion
Adipose tissue storage
CHOLINESTERASE BLOCKAGE

Chlorpyrifos: NEUROTOXIC Pesticide for Children

TOXDetect PROFILE

- In children aged 1-2 years: dietary exposures are over **140 times** higher than EPA's level of concern .
- Children carry particularly high levels of chlorpyrifos — almost twice those of adults (CDC NHANES study). Chronic exposure levels were 4.6 times the "acceptable" level for children (6–11 years) and 3.0 times the "acceptable" level for youth (12–19 years).
- Children 2 yrs. and younger are approx. 60 times more susceptible to chlorpyrifos than others because **they do not produce PON1 enzymes which are critical for detoxification of organophosphates.**

https://www.regulations.gov/document/EPA-HQ-OPP-2015-0653-0437
https://www.epa.gov/pesticides/updated-human-health-risk-analyses-chlorpyrifos

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Pediatrics 2006

PMID: 17116700

NIH Public Access
Author Manuscript
Pediatrics. Author manuscript; available in PMC 2012 July 06.

Published in final edited form as:
Pediatrics. 2006 December ; 118(6): e1845–e1859. doi:10.1542/peds.2006-0338.

Impact of Prenatal Chlorpyrifos Exposure on Neurodevelopment in the First 3 Years of Life Among Inner-City Children

Virginia A. Rauh, ScD[a], **Robin Garfinkel, PhD**[a], **Frederica P. Perera, DrPH**[a], **Howard F. Andrews, PhD**[a], **Lori Hoepner, MPH**[a], **Dana B. Barr, PhD, DLS**[b], **Ralph Whitehead, MPH**[b], **Deliang Tang, DrPH**[a], and **Robin W. Whyatt, DrPH**[a]

[a]Columbia Center for Children's Environmental Health, Mailman School of Public Health, Columbia University, New York, New York

[b]National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia

- Highly exposed children (chlorpyrifos levels of >6.17 pg/g plasma) were significantly more likely to experience Psychomotor Development Index and Mental Development Index delays, attention problems, attention-deficit/hyperactivity disorder problems, and **pervasive developmental disorder problems at 3 years of age**.

Research | Children's Health

Seven-Year Neurodevelopmental Scores and Prenatal Exposure to Chlorpyrifos, a Common Agricultural Pesticide

Virginia Rauh,[1] Srikesh Arunajadai,[2] Megan Horton,[3,4] Frederica Perera,[4] Lori Hoepner,[4] Dana B. Barr,[5] and Robin Whyatt[4]

[1]Heilbrunn Center for Population and Family Health, Mailman School of Public Health, [2]Department of Biostatistics, Mailman School of Public Health, [3]Sergievsky Center, and [4]Columbia Center for Children's Environmental Health, Mailman School of Public Health, Columbia University, New York, New York, USA; [5]Emory University, Atlanta, Georgia, USA

- "Conclusions : We report evidence of deficits in Working Memory Index and **Full-Scale IQ** as a function of prenatal CPF exposure at 7 years of age.
- These findings are important in light of continued widespread use of CPF in agricultural settings and possible **longer-term educational implications** of **early cognitive deficits**."

PMID: 21507777

Prenatal Exposure to Organophosphate Pesticides and IQ in 7-Year-Old Children

Maryse F. Bouchard,[1,2] Jonathan Chevrier,[1] Kim G. Harley,[1] Katherine Kogut,[1] Michelle Vedar,[1] Norma Calderon,[3] Celina Trujillo,[1] Caroline Johnson,[1] Asa Bradman,[1] Dana Boyd Barr,[4] and Brenda Eskenazi[1]

[1]University of California–Berkeley, Center for Environmental Research and Children's Health, School of Public Health, Berkeley, California, USA; [2]CHU Sainte-Justine Research Center and Université de Montréal, Department of Environmental and Occupational Health, Montreal, Quebec, Canada; [3]Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS), Clinica de Salud del Valle de Salinas, Salinas, California, USA; [4]Emory University, Rollins School of Public Health, Atlanta, Georgia, USA

A California's Salinas Valley group exposed to the highest levels of organophosphate during pregnancy was associated with **a 7-point drop** in IQ scores in 7-year-olds:

Average maternal **DAP (urinary organophosphate metabolite)** concentrations were associated with poorer scores for Working Memory, Processing Speed, Verbal Comprehension, Perceptual Reasoning, and Full-Scale intelligence quotient (IQ). Children in the highest quintile of maternal DAP concentrations had an average deficit of **7.0 IQ** points compared with those in the lowest quintile.

PMID: 21507776

What is an IQ drop of 7 points?

- This is an association of magnitude similar to that observed with an increase in blood lead concentrations from **1 to 10 µg/dL.**
- **It is estimated that since 1940 US inhabitants have lost a collective 824 million points since the 1940s due to lead toxicity.**
- **The government fully banned lead from gasoline in 1996.**

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Formerly Great Plains Laboratory

PNAS 2012

Brain anomalies in children exposed prenatally to a common organophosphate pesticide

Virginia A. Rauh[a,b,1], Frederica P. Perera[b,c], Megan K. Horton[b,d], Robin M. Whyatt[b,c], Ravi Bansal[e], Xuejun Hao[e], Jun Liu[e], Dana Boyd Barr[f], Theodore A. Slotkin[g], and Bradley S. Peterson[e,h]

[a]Heilbrunn Center for Population and Family Health, [b]Columbia Center for Children's Environmental Health, and Departments of [c]Environmental Health Sciences and [d]Epidemiology, Mailman School of Public Health, Columbia University, New York, NY 10032; [e]Division of Child and Adolescent Psychiatry, Columbia University College of Physicians and Surgeons, New York, NY 10032; [f]Rollins School of Public Health, Emory University, Atlanta, GA 30322; [g]Department of Pharmacology and Cancer Biology, Duke University Medical Center, Durham, NC 27710; and [h]Department of Child and Adolescent Psychiatry, New York State Psychiatric Institute, New York, NY 10032

"We investigated associations between CPF(chlorpyrifos) exposure and brain morphology using magnetic resonance imaging in 40 children (6-11 y.o.) with identified CPF exposure:

- Significant associations of prenatal exposure to a widely used environmental neurotoxicant, at standard use levels, with structural changes in the developing human brain related to:
- Lowering of IQ even at low exposures
- High-exposure children did not show expected sex differences in the right inferior parietal lobe and superior marginal gyrus, and displayed reversal of sex differences in the right mesial superior frontal gyrus, consistent with disruption by CPF of normal behavioral sexual dimorphism."

PMID: 22547821

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Autism Spectrum Disorder and Chlorpyrifos

- Proximity to organophosphates at some point during gestation was associated with a 60% increased risk for ASD, higher for third-trimester exposures (OR = 2.0)
- **Second-trimester chlorpyrifos** applications were associated with increased risk for ASD: **OR = 3.3**

MOSAIC DIAGNOSTICS
Formerly Great Plains Laboratory

PMID: 24954055

Chlorpyrifos: The DDT/Lead of our Time

- In November 2023, the 8th Circuit Court of Appeals reversed the EPA's ban on chlorpyrifos enacted in 2021.
- In rolling back this ruling, the 8th Circuit Court will open the market for chlorpyrifos to be used in food production starting in 2024- which would continue until the EPA reinstates the ban.

Classes of Pesticides We Can Test for (in pink)

TOXDetect PROFILE

- **Organochlorine pesticides: ex. DDT**
- **Organophosphate pesticides: cholinesterase inhibitors ex. Malathion, Chlorpyrifos**
- Carbamates: weaker cholinesterase inhibitors ex. Carbofuran
- **Pyrethroids: while related to naturally occurring pyrethrins, they are mostly synthetic and very strong sensitizing (allergy-inducing) agents, ex. Cyfluthrin Cypermethrin, Deltamethrin, Permethrin**
- Fungicides: commonly used on foods like grapes and strawberries ex. chlorothalonil, mancozeb
- **Chlorophenoxy herbicides: ex. 2,4-D**
- **Triazine herbicides: ex. atrazine**
- Neonicotinoids: ex. Imidaclopirid
- Fumigants- used in air, soil, and on grains and crops post-harvest to reduce insects- a potential source of exposure to pesticide residues on food. ex. methyl bromide (phased out in 2005 but still produced in US for restrictive use)
- Phosphonoglycine herbicides: **Glyphosate**

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Pyrethroid Pesticides

TOXDetect PROFILE

- Acute exposures: dizziness and headaches, nausea, fatigue, blurred vision, a burning sensation and tingling of the face, tremor of the arms and legs, convulsions, sun sensitivity and unconsciousness PMID: 3359951
- Paresthesia, itching, burning, tingling PMID:1964560
- Dermal sensitization PMID: 30344292
- Respiratory irritation PMID:1578509
- In utero exposure alters cognitive development PMID: 26057254
- Hypothyroidism (farmers) PMID: 30256155
- Asthma (nonatopic)
- Chronic lymphocytic leukemia/small lymphocytic lymphoma
- Allergic and nonallergic respiratory symptoms

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TOXDetect Profile
Pesticide Metabolites

TOXDetect PROFILE

14) 3-Phenoxybenzoic Acid (3-PBA)

Pyrethoids, Permethrin, Cypermethrin, Cyhalothrins, Fenpropathrin, Deltamethrin, Trihalomethrin

Parent Compound: Pyrethroids

Pyrethroids are widely used in agriculture, household insect control, and veterinary medicine. Pyrethroids work by targeting the nervous system of insects, causing hyperexcitation and paralysis. The most common potential impacts to health include neurobehavioral, neurodevelopmental, and endocrine disruption. Exposure has also been associated with an increased risk of all-cause and cardiovascular disease mortality.

Pyrethroids are not “Natural”

TOXDetect PROFILE

- Pyrethroid insecticides are a synthetic molecule similar but not identical to Chrysanthemum-extracted pyrethrins.

- Approximately 30% of the US population has detectable 3-PBA in their urine.

doi:10.1289/ehp.0901275

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Less Toxic Pesticides?

TOXDetect PROFILE

- A Center for Public Integrity review of the past 10 years' worth of more than **90,000 adverse-reaction reports**, filed with the EPA by pesticide manufacturers, found that **pyrethrins and pyrethroids** together **accounted for more than 26 percent of all fatal, "major," and "moderate" human incidents in the United States in 2007**, up from 15 percent in 1998.
- The amount of moderate and serious incidents attributed to the group-more than **6,000 - is significantly greater than any other class of insecticide**.

https://publicintegrity.org/inequality-poverty-opportunity/workers-rights/safe-pesticides-now-first-in-poisonings/

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JAMA Internal Medicine 2019

TOXDetect PROFILE

- Pyrethroid exposure can cause oxidative stress, inflammation, and DNA damage.
- Environmental pyrethroid exposure may impair neurodevelopment, interfere with reproductive health, and increase the risk of major chronic diseases, such as diabetes, cardiovascular disease (CVD), and Parkinson disease.
- In a 14 year observational study, use of pyrethroid insecticides was associated with increased risk for:
  - higher risk of death from all causes
  - Higher risk of death from cardiovascular disease (HR=3.0)

doi:10.1001/jamainternmed.2019.6019

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Cross Reaction to Pyrethrin and Ragweed

TOXDetect PROFILE

- Those with ragweed allergies and **asthma** may be particularly sensitive to pyrethrins and pyrethroids.
- Up to 1 in 5 Americans have ragweed allergies.
- Pyrethrins are extracted from chrysanthemum plants and like the plant can trigger allergic reactions in some people.

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Involuntary Exposure: Another Reason to Avoid Fast Food

TOXDetect PROFILE

- Jerome Blondell, who retired from EPA in 2005 after 30 years with the agency, said he was especially troubled by reports of people being sprayed with pyrethroid pesticides by automatic misting devices, used to kill insects by some fast-food restaurants.

https://publicintegrity.org/inequality-poverty-opportunity/workers-rights/safe-pesticides-now-first-in-poisonings/

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Pyrethroid anaphylaxis

29-year-old woman with unremarkable medical history took her first trip to Africa, flying from Brussels to Kinshasa via Douala.

After closing the doors, cabin crew sprayed insecticides as part of routine vector control procedures for flights originating in territories with endemic malaria, yellow fever, or other insect vector-borne diseases as defined in the International Health Regulations.

Journal of TRAVEL MEDICINE

Anaphylaxis in an Airplane After Insecticide Spraying

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DOI: 10.1111/j.1708-8305.2010.00455.x

Flights departing from malarious areas are sprayed with pyrethroids. They are presumed to be safe since reports of adverse responses among passengers or crew were only anecdotal. However, asthmatic reactions after domestic and occupational exposure have been published. We present the first case description of pyrethroid allergy in an airplane.

PMID: 21050327

Sensitized to Pyrethroids

Shortly after the cabin spraying, the woman's lips and eyelids became swollen, she developed diarrhea, shortness of breath and felt as if she would lose consciousness. Is there a doctor on board?

This time there was. He found a dyspneic woman with a red face, slightly edematous eyes, and pronounced edema of the lips. She appeared to be suffocating and he noticed a prolonged expiration. Her pulse rate and blood pressure were normal. He administered albuterol inhalation and oral corticosteroids which he carried in his luggage since the flight crew brought only a first-aid kit containing bandages, not the emergency medical kit containing epinephrine.

Once in Kinshasa, the woman suffered from persistent mild wheezing, which she had never experienced before. This wheezing resolved after nighttime use of an electric anti-mosquito vaporizer was turned off.
One month later.....

Figure 1 Itchy swollen eyelid after rubbing a dog that had just been treated with flea powder containing pyrethroids.

Treatment

- **Rule #1- Avoidance, Avoidance, Avoidance**

What does this mean?

Air filtration

Water filtration

Organically grown food

No carpets/take shoes off at the door

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Water Filtration

TOXDetect PROFILE

Water filtration-

Why test your water for pesticide contamination?

US Department of Agriculture estimates that **50 million people** in the United States obtain their drinking water from groundwater that is potentially contaminated by pesticides and other agricultural chemicals.

Only 13 pesticides are regulated with maximum contaminant levels (MCLs) under the Safe Drinking Water Act, such as **glyphosate**, **atrazine, simazine**, and **2,4-D**. Not included are about **900** other pesticides registered for use in the U.S. in parks, golf courses, and on agricultural crops.

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Organically grown food is less contaminated with pesticide residue

TOXDetect PROFILE

- **73%** of USDA's conventionally grown samples had residues. For five crops (apples, peaches, pears, strawberries and celery) more than 90 percent of samples had residues.
- Consumer's Union found residues in **79%** of their conventionally grown samples.
- **Organically** grown samples consistently had far smaller percentages with residues:
  - USDA 23%
  - CA DPR 6.5%
  - Consumer's Union 27%
- IPM (Integrated Pest Management):
  - USDA: 47%
  - Consumer's Union 51%

Food Additives and Contaminants. 2002;19(5): 437-446.

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Organic vs. Conventional

TOXDetect PROFILE

- Higher levels of polyphenols: phenolic acids, flavanones, stilbenes, flavones, flavonols and anthocyanins (19-69% higher)
- Organic crops had on average 48% lower cadmium (Cd) levels than conventional crops.
- CAVEAT: imported organic food is subject to little or no regulation

British Journal of Nutrition 2014;112, 794–811.
OrganicEye June 18, 2024 2 OrganicEye, About
Globe Newswire April 30, 2024
Organic Insider November 8, 2023
The New Yorker November 15, 2021 15, 16 SC Times January 26, 2023
Reason February 4, 2023

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Organic Grains Contain Fewer Mycotoxins

TOXDetect PROFILE

- *Fusarium* infestation in barley, oats and wheat was significantly lower when grown organically than conventionally
- The most toxic trichothecenes, HT-2 and T-2 toxin were lower in organic oats and barley vs conventional.
- Wheat had lower concentrations of deoxynivalenol (DON) and moniliformin (MON) when organically produced.

Food Additives & Contaminants: 2009; Part A, 26, 1063–1069./*Food Control, 2014;38*, 61–66./*Food Additives & Contaminants: 2010;Part A, 27*, 842–852.

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Open Access Research

BMJ Open

Reduced risk of pre-eclampsia with organic vegetable consumption: results from the prospective Norwegian Mother and Child Cohort Study

TOXDetect PROFILE

- Between 1999 and 2008 28,000 women were given questionnaires asking if the ate organic food "often" "mostly" "rarely" or "never" and then followed for presence of pre-eclampsia.
- The prevalence of pre-eclampsia in the study sample was 5.3% (n=1491).
- Women who reported eating organic vegetables 'often' or 'mostly' (9% of them), had lower risk of pre-eclampsia than those who reported 'never/rarely' or 'sometimes'
- The women who ate organic vegetables often or mostly had a 21% lower risk for eclampsia.
- Eating any other class of organic food (fruit, dairy, meat) did not appear to have an effect

LOE: 3

BMJ Open 2014;4:e006143. doi:10.1136/bmjopen-2014- 006143

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The New Dirty Thirty

TOXDetect PROFILE

- Non-organic soy, corn
- Non-organic grains/beans Why? They are often dessicated w glyphosate: oats, barley, wheat, beans (**garbanzo beans**, canola (non-GMO non-organic)
- Non-organic vegetables treated with toxic OP: broccoli, cauliflower, wheat, non-GMO corn.
- Imported fruit/veg that are at high risk for toxic pesticide residue: orange, cucumber, apple, melon, banana.
- What's Left? USDA-certified U.S.vorganically grown food or locally grown food from growers you can trust

Global Health 2012; 8:2 PMC3297498
Environ Health Perspect 2003;111:377–382

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Treatment: Organophosphate Pesticide exposure

TOXDetect PROFILE

- N-acetyl cysteine (NAC)-animal studies
- Curcumin alone dosage equivalent 2500 mg. (50 mg/kg) or with NAC-prevents DNA damage and lipid peroxidation dosage: 1800 mg NAC
- Melatonin- with vit. C and vit. E prevents DNA damage and lipid peroxidation dosage associated with chorpyrifos dosage equivalent: melatonin 3 mg hs
- Melatonin-used in treatment of acute OP poisoning in India

J Biochem Mol Toxicol. 2010 Sep-Oct;24(5):286-92./ *Arch Toxicol* 2001;75(2):88–96.
Biol Pharm Bull. 2007 Mar;30(3):490-4
Cell Biol Toxicol. 2008 Apr;24(2):151-8.
Toxicol Ind Health 2012 DOI: 10.1177/0748233712446726

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PON1 RISK ALLELE- the canary of pesticide toxicity

TOXDetect PROFILE

- PON1- paraoxonase 1 determines the rate at which organophosphate pesticides are metabolized
- Those with the "slower" PON1 snps:
  - PON1-192QQ and PON155MM who reported using OP pesticides at their homes had an increased risk of Parkinson's Disease **of 2.84/3.57** respectively.
- "Genetic susceptibility alone does not increase the risk of PD in the absence of exposure to OP pesticides."

PMID: 23602893

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Upregulate PON1 Activity

TOXDetect PROFILE

Increased activity of PON1 **even w PON1 snps:**

- Exercise
- Mediterranean Diet
- Olive Oil
- Fish Oil
- **Pomegranate**
- Anthocyanins
- Coconut Oil
- Quercitin
- Walnuts
- Aspirin

PMID: 23710701, 25963585, 26761772, 16276071, 22924372, 23510814, 24285687, 25758596, 20228421, 17585031, 23892389, 19891963

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Treatment: Preserve Glutathione Status

TOXDetect PROFILE

Decrease oxidative stress:

- Alpha lipoic acid has been shown to increase glutathione levels and upregulate ATP production acting as an antioxidant in mitochondria. When rats are pre-treated with ALA (20 mg/kg) and then exposed to malathion they did not have liver, kidney degenerative changes that occurred without the ALA.
- Vit. D- sufficient to raise blood levels to 50-80 ng/ml: for every 1000 IU vit. D you supplement- blood levels go up: 10 mg/ml or 25 nmol/L

Neurochem Res 2008;33:194-203.
Am J. Clin Nutr 2003;77:204-210.
Trends Endocrinol Metab. 2002 Apr;13(3):100-5.
Am J Kidney Dis. 2001 Apr;37(4):750-7.
J Biomed Biotechnol. 2010; 2010: 203503.

LOE: C

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DHA

TOXDetect PROFILE

- DHA crosses the blood-brain barrier, protecting cell membranes from toxin-induced oxidative damage, particularly from organophosphate and carbamate pesticides.
- DHA (omega-3 docosahexaenoic acid) from marine algae or fish/krill oil: 750 mg daily

LOE: B

Neurochem Int. 2011; 59:664–70.

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Ascorbate

TOXDetect PROFILE

- Buffered ascorbate (calcium, magnesium, potassium, zinc) also alkalinizes urine leading to improved renal excretion of toxicants.
- Functions as an electron donor to enhance cell energy. Ascorbate is uniquely able to donate an electron and restore ATP-generating capacity to the mitochondria of the cell, thus increasing its energy output.
- Functions as an antioxidant to reduce and support glutathione.
- Individual needs vary, minimum dose 3000 mg. Tolerance test may show need for greater doses.

Int J Vitam Nutr Res.2009 Sep; 79(5-6):281-7. Intl J Integrative Med, 2000; 2(6):7-18.
Annu Rev Nutr. 1986; 6:365-406

LOE C

Vit. E Complex

TOXDetect PROFILE

- Vitamin E (1000 IU) –helps stabilize cell membranes while quenching free radical damage.
- Organophosphates and carbamates cause extensive oxidative damage, especially to the cardiovascular and nervous systems- data indicate vit. E prevents damage in organophosphate exposure.

J Neurochem 2007;100(6):1469./Oxid Med Cell Longevity 2014 Article ID 671539.

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Vit. A/Carotenoids

TOXDetect PROFILE

- 50,000 IU daily
- Organophosphates and PCBs decrease liver Vit. A content which increases their toxicity.
- IM injection of 1,500,000 units Vit A given yearly to cattle to treat organophosphate poisoning.
- Other items that lower Vit. A stores are: alcohol, coffee, cold weather, cortisone, diabetes, excessive Fe, infections, laxatives, liver disease, mineral oil, nitrates, sugar, tobacco, Vit. D deficiency, Zn deficiency.
- Carotenoids have no vit. A-related toxicity as the conversion to vit. A is rate-limited in intestinal lining but conversion is limited in diabetics and documented increased risk for lung CA in smokers.

Mar. Drugs **2015**, *13*, 6152-6209.

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TREATMENT

- Air filtration unit if any current exposure
- Add point-of-use water filter (previous water was from plastic bottled water)
- Vit. A: 50,000 IU day
- Vit. E: complex 1,000 IU day
- B1: 200 mg. daily in B complex
- R-Alpha lipoic acid: 600 mg. qd
- Melatonin 3 mg. hs**
- Urine Alkalinization: potassium citrate 300-500 mg.
- Sauna 3 times weekly x 6 weeks
- IV magnesium, B complex, vit. C and GSH weekly times 8 weeks
- Organic Food ONLY (a study commissioned by Michelle Perro MD showed that purchasing whole USDA organic food diet was no more expensive than the average family's standard grocery bills.)

**Indian J Anaesth. 2016 Nov; 60(11): 814–820.

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Questions?

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