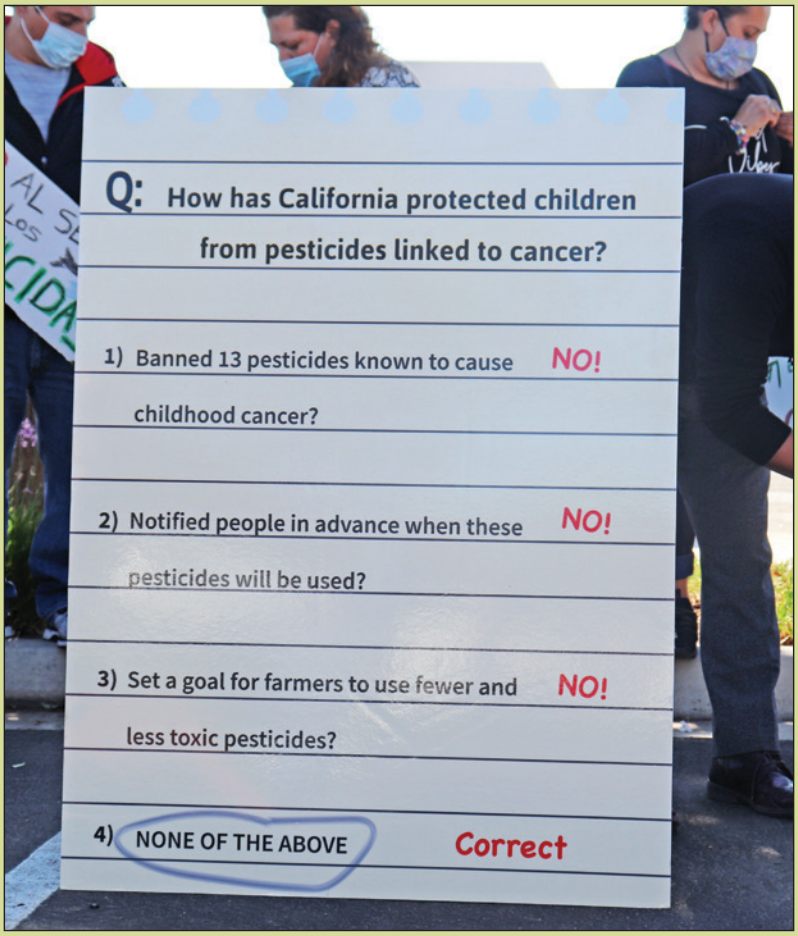
There's Something in the Air, and It Causes Childhood Cancers



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Californians for Pesticide Reform is a diverse, statewide coalition of 200+ member groups working to strengthen pesticide policies in California to protect public health and the environment. Member groups include public and children's health advocates, clean air and water groups, health practitioners, environmental justice groups, labor, education, farmers, and sustainable agriculture advocates from across the state.

There's Something in the Air, and It Causes Childhood Cancers

"In the old days, miners would carry birds with them to warn against poison gas. Hopefully, the birds would die before the miners.

Farm workers are society's canaries.

Farm workers — and their children — demonstrate the effects of pesticide poisoning before anyone else."

— Cesar Chavez
United Farm Workers President, 1989, a year after his last and longest fast, a protest against pesticide use*

"There's something in the air . . . and it causes cancer."

— Yanely Martinez
Greenfield City Councilmember, 2021†

* "Address by Cesar Chavez, President United Farm Workers of America, AFL-CIO, Pacific Lutheran University," March 1989-Tacoma, Washington, https://ufw.org/cesar-chavezs-first-major-address-36-day-1988-fast-pesticide-poisoning-farm-workers-2/

† At a meeting with the author in Greenfield, California, October 8, 2021.

There's something in the air, and it causes childhood cancers[1]

This short paper is presented out of concern that a cruel historical pattern is repeating itself: that the evidence of pesticide harms that farmworkers and their children have demonstrated through their damaged bodies for generations, and that the confirmatory evidence of scientific studies regarding this pesticide damage, will once again be ignored or protections delayed for decades by our county and state regulators. We must break with that past.

Executive summary

A pair of studies published in 2020 and 2021 have established a statistically significant link between several childhood cancers and prenatal residential proximity to applications of 13 agricultural pesticides, which we are calling "The Toxic 13." The two California studies, by researchers at UCLA and other universities in Southern California, are notable for establishing links between specific childhood cancers and specific pesticides when they are applied *in any amount* at a distance of up to 2.5 miles (4000m) from a residence.

The authors of the second study concluded:

> **"Policy interventions to reduce pesticide exposure in individuals residing near agricultural fields should be considered to protect the health of children."**

This report:

- analyzes use patterns of the 13 pesticides identified in the two studies by acreage and racial composition in California and in six key agricultural counties in the San Joaquin Valley and Central Coast;
- outlines current restrictions on the pesticides, if any, in California and globally;
- makes specific policy recommendations to address the health threat posed by continued use of these chemicals.

Our analysis indicates that, while average annual acreage treated with any of the Toxic 13 has slightly decreased in the years since the period covered by the study, use remains very high for most of the pesticides, and use of five of the pesticides is actually increasing.

Moreover, there is a marked racial disparity in impact, with pesticide use heavily concentrated in the counties and zip codes with the highest proportion of Latinx[2] residents.

In the case of the Toxic 13, California's system of designating certain harmful pesticides as Restricted Materials, which require a permit for their use, is largely a failure. Of the 12 of these pesticides still registered for use in California, only four are Restricted. By contrast, all but two are banned or not approved in other countries, and 10 of them are widely banned, in at least 28 countries.

We echo the study authors' call for policy interventions to reduce the threat posed by these chemicals. Specifically, we call on California to:

- Designate all twelve pesticides still registered for use in California as Restricted Materials.
- Immediately provide advance public notice for all Restricted Material pesticide applications in California.
- Establish emergency 2.5-mile buffer zones around all residences, schools, hospitals, and other sensitive sites.
- Initiate proceedings to ban all 13 of these chemicals.
- Overhaul the pesticide regulatory system which continues to perpetrate gross race-based inequities, beginning with the provisions of the "Protect America's Children from Toxic Pesticides Act", proposed in the U.S. Senate in the summer of 2020.
- Set bold statewide targets for reduction of pesticide use and expansion of organic acreage.

Two recent California studies indicate elevated childhood cancer risk from pesticides applied up to 2.5 miles away

In two recent peer-reviewed scientific journal studies, teams of researchers found concerning statistically significant correlations between use of 13 individual pesticides and early childhood cancers.

The first study of pesticide links to childhood leukemias, *Prenatal pesticide exposure and childhood leukemia – A California statewide case-control study*[3] focused on "the association of pesticide exposure in pregnancy and early childhood with childhood acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML)." Their methods "identified cancer cases less than six years of age from the California Cancer Registry and cancer-free controls from birth certificates." The team's analyses were restricted to rural Californians born between 1998 and 2011, using EPA-classified carcinogens identified in the California Department of Pesticide Regulation's (DPR) Pesticide Use Reporting (PUR) system and then linked to land-use surveys. "Exposures for subjects were assessed using a 4000m buffer [2.5 miles] around the ... residential addresses at birth." The scientists concluded: "Our findings suggest that in rural areas of California exposure to certain pesticides or pesticide classes during pregnancy due to residential proximity to agricultural applications may increase the risk of childhood ALL and AML."[4]

The second study, *Residential proximity to pesticide application as a risk factor for childhood central nervous system tumors,*[5] was released in the summer of 2021 and focused on childhood brain tumors. Using similar methods to the previous study, the researchers found eight pesticides with statistically significant correlations to childhood brain cancers, including diffuse astrocytoma, medulloblastoma, and ependymoma. The authors conclude: "Our study suggests that exposure to certain pesticides through residential proximity to agricultural applications during pregnancy may increase the risk of childhood central nervous system tumors... Our results suggest that exposure to specific pesticides may best explain the results of previous studies that reported relationships between broader pesticide types and central nervous system tumors. Policy interventions to reduce pesticide exposure in individuals residing near agricultural fields should be considered to protect the health of children."[6]

The scientific links to childhood cancer and pesticide exposure have been mounting for decades.[7] What is new about these recent studies is that they are California-specific, provide correlations of individual pesticides to specific childhood cancer sub-types, and establish links to in utero exposure over a long distance — up to 2.5 miles from the pregnant mother's residence.

Current state regulations do not address exposure from applications at such distances and therefore do not account for normal pesticide drift. For example, a policy implemented in 2018 that restricts pesticide use around California public schools and daycares applies only within a ¼ mile of schools.[8]

Table 1. Cancer-Causing Pesticide Use, 1990s versus 2010s: California, Fresno, Kern, Monterey, Santa Cruz, Tulare and Ventura Counties

Region	Ave Pounds/Year 1991–1999	Ave Pounds/Year 2010–2018	Percent Increase
California	**25,023,438**	**39,222,458**	**56.7%**
Fresno County	5,372,790	7,291,115	35.7%
Kern County	4,467,035	7,389,807	65.4%
Monterey County	955,455	1,722,190	80.2%
Santa Cruz County	195,884	409,591	109.1%
Tulare County	1,293,955	1,955,995	51.2%
Ventura County	512,143	1,374,073	168.3%

Increasing generational risk of carcinogenic pesticides

While pesticide regulators often state that California has the most stringent pesticide regulatory system in the country, the fact is that use of state-listed cancer-causing pesticides has increased dramatically since the 1990s, when official records were first kept.[9] The statewide average annual use of carcinogenic pesticides increased 57%, from 25.0 million pounds in the 1990s to 39.2 million in the 2010s.[10] Increases in Kern, Monterey, Santa Cruz and Ventura Counties were even higher, at 65%, 80%, 109% and 168% respectively.

While use of cancer-causing pesticides in the six counties decreased in the last few recorded years, recent use remains above even the highest spikes in annual use in the 1990s. The screenshot graphs from the California Department of Public Health in Figures 1-7 illustrate this historical pattern.[11]

Figure 1-6. Screenshots of Department of Public Health graphs of carcinogenic pesticide use, 1991–2018, pounds, Fresno County, Kern County, Monterey County, Santa Cruz County, Tulare County and Ventura County.

Figure 7. Screenshot of Department of Public Health graph of carcinogenic pesticide use, 1991–2018, pounds, California.

A sobering result of the study of childhood leukemia is that a child born to a pregnant mother living within 2.5 miles of use of any state-identified cancer-causing pesticide had a 183% higher risk of developing childhood acute lymphoblastic leukemia.[12]

The "Toxic 13" pesticides linked to childhood cancers

The two studies found a combined 13 individual pesticides that displayed a statistically significant increase in the rates of certain childhood cancers, at 95% confidence levels for both single- and multiple-pesticide tests performed by the researchers. This "Toxic 13" [our term, not that of the scientific journal articles' authors] indicated the risk of children developing specific cancers if their mother was exposed to these pesticides was 1½ to 3 times greater than the risk for children not exposed. The findings are summarized in the tables for each study below, including information about each pesticide's regulatory status in California and beyond.

Internationally, all but two of these 13 pesticides (Phosmet and Kresoxim-methyl) are forbidden for use in other countries — and 10 are banned or not approved in at least 28 nations. Of the 13 pesticides, one, Triforine, is no longer registered for use in California, while only four are classified as Restricted Use materials — pesticides considered especially hazardous and so requiring a permit from County Agricultural Commissioners before use.

Use of the Toxic 13 pesticides linked to childhood cancers in the six counties

The association of the Toxic 13 pesticides with early childhood cancers is based upon any-or-none analyses. That is, the comparison groups were pregnant mothers who lived within any amount versus those who lived near none of the pesticide in question applied within 2.5 miles. Given such analyses, the acreage or spread of pesticide applications is a more apt measure of exposure threat than pounds applied, as pounds could be concentrated in small areas.

Tables 4 and 5 below compare the average annual acreage of the Toxic 13 pesticides during the period examined in both studies, 1998–2011, with the most recent DPR data from 2012–2018. There has been a 27% increase in acreage treated with childhood leukemia-linked pesticides in Monterey County, and a slight decrease in

Table 2. Pesticides linked to Childhood Leukemias, Odds Ratios,[1] and regulation status

Pesticide	Type	Childhood Cancer	Association (and 95% Confidence Interval)	Other Countries Banned/Not approved[2]	CA Restricted[3]
Propanil	herbicide	acute lymphoblastic leukemia (ALL)	2.58 (1.44–4.63)	29	yes
Diuron	herbicide	acute lymphoblastic leukemia (ALL)	2.38 (1.57–3.60)	29	no
Phosmet	insecticide	acute lymphoblastic leukemia (ALL)	2.10 (1.46–3.02)	0	no
Kresoxim-methyl[4]	fungicide	acute lymphoblastic leukemia (ALL)	1.77 (1.14–2.75)	0	no
Metam-sodium	fumigant	acute myeloid leukemia (AML)	2.56, (1.19–5.49)	2	yes
Paraquat dichloride	herbicide	acute myeloid leukemia (AML)	3.38 (1.23–9.27)	48	yes
1st Study		**Childhood leukemia**	**from 1.77 to 3.38 average**	**4 of 6 pesticides banned**	**3 of 6**

1. *International Journal of Hygiene and Environmental Health*, Volume 226, May 2020, 113486, https://doi.org/10.1016/j.ijheh.2020.113486
2. The Pesticide Action Network International Consolidated List of Banned Pesticides, https://pan-international.org/pan-international-consolidated-list-of-banned-pesticides/
3. "California Restricted Materials Requirements," https://www.cdpr.ca.gov/docs/enforce/dpr-enf-013a.pdf
4. Kresoxim-methyl was identified in both studies

Table 3. Pesticides linked to Childhood Brain Tumors, Odds Ratios,[1] and regulation status

Pesticide	Type	Childhood Cancer	Association (and 95% Confidence Interval)	Other Countries Banned/Not approved[2]	CA Restricted[3]
Triforine	fungicide, insecticide	diffuse astrocytoma	2.38 (1.44–3.92)	29	not registered in CA
Bromacil	herbicide	diffuse astrocytoma	2.12 (1.13–3.97)	32	yes
Kresoxim-methyl[4]	fungicide	diffuse astrocytoma	2.09 (1.03–4.21)	0	no
Thiophanate-methyl	fungicide	diffuse astrocytoma; ependymoma	1.64 (1.02–2.66) 1.72 (1.10–2.68)	28	no
Linuron	herbicide	medulloblastoma	2.52 (1.25–5.11)	32	no
Chlorothalonil	fungicide	medulloblastoma	1.78 (1.15–2.76)	32	no
Dimethoate	insecticide	medulloblastoma	1.60 (1.06–2.43)	33	no
Propiconazole	fungicide	medulloblastoma	1.60 (1.02–2.53)	28	no
2nd Study		**Childhood brain cancers**	**from 1.60 to 2.52 average**	**7 of 8 pesticides banned**	**1 of 8**

1. Environmental Research, Volume 197, June 2021, 111078, https://doi.org/10.1016/j.envres.2021.111078
2. The Pesticide Action Network International Consolidated List of Banned Pesticides, https://pan-international.org/pan-international-consolidated-list-of-banned-pesticides/
3. "California Restricted Materials Requirements," https://www.cdpr.ca.gov/docs/enforce/dpr-enf-013a.pdf
4. Kresoxim-methyl was identified in both studies

Table 4. Average annual use of pesticides linked to childhood cancers in the San Joaquin Valley Counties of Fresno, Kern and Tulare, in acres*

	Fresno County		Kern County		Tulare County	
Pesticide	Ave Acres/Year 1998–2011	Ave Acres/Year 2012–2018	Ave Acres/Year 1998–2011	Ave Acres/Year 2012–2018	Ave Acres/Year 1998–2011	Ave Acres/Year 2012–2018
Bromacil	6,782	1,962	7,152	4,161	9,224	3,190
Chlorothalonil	74,430	77,533	69,462	64,086	3,338	3,069
Dimethoate	70,616	97,035	29,453	17,413	36,443	24,816
Diuron	168,357	80,962	107,010	41,310	124,257	41,129
Kresoxim-methyl	20,481	60,895	9,942	21,092	6,319	13,029
Linuron	677	1,468	32,163	21,614	3	5
Metam-sodium	41,101	7,587	24,296	8,445	602	218
Paraquat dichloride	276,762	178,692	239,767	241,657	122,306	90,777
Phosmet	33,153	2,821	41,481	1,280	27,660	3,101
Propanil	859	1,153	0	0	0	0
Propiconazole	32,635	109,885	16,572	29,491	30,458	43,027
Thiophanate-methyl	7,439	17,843	12,016	12,045	4,093	6,933
Triforine	73	0	22	0	87	0
Total Leukemia-linked	**539,855**	**330,956**	**422,497**	**313,782**	**281,144**	**148,254**
Total Brain Cancer-linked	**213,132**	**366,621**	**176,781**	**169,902**	**89,966**	**94,069**
Total Carcinogens	**1,524,657**	**1,595,666**	**1,134,083**	**1,147,421**	**823,720**	**831,605**

* Compiled from California Department of Public Health's Agricultural Pesticide Mapping Tool, https://trackingcalifornia.org/pesticides/pesticide-mapping-tool

the other counties. Use of the group of childhood brain cancer-linked pesticides increased by acreage in Fresno and Tulare, and decreased slightly in Kern, Monterey, Santa Cruz and Ventura.

Use of one pesticide – Propiconazole — has significantly increased by acreage in all six counties.

Other pesticides have also seen increases in use in specific counties:

- Chlorothalonil: Fresno, Monterey, Santa Cruz
- Dimethoate: Fresno (up 37%)
- Kresoxim-methyl: Fresno, Kern, Monterey, Tulare, Ventura
- Linuron: Monterey, Ventura, Fresno, Tulare
- Metam Sodium: Ventura (up 16%)
- Paraquat dichloride: Kern, Monterey (up 34%), Ventura
- Propanil: Fresno (up 34%)
- Thiophanate-methyl: Fresno, Monterey, Tulare

Table 5. Average annual use of pesticides linked to childhood cancers in the coastal counties of Monterey, Santa Cruz and Ventura, in acres*

	Monterey County		Santa Cruz County		Ventura County	
Pesticide	**Ave Acres/Year 1998–2011**	**Ave Acres/Year 2012–2018**	**Ave Acres/Year 1998–2011**	**Ave Acres/Year 2012–2018**	**Ave Acres/Year 1998–2011**	**Ave Acres/Year 2012–2018**
Bromacil	120	4	0	0	1,731	92
Chlorothalonil	15,745	24,079	2,569	2,663	31,755	22,105
Dimethoate	87,576	19,840	3,287	767	4,223	3,233
Diuron	2,097	2,088	54	43	3,288	825
Kresoxim-methyl	8,036	9,445	34	7	63	106
Linuron	5,402	6,962	128	69	6,081	8,014
Metam-sodium	817	72	170	0	1,919	2,230
Paraquat dichloride	33,815	45,456	701	326	1,885	2,905
Phosmet	115	33	647	98	54	16
Propanil	0	0	0	0	3	0
Propiconazole	4,424	12,999	441	942	18,630	26,100
Thiophanate-methyl	4,197	8,455	1,333	1,107	3,386	3,233
Triforine	39	0	7	0	7	0
Total Leukemia-linked	**44,879**	**57,094**	**1,605**	**475**	**7,208**	**6,082**
Total Brain Cancer-linked	**125,539**	**81,785**	**7,798**	**5,555**	**65,876**	**62,882**
Total Carcinogens	**478,970**	**402,856**	**37,738**	**30,936**	**238,004**	**230,673**

* Compiled from California Department of Public Health's Agricultural Pesticide Mapping Tool, https://trackingcalifornia.org/pesticides/pesticide-mapping-tool

Disproportionate use of pesticides linked to childhood cancers in Latinx areas of California

The Department of Pesticide Regulation "Environmental Justice" webpage states: "Fair treatment means that no one group of people, including racial, ethnic, or socioeconomic groups, should be disproportionately impacted by pesticides."[13]

When examining where the pesticides linked to childhood cancers are used, it quickly becomes clear that DPR and County Ag Commissioners are not living up to the "fair treatment" standard of Environmental Justice, but rather allowing for environmental injustice, with disproportionate use of these childhood cancer-threatening pesticides in Latinx regions of the state.

Fresno, Kern and Tulare Counties are among the 11 counties in the state with populations that are majority Latinx, with a total population of roughly six million in these 11 counties. More than a combined eight million pounds of the Toxic 13 pesticides linked to childhood cancers were applied in these majority-Latinx counties in 2019.

The 25 counties with the smallest proportions of Latinx residents, at under 24%, also have about six million people. But those "least Latinx" counties had less than

Table 6. Disproportionate use of pesticides linked to childhood cancer, Counties with highest and lowest Latinx population percentages, Fresno, Kern and Tulare Counties, pounds per person[1]

Counties	Population[2]	Latinx population[3]	All Carcinogens (2018) pounds/ person[4]	Times more than smallest Latinx counties	Toxic 13 (2019) pounds/ person	Times more than smallest Latinx counties	Childhood Leukemia-linked (2019) pounds/ person	Times more than smallest Latinx counties	Brain Cancer-linked (2019) pounds/ person	Times more than smallest Latinx counties
25 smallest Latinx %[5]	6,258,378	19%	0.35		0.12		0.11		0.01	
11 highest Latinx %[6]	5,863,161	57%	4.20	12.0	1.36	11.3	1.25	11.0	0.12	12.8
Fresno	999,101	54%	6.81	19.5	1.21	10.0	1.05	9.2	0.17	17.8
Kern	900,202	54%	8.01	22.9	2.53	20.6	2.42	20.3	0.12	12.1
Tulare	466,195	65%	4.21	12.1	0.27	2.2	0.21	1.9	0.06	6.9

1. Pesticide use data downloaded from UC Davis PUR Web GIS v. 2 at http://purwebgis.ucdavis.edu/PURwebGIS.html
2. https://www.california-demographics.com/counties_by_population
3. Compiled from https://www.indexmundi.com/facts/united-states/quick-facts/california/hispanic-or-latino-population-percentage#table
4. Generated from the California Department of Public Health's Agricultural Pesticide Mapping Tool, which counts only agricultural applications: https://trackingcalifornia.org/pesticides/pesticide-mapping-tool
5. From highest to lowest Latinx percentage, ranging from 24% to 7.5%: Sacramento, San Luis Obispo, Inyo, Alameda, Lake, Del Norte, Lassen, Butte, Marin, San Francisco, Amador, Placer, Modoc, El Dorado, Siskiyou, Tuolumne, Calaveras, Sierra, Humboldt, Mariposa, Alpine, Shasta, Nevada, Plumas, and Trinity. https://www.indexmundi.com/facts/united-states/quick-facts/california/hispanic-or-latino-population-percentage#table
6. From highest to lowest Latinx percentage, ranging from 85% to 54%: Imperial, Tulare, San Benito, Colusa, Merced, Monterey, Madera, Kings, Kern, San Bernardino, Fresno. https://www.indexmundi.com/facts/united-states/quick-facts/california/hispanic-or-latino-population-percentage#table

Table 7. Disproportionate use of pesticides linked to childhood cancers in Monterey and Santa Cruz Counties, Latinx-majority zip codes, 2019

County	Zip code(s)	% of all lbs pesticides w/ childhood leukemia link[1]	% of all lbs pesticides w/ childhood brain cancer link[2]	Latinx %[3]	White %[4]
Monterey	Salinas Valley-12	88.2	90.3	58.7	14.6
Santa Cruz	95076	98.5	95.2	70.7	24.3

1. http://purwebgis.ucdavis.edu/PURwebGIS.html
2. http://purwebgis.ucdavis.edu/PURwebGIS.html
3. https://statisticalatlas.com
4. https://statisticalatlas.com

Table 8. Disproportionate use of pesticides linked to childhood cancer, Oxnard versus the rest of Ventura County, ethnicity, pounds per person[1]

Counties	Population[2]	Latinx population[3]	Toxic 13 (2019) pounds/ person	Times more than rest of Ventura County	Childhood Leukemia-linked (2019) pounds/ person	Times more than rest of Ventura County	Brain Cancer-linked (2019) pounds/ person	Times more than rest of Ventura County
Oxnard: zip codes 93030, 93033, 93036	190,013	78%	0.71	2.60	0.64	2.56	0.07	2.98
The rest of Ventura County	653,830	25%	0.27		0.25		0.02	

1. Data downloaded from http://purwebgis.ucdavis.edu/PURwebGIS.html
2. https://www.california-demographics.com/counties_by_population and https://statisticalatlas.com
3. https://www.california-demographics.com/counties_by_population and https://statisticalatlas.com

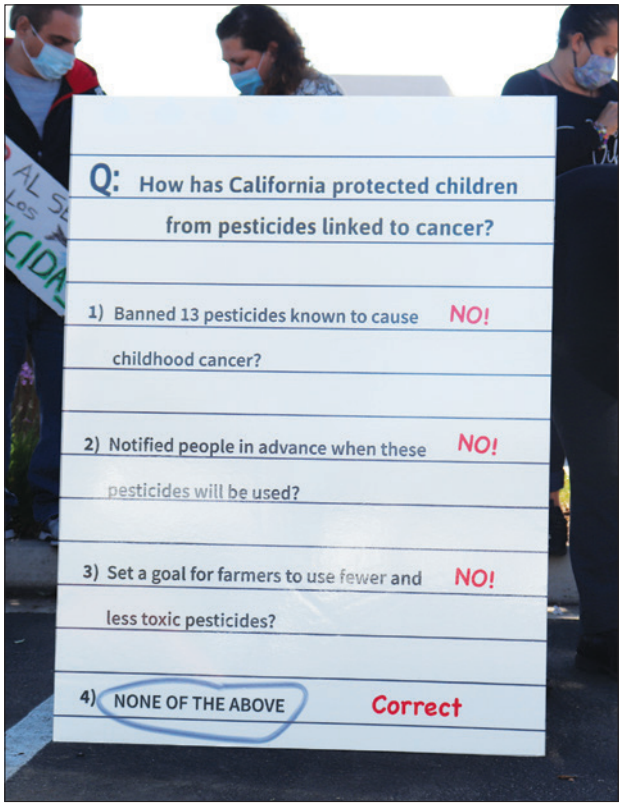
770,000 pounds of the Toxic 13 applied in 2019. Per person, there were 11 times more childhood cancer-linked pesticides applied in majority Latinx counties than counties with Latinx populations below 24%.[14] The two groups of counties are similar in total area[15].

Disproportionate use in majority Latinx regions of carcinogens and the Toxic 13 pesticides was also a characteristic of agricultural applications in Fresno, Kern and Tulare Counties. The ratios compared to counties with under 24% Latinx populations ranged from 1.9 times more childhood leukemia-linked pesticides in Tulare County to 23 times higher for all cancer-causing pesticides and 20 times higher for total use of the Toxic 13 in Kern County, when measured by pounds of pesticides applied per person. More detailed comparisons are in Table 6.

In the zip codes that encompass Santa Cruz County,[16] the 95076 zip code stands out as one of the few in the county that has a majority Latinx population at 70.7%.[17] A full 60% of all Latinx residents in all the Santa Cruz County zip codes live within the 95076 zip, which includes Watsonville, while only 12.6% of the county's white population lives there.[18] However, 98.5% (168.9 of 171.4 pounds) of the pesticides associated with childhood leukemia and 95.2% (2113.1 of 2220.1 pounds) of the pesticides tied to childhood brain cancer were applied in 2019 in the 95076 zip code alone.[19] (See Table 7 above.)

Similarly in Monterey County, the application of pesticides linked to childhood cancers is concentrated in the Latinx-majority region of the Salinas Valley, where 58.7% of residents are Latinx compared to just 14.6% white in the 12 zip codes that cover the region. 88.2% (24,793 of 28,124 pounds) of the pesticides linked to childhood leukemias in Monterey County were applied in the Salinas Valley in 2019; and 90.3% (35,235 of 39,022 pounds) of pesticides associated with childhood brain cancer.[20] (See Table 7 above.)

In Ventura County, which is 47% white and 42% Latinx,[21] use of the pesticides linked to childhood cancers in 2019 was concentrated in three zip codes of the City of Oxnard, where the population is 78% Latinx and only 10% white.[22] In this area, 43% of all the Toxic 13 pesticides in Ventura County were applied — more than 2½ times (260%) the rate per person of the rest of the county. Table 8 compares Toxic 13 pesticide use in Oxnard to other Ventura County areas.



Another way to see the environmental injustice of the current pesticide regulatory system: there were more pounds applied of the pesticides linked to childhood cancers in Fresno County (54% Latinx) alone, than in all 25 of the counties with the lowest proportional Latinx populations *combined*.

Table 9. Disproportionate use of pesticides linked to childhood cancer, Fresno County versus 25 counties with smallest Latinx percentages, total pounds, 2019

Childhood cancer-linked pesticide	Pounds applied in 2019 Fresno County	Pounds applied in 2019 in the 25 counties <24% Latinx
Bromacil	437	57
Chlorothalonil	85,193	27,705
Dimethoate	30,045	2,661
Diuron	7,979	11,429
Kresoxim-methyl	4,180	1,319
Linuron	2,055	1,812
Metam-sodium	847,575	232,733
Paraquat dichloride	178,491	57,143
Phosmet	1,130	520
Propanil	6,398	407,349
Propiconazole	29,561	12,450
Thiophanate-methyl	15,382	12,568
Triforine[1]	0	0
Total toxic 13 pesticides	**1,208,425**	**767,746**

* Not registered in California in 2019

California communities call for justice: Ending pesticide secrecy, restricting the use of the pesticides linked to childhood cancers, and adopting bold models of regulatory and agricultural change

There is something in the air, and it causes childhood cancers, according to these two new studies, as well as decades of others linking pesticide exposures to childhood cancers (See attached annotated bibliography of pesticides and childhood cancer research from Beyond Pesticides).

Stop pesticide secrecy: Immediately web-post pesticide warnings

The use of these carcinogenic pesticides is kept secret from the public. If a parent, teacher, nurse, or union organizer wants to know what, when, and where hazardous pesticides will be applied in order to warn their loved ones, students, patients, or workers to take safety precautions, there is no current way to find out. County Agricultural Commissioners already receive from growers Notices of Intent (NOIs) to apply "restricted" pesticides—those recognized by the State as most hazardous—at least 24 hours before the planned application. The Ag Commissioners could simply web-post those NOIs, so the public could have access to the application information and take precautions recommended by scientists to reduce pesticide exposure, like shutting windows and doors, keeping more vulnerable people inside, refraining from drying clothes outside, and avoiding application areas—especially if one is pregnant.

The public has a right to know about upcoming pesticide applications, and has been demanding it throughout the state.

DPR has embarked upon plans to develop a statewide notification system or regulation, but has scheduled a planning process that extends through June 2024. Community members argue that NOIs are public documents that can be made public *now*, without spending years on the regulatory process. Previous efforts by DPR to develop a fumigant notification rule in 2016 quickly withered under a blast of opposition from industry, which adamantly opposes any move toward greater transparency.

"Agricultural Commissioners act under the direction and supervision of the director of the Department of

Pesticide Regulation. The state can use its existing authority to require county agricultural commissioners to post NOIs in advance on a public website," argues Paulina Torres, staff attorney with Delano-based Center on Race, Poverty and the Environment. "Since no burden would be placed on growers and pesticide applicators, no regulation is needed. The time to require more transparency is now, not years from now."[23]

Restrict use of pesticides linked to childhood cancers

One of the reasons rural California communities demand pesticide warnings is because pesticide regulators have a long history of delayed action even after overwhelming scientific evidence of pesticide harms. Here are three prominent examples:

- The DDT ban took 10 years after Rachel Carson's *Silent Spring* warning.
- Ten years after the 2005 International Montreal Protocol ban, 2.4 million pounds of methyl bromide were used in California, as strawberry growers took advantage of "emergency exemptions."
- Brain- and lung-harming chlorpyrifos was cancelled in the fields 20 years after its phaseout for residential use.

While we wait, we at least want to have a chance to take care of ourselves, to the extent possible. We can't do that if pesticide applications continue to be a secret known only to growers and County Ag Commissioners.

Notification is not enough; the use of pesticides linked to childhood cancers must be restricted in an expedited way. As noted above, dozens of countries have banned or not approved 10 of the Toxic 13, while an 11th, metam-sodium, is banned in two countries. We don't need to use these pesticides.

The State as well as County Ag Commissioners could and should follow the science and apply *immediate emergency safety buffers of 2.5 miles around all residences, schools, hospitals, and other sensitive sites in which the Toxic 13 cannot be applied*. This stopgap measure should at least be in place until the process to end their use entirely is complete.

Begin bold actions to reform pesticide regulation and the pesticide-intensive agricultural system

The Toxic 13 is just one group of many pesticides that threaten children's health. While California may indeed be among this country's leaders in many aspects of pesticide regulation, it is the leader of a poorly regulated nation. Dozens of countries better protect their residents from pesticide harms simply by banning the worst of them. In a recent article in *Environmental Health* comparing pesticide regulations amongst agricultural powers, the authors found:

> Of the pesticides used in USA agriculture in 2016, 322 million pounds were of pesticides banned in the EU, 26 million pounds were of pesticides banned in Brazil and 40 million pounds were of pesticides banned in China. Pesticides banned in the EU account for more than a quarter of all agricultural pesticide use in the USA. The majority of pesticides banned in at least two of these three nations have not appreciably decreased in the USA over the last 25 years and almost all have stayed constant or increased over the last 10 years.[24]

A U.S. Senate Bill from 2020 noted similarly:

> United States lags behind the European Union and other developed nations in protecting its people and its environment from toxic chemicals, allowing the use of 72 pesticides that have been banned or are being phased out in the European Union alone.[25]

To better protect U.S. residents from highly hazardous pesticides, our regulatory system requires a major overhaul. One model for such a systematic change in pesticide regulation aimed at protecting public health can be found in the "Protect America's Children from

Toxic Pesticides Act", proposed in the U.S. Senate in the summer of 2020. The bill calls for comprehensive regulatory changes, including the following:

- Ending indefinite delays in pesticide review
- Requiring emergency review of pesticides banned in other nations
- Ending abuse of emergency exemptions
- Cancelling use of organophosphates, neonicotinoids, and paraquat
- Ending state preemption of local pesticide laws[26]

DPR should adopt the elements of the "Protect America's Children from Toxic Pesticides Act."

Finally, to realize a truly healthy California agricultural industry, pesticide regulation is certainly not enough. The way we grow food must be safer for workers, for our communities, for our soil, water, and air, and for our climate.

The European Union's "Farm to Fork Strategy" puts forward a bold model for significant change in a healthier-for-all direction, driven by goals of 50% decrease in the use of synthetic pesticides by 2030 and growing organic acreage to 25% of total ag land by the same year.[27]

That could and should be the plan for our state.

Notes

1 Exposure to drifting pesticides could come through the air, but also through water contamination, and by dusts that accumulate in homes and other areas.

2 We use the term *Latinx* where government data bases use *Hispanic*. Hispanic or Latinx refers to a person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin regardless of race. The term is separate from the category *white* in databases we used.

3 Authored by Andrew Park, Beate Ritz, Fei Yu, Myles Cockburn, and Julia Heck, all affiliated with prominent Los Angeles-area research institutions, UCLA (three of the four at the Fielding School of Public Health) and USC (Cockburn) in 2020. *International Journal of Hygiene and Environmental Health*, Volume 226, May 2020, 113486, https://doi.org/10.1016/j.ijheh.2020.113486

4 *International Journal of Hygiene and Environmental Health*, Volume 226, May 2020, 113486, https://doi.org/10.1016/j.ijheh.2020.113486

5 Lead authors Christina Lombardi and Shiraya Thompson, were joined by three co-authors from the previous study, Professors Ritz, Cockburn, and Heck. *Environmental Research,* Volume 197, June 2021, 111078, https://doi.org/10.1016/j.envres.2021.111078

6 *Environmental Research*, Volume 197, June 2021, 111078, https://doi.org/10.1016/j.envres.2021.111078

7 See extensive annotated bibliography by Beyond Pesticides attached to this paper.

8 Pesticide Use Near Schoolsites, https://www.cdpr.ca.gov/docs/legbills/rulepkgs/16-004/16-004_final_text.pdf

9 Not all of the Toxic 13 are state-listed carcinogens, as paraquat dichloride is not included, but is listed as a possible carcinogen by U.S. EPA.

10 Data calculated from annual figures from the California Department of Public Health's "Agricultural Pesticide Mapping Tool" at https://trackingcalifornia.org/pesticides/pesticide-mapping-tool. The decade calculations included only years available from the site, 1991-1999 and 2010-2018.

11 https://trackingcalifornia.org/pesticides/pesticide-mapping-tool

12 Adjusted Odds Ratio (aOR): 2.83, 95% CI: 1.67–4.82. *International Journal of Hygiene and Environmental Health*, Volume 226, May 2020, 113486, https://doi.org/10.1016/j.ijheh.2020.113486

13 https://www.cdpr.ca.gov/docs/envjust/

14 Demographic race/ethnicity data from https://www.indexmundi.com/facts/united-states/quick-facts/california/hispanic-or-latino-population-percentage#table; Total county population data from https://www.california-demographics.com/counties_by_population. Pesticide use data downloaded from UC Davis PUR Web GIS v. 2 at http://purwebgis.ucdavis.edu/PURwebGIS.html

15 The 11 most Latinx counties are 54,429 mi2 in total area, and the 25 least Latinx counties are 58,510 mi2 http://www.usa.com/rank/california-state--land-area--county-rank.htm

16 While all of Santa Cruz County is included, some zip codes extend beyond Santa Cruz County boundaries. The data can not be parsed by county only, so some residents from other counties are included in these figures.

17 https://statisticalatlas.com/zip/95076/Race-and-Ethnicity

18 Compiling "White" versus "Hispanic" data for all zip codes encompassing Santa Cruz County on https://statisticalatlas.com yields 165,142 white residents versus 100,214 Latinx residents. Zip 95076 had 20,820 whites (20,820/165,142 = 12.6%) and 60,574 Latinx (60,574/100,214 = 60.4%).

19 Data downloaded from http://purwebgis.ucdavis.edu/PURwebGIS.html

20 Data downloaded from http://purwebgis.ucdavis.edu/PURwebGIS.html for zips 93450, 93901, 93905, 93906, 93907, 93908, 93926, 93927, 93930, 93960, 95012, and 95039.

21 https://www.indexmundi.com/facts/united-states/quick-facts/california/hispanic-or-latino-population-percentage#table

22 https://statisticalatlas.com

23 Californians for Pesticide Reform News Release, May 27, 2021.

24 Donley, Environmental Health (2019) 18:44, https://doi.org/10.1186/s12940-019-0488-0

25 Senate Bill 4406, "Protect America's Children from Toxic Pesticides Act", August 4, 2020

26 Senate Bill 4406, "Protect America's Children from Toxic Pesticides Act", August 4, 2020

27 "European Union's Farm to Fork Strategy – for a fair, healthy and environmentally-friendly food system," https://www.fao.org/agroecology/database/detail/en/c/1277002/ ; Full text available at: https://ec.europa.eu/food/sites/food/files/safety/docs/f2f_action-plan_2020_strategy-info_en.pdf

Pesticides Linked to Childhood Cancers – Annotated Bibliography

Childhood Brain Cancer

Exposure to pyrethroid pesticides and the risk of childhood brain tumors in East China

Pesticide exposure is hypothesized as one of the risk factors for the development of childhood brain tumors (CBT). This hospital-based case-control study evaluated the association of pyrethroid pesticide exposure with the risk for CBT in a children population in East China. In total, 161 CBT cases and 170 controls were recruited from two children's medical centers in Shanghai (Xinhua Hospital and Shanghai Children's Medical Center) between September 2012 and June 2015. The cases and controls were matched for age, sex, and province of residence. Pyrethroid pesticide exposure was evaluated by urinalysis of three nonspecific metabolites of pyrethroids (cis-DCCA, trans-DCCA, and 3-PBA) using gas chromatography-mass spectrometry (GC-MS) detection and by administering a questionnaire. Unconditional logistic regression showed that trans-DCCA, 3-PBA, and total metabolites (sum of the three metabolites) were positively associated with the increased risk of CBT. Children in the highest quartile had a nearly three-fold increased risk of CBT compared with those in the lowest quartile after adjusting for confounding factors (trans-DCCA, odds ratio (OR) = 2.58, 95% confidence interval (CI), 1.38-4.80, p = 0.003; 3-PBA, OR = 3.26, 95% CI, 1.73-6.14, p < 0.0001; total metabolites, OR = 3.60, 95% CI, 1.87-6.93, p < 0.0001). We also found that exposure to both mosquitocide and cockroach killer was related to the increased risk of CBT (mosquitocide, OR = 1.68, 95% CI, 1.06-2.67, p = 0.027; cockroach killer, OR = 1.83, 95% CI, 1.13-2.95, p = 0.013). These findings indicate that exposure to pyrethroid pesticides might be associated with increased risk of CBT. Prospective cohort studies with larger sample sizes are required to confirm this conclusion

Chen S, Gu S, Wang Y, Yao Y, et al. 2016. Environ Pollut. 218:1128-1134.

Increased risk of childhood brain tumors among children whose parents had farm-related pesticide exposures during pregnancy

Malignant brain tumors rank second in both incidence and mortality by cancer in children, and they are the leading cause of cancer death in children. While there are several studies which link pesticide exposure to increased risk of CBT, findings have been inconsistent. Authors performed a meta-analysis on 15 published epidemiological studies to test that in utero exposure to pesticides may be involved in the development of brain cancer in children. Findings of meta-analyses revealed a significantly increased risk of CBT among children whose mothers had farm-related exposures during pregnancy (RR=1.48, 95% CI=1.18-1.84). A dose response was recognized when this risk estimate was compared to those for risk of CBT from maternal exposure to non-agricultural pesticides (e.g., home extermination, pest strips) during pregnancy (RR=1.36, 1.10-1.68), and risk of CBT among children exposed to agricultural activities (RR=1.32, 1.04-1.67). Three studies combined for the paternal exposure to pesticides during preconception produced a calculated summary risk estimate of odds ratio (OR) = 2.29 (95% CI: 1.39-3.78). Meta-analysis of five studies of paternal exposure to pesticides during pregnancy produced a final calculated summary risk estimate of OR = 1.63 (95% CI: 1.16-2.31). The search of the CTD databases revealed association between herbicide and astrocytoma and more than 300 genes are altered by exposure to herbicide, fungicide, insecticide or pesticides. Based on the collective results of these meta-analyses, it appears that pesticide exposure may increase risk of CBT, with preconception and prenatal exposures being especially important factors in increasing risk of its development.

Kunkle B, Bae S, Singh KP, Roy D. 2014. JP J Biostat. 11(2):89-101

Exposure to pesticides and the risk of childhood brain tumors

Previous research has suggested positive associations between parental or childhood exposure to pesticides and risk of childhood brain tumors (CBT). This Australian case-control study of CBT investigated whether exposures to pesticides before pregnancy, during pregnancy and during childhood, were associated with an increased risk. Cases were recruited from 10 pediatric oncology centers, and controls by random-digit dialing, frequency matched on age, sex, and State of residence. The odds ratios (ORs) for professional pest control treatments in the home in the year before the index pregnancy, during the pregnancy, and after the child's birth were 1.54 (95% confidence interval (CI): 1.07, 2.22), 1.52 (95% CI: 0.99, 2.34) and 1.04 (95% CI: 0.75, 1.43), respectively. ORs for treatments exclusively before pregnancy and during pregnancy were 1.90 (95% CI: 1.08, 3.36) and 1.02 (95% CI: 0.35, 3.00), respectively. The OR for the father being home during the treatment was 1.79 (95% CI: 0.85, 3.80). The OR for paternal occupational exposure in the year before the child's conception was 1.36 (95% CI: 0.66, 2.80). ORs for prenatal home pesticide exposure were elevated for low- and high-grade gliomas; effect estimates for other CBT subtypes varied and lacked precision. These results suggest that preconception pesticide exposure, and possibly exposure during pregnancy, is associated with an increased CBT risk. It may be advisable for both parents to avoid pesticide exposure during this time.

Greenop KR, Peters S, Bailey HD, et al. 2013. Cancer Causes Control. 24(7):1269-78

Childhood brain tumors, residential insecticide exposure, and pesticide metabolism genes

Insecticides that target the nervous system may play a role in the development of childhood brain tumors (CBTs). Constitutive genetic variation affects metabolism of these chemicals. We analyzed population-based case-control data to examine whether CBT is associated with the functional genetic polymorphisms PON1C-108T, PON1Q192R, PON1L55M, BCHEA539T, FMO1C-9536A, FMO3E158K, ALDH3A1S134A, and GSTT1 (null). DNA was obtained from newborn screening archives for 201 cases and 285 controls, <or= 10 years of age, and born in California or Washington State between 1978 and 1990. Conception-to-diagnosis home insecticide treatment history was ascertained by interview. We observed no biologically plausible main effects for any of the metabolic polymorphisms with CBT risk. However, we observed strong interactions between genotype and insecticide exposure during childhood. Among exposed children, CBT risk increased per PON1-108T allele [odds ratio (OR) = 1.8; 95% confidence interval (CI), 1.1-3.0] and FMO1-9536A (*6)

allele (OR = 2.7; 95% CI, 1.2-5.9), whereas among children never exposed, CBT risk was not increased (PON1: OR = 0.7; 95% CI, 0.5-1.0, interaction p = 0.005; FMO1: OR = 1.0; 95% CI, 0.6-1.6, interaction p = 0.009). We observed a similar but statistically nonsignificant interaction between childhood exposure and BCHEA539T (interaction p = 0.08). These interactions were present among both Hispanic and non-Hispanic white children. Based on known effects of these variants, these results suggest that exposure in childhood to organophosphorus and perhaps to carbamate insecticides in combination with a reduced ability to detoxify them may be associated with CBT. Confirmation in other studies is required.

Nielsen, S.S., et al. 2010. Childhood brain tumors, residential insecticide exposure, and pesticide metabolism genes. Environmental Health Perspectives 118(1):144-149

Critical Confluence: Gene Variants, Insecticide Exposure May Increase Childhood Brain Tumor Risk

Epidemiologic data have suggested a link between pesticide exposures and childhood brain tumors. The link may be specific to insecticides such as organophosphorus and carbamate compounds, which are known to target the nervous system. Previously published work investigated the role of individual genetic variation with a focus on paraoxonase (PON1), a key enzyme in the metabolism of organophosphorus insecticides commonly used in homes at the time but now banned for residential use. This work showed that children with brain tumors were more likely to carry a common single-nucelotide polymorphism (SNP) gene variant in the promoter region of the PON1 gene (PON1C-108T) than other children, and that the association between this SNP and brain tumors was stronger in children with a history of home insecticide exposure. Research in an expanded study population now provides additional evidence that exposure to insecticides, paired with specific metabolism gene variants, may increase the risk of childhood brain tumors.

Barrett, J. 2010. Environ Health Perspect. 118(1): A35

Parental exposure to pesticides and childhood brain cancer: U.S. Atlantic coast childhood brain cancer study

The etiology of childhood brain cancer remains largely unknown. However, previous studies have yielded suggestive associations with parental pesticide use. Study aimed to evaluate parental exposure to pesticides at home and on the job in relation to the occurrence of brain cancer in children. Authors included 526 one-to-one-matched case-control pairs. Brain cancer cases were diagnosed at < 10 years of age, and were identified from statewide cancer registries of four U.S. Atlantic Coast states. Using information on residential pesticide use and jobs held by fathers during the two-year period before the child's birth, authors assessed potential exposure to insecticides, herbicides, and fungicides. A significant risk of astrocytoma was associated with exposures to herbicides from residential use. Combining parental exposures to herbicides from both residential and occupational sources, the elevated risk remained significant. However, these findings should be viewed in light of limitations in exposure assessment and effective sample size.

Shim YK, Mlynarek SP, van Wijngaarden E. 2009. Environ Health Perspect. 117(6):1002-6.

A case-control study of childhood brain tumors and fathers' hobbies: a Children's Oncology Group study

A case-control study evaluating parental risk factors for childhood brain tumors finds a significant association for home lawn care pesticide applications during pregnancy (OR 1.6) and after birth (OR 1.8) and thus pesticides may increase the risk of medulloblastoma and primitive neuroectodermal tumors in children.

Rosso, A.L., et al. 2008. Cancer Causes Control 19(10)1201-1207

The Upper Midwest Health Study: a case-control study of primary intracranial gliomas in farm and rural residents

A NIOSH population based case control study finds moving to a farm as an adolescent (between the ages of 11 and 20), rather than moving to a farm as an adult, is associated with a greater risk for gliomas.

Ruder, A.M., et al. 2006. J Agric Saf Health 12(4):255-274

Risk of brain tumors in children and susceptibility to organophosphorus insecticides: the potential role of paraoxonase (PON1)

Prior research suggests that childhood brain tumors (CBTs) may be associated with exposure to pesticides. Organophosphorus insecticides (OPs) target the developing nervous system, and until recently, the most common residential insecticides were chlorpyrifos and diazinon, two OPs metabolized in the body through the cytochrome P450/paraoxonase 1 (PON1) pathway. To investigate whether two common PON1 polymorphisms, C-108T and Q192R, are associated with CBT occurrence, authors conducted a population-based study of 66 cases and 236 controls using DNA from neonatal screening archive specimens in Washington State, linked to interview data. The risk of CBT was nonsignificantly increased in relation to the inefficient PON1 promoter allele [per PON1(-108T) allele, relative to PON1(-108CC): odds ratio (OR) = 1.4; 95% confidence interval (CI), 1.0-2.2; p-value for trend = 0.07]. Notably, this association was strongest and statistically significant among children whose mothers reported chemical treatment of the home for pests during pregnancy or childhood (per PON1(-108T) allele: among exposed, OR = 2.6; 95% CI, 1.2-5.5; among unexposed, OR = 0.9; 95% CI, 0.5-1.6) and for primitive neuroectodermal tumors (per PON1(-108T) allele: OR = 2.4; 95% CI, 1.1-5.4). Larger studies that measure plasma PON1 levels and incorporate more accurate estimates of pesticide exposure will be required to confirm these observations.

Searles Nielsen S, Mueller BA, De Roos AJ, et al. 2005. Environ Health Perspect.113(7):909-13.

Farm-related exposures and childhood brain tumours in seven countries: results from the SEARCH International Brain Tumour Study

A total of 1218 cases of childhood brain tumours (CBT) and 2223 control subjects from the general population were included in a population-based case-control study conducted in nine centres in seven countries. Mothers were asked about farm- or agriculture-related exposures. Significantly elevated odds ratios (OR) for CBT were associated with children's personal and maternal prenatal exposure while living on a farm with pigs (child OR = 1.7, mother OR = 2.3), horses (child OR = 1.6, mother OR = 1.8), dogs (child OR = 1.5, mother OR = 1.5) and cats (child OR = 1.5, mother OR = 1.7). Children who were exposed to pigs, horses and cats combined, while living on a farm, had a threefold elevated OR for CBT. Increased ORs for primitive neuroectodermal tumours (PNET) were associated with children's farm exposure to dogs (OR = 1.9) and cats (OR = 2.2), and maternal farm exposure to pigs (OR = 4.2). The OR for CBT was elevated (OR = 2.3) for children of mothers who had preconception/prenatal farm- or agriculture-related employment involving potential contact with animals, relative to no farm- or agriculture-related employment. In particular, increased ORs for CBT were observed for children of mothers who were employed as general farmers (OR = 4.1) or general farm workers (OR = 3.8). During the 5 years preceding the index child's birth, maternal exposures were related

to CBT, relative to no maternal exposure to agricultural chemicals or animal products: fertilisers (OR = 1.8), pesticides (OR = 2.0), animal manure (OR = 2.0) and unprocessed wool (OR = 3.0). Our findings suggest that various farm-related exposures are positively associated with CBT and warrant further investigation into the public health importance of these associations.

Efird, J.T., et al. 2003. Paediatr Perinat Epidemiol 17(2):201-211

Parental occupational exposure to pesticides and childhood brain cancer

A community-based case-control study of parental occupational pesticide exposure and childhood brain cancer finds a slightly elevated risk of astrocytoma for paternal exposure to insecticides, herbicides, and fungicides; a slightly elevated risk of primitive neuroectodermal tumors (PNET) for paternatal exposure to herbicides. The study also finds a small elevated risk for astrocytoma for maternal exposure to insecticides and non-agricultural fungicides.

Van Wijngaarden, E., et al. 2003. American Journal of Epidemiology 157(11):989-997

Farm and animal exposures and pediatric brain tumors: results from the U.S. West Coast Childhood Brain Tumor Study

Nineteen counties from San Francisco and Los Angeles, California, and Seattle, Washington, were the United States sites for a large population-based case-control study of childhood brain tumors (CBTs), sponsored by the National Cancer Institute. CBT patients who were <20 years of age and were diagnosed between 1984 and 1991 were reported to each region's cancer registry. The 801 control subjects were obtained by random digit dial and were frequency-matched to the 540 CBT patients in San Francisco and Seattle (one patient to two controls) and in Los Angeles (one patient to one control). Data collected by in-person interview with subjects' mothers were analyzed to investigate an association between risk for CBTs and life on a farm, exposure to farm animals (dairy cattle, beef cattle, pigs, sheep/goats, poultry, and horses), and some cat and non-farm horse exposures. Elevated risks for CBTs were observed in association with mothers' exposure to pigs [odds ratio (OR) = 3.8, 95% confidence interval (CI) = 1.2-12] and horses (OR = 2.2, 95% CI = 1.0-4.8) on a farm during the index pregnancy. Children diagnosed with primitive neuroectodermal tumors showed elevated risks for CBTs with personal and maternal prenatal exposure to pigs (child, OR = 4.0, 95% CI = 1.2-13; mother, OR = 11.9, 95% CI = 2.8-51) and poultry (child, OR = 3.0, 95% CI = 1.1-8.0; mother, OR = 4.0, 95% CI = 1.2-14). No other animal exposures of children or mothers were found to be consistently related to CBTs. Children diagnosed with primitive neuroectodermal tumors who were on a farm for > 1 year and were first on a farm when they were < 6 months of age also had increased risk for CBTs (OR = 3.9, 95% CI = 1.2-13). A somewhat increased risk for CBTs was found for children of mothers who ever had worked on livestock farms compared with mothers who never had worked on a farm (OR = 7.4, 95% CI = 0.86-64, based on five case mothers and one control mother who worked on livestock farms during the five years preceding the birth of the index child). The associations are consistent with those of two previous studies in Norway (P. Kristensen et al., Int. J. Cancer, 65: 39-50, 1996) and the United States and Canada (G. R. Bunin et al., Cancer Epidemiol. Biomark. Prev., 3: 197-204, 1994) that investigated the role of farm-related exposures in the etiology of CBTs.

Holly, E.A., et al. 1998. Cancer Epidemiol Biomarkers Prev 7(9):797-802

Household pesticides and risk of pediatric brain tumors

A follow-up to a population-based case-control study of pediatric brain tumors in Los Angeles County, California, involving mothers of 224 cases and 218 controls, investigated the risk of household pesticide use from pregnancy to diagnosis. Risk was significantly elevated for prenatal exposure to flea/tick pesticides -odds ratio (OR) = 1.7; 95% confidence interval (CI), 1.1-2.6-, particularly among subjects less than five years old at diagnosis (OR = 2.5; CI, 1. 2-5.5). Prenatal risk was highest for mothers who prepared, applied, or cleaned up flea/tick products themselves (OR = 2.2; CI, 1.1-4.2; for subjects less than five years of age, OR = 5.4; CI, 1.3-22.3). A significant trend of increased risk with increased exposure was observed for number of pets treated (p = 0.04). Multivariate analysis of types of flea/tick products indicated that sprays/foggers were the only products significantly related to risk (OR =10.8; CI, 1.3-89.1). Elevated risks were not observed for termite or lice treatments, pesticides for nuisance pests, or yard and garden insecticides, herbicides, fungicides, or snail killer. Certain precautions,if ignored, were associated with significant increased risk: evacuating the house after spraying or dusting for pests (OR = 1.6; CI, 1.0-2.6), delaying the harvest of food after pesticide treatment (OR = 3.6; CI, 1.0-13.7), and following instructions on pesticide labels (OR = 3. 7;CI, 1.5-9.6). These findings indicate that chemicals used in flea/tick products may increase risk of pediatric brain tumors and suggest that further research be done to pinpoint specific chemicals involved.

Pogoda, J.M. and Preston-Martin, S. 1997. Environmental Health Perspectives 105:1214-1220

Cancer in offspring of parents engaged in agricultural activities in Norway: incidence and risk factors in the farm environment

In this study of cancer in offspring we demonstrate that factors linked to horticulture and use of pesticides are associated with cancer at an early age, whereas factors in animal husbandry, in particular poultry farming, are associated with cancers in later childhood and young adulthood. Incident cancer was investigated in offspring born in 1952–1991 to parents identified as farm holders in agricultural censuses in Norway in 1969–1989. In the follow-up of 323,292 offspring for 5.7 million person-years, 1,275 incident cancers were identified in the Cancer Registry for 1965–1991. The standardized incidence for all cancers was equal to the total rural population of Norway, but cohort subjects had an excess incidence of nervous-system tumours and testicular cancers in certain regions and strata of time that could imply that specific risk factors were of importance. Classification of exposure indicators was based on information given at the agricultural censuses. Risk factors were found for brain tumours, in particular non-astrocytic neuroepithelial tumours: for all ages, pig farming tripled the risk [rate ratio (RR), 3.11; 95% confidence interval (CI), 1.89-5.13]; indicators of pesticide use had an independent effect of the same magnitude in a dose-response fashion, strongest in children aged 0 to 14 years (RR, 3.37; 95% CI, 1.63-6.94). Horticulture and pesticide indicators were associated with all cancers at ages 0 to 4 years, Wilms' tumour, non-Hodgkin's lymphoma, eye cancer and neuroblastoma. Chicken farming was associated with some common cancers of adolescence, and was strongest for osteosarcoma and mixed cellular type of Hodgkin's disease. The main problem in this large cohort study is the crude exposure indicators available; the resulting misclassification is likely to bias any true association towards unity.

Kristensen, P., et al. 1996. Int J Cancer 65(1):39-50

Incidence and risk factors for childhood brain tumors in the Ile de France

A case-control study in France coordinated by International Agency for Research on Cancer finds a statistically significant association for farm residence and home treated with pesticides for childhood brain tumors

Cordier, S., et al. 1994. Int J Cancer 59(6):776-782

Risk factors for astrocytic glioma and primitive neuroectodermal tumor of the brain in young children: a report from the Children's Cancer Group

A case-control study focusing on gestational exposures find elevated risks for primitive neuroectodermal tumor (PNET), one the of the most common subtypes of brain tumors in children, for mother's residence on a farm during pregnancy and for the child's residence on a farm for at least one year. Mothers of astrocytoma brain cancer cases were more likely than their controls to report weekly use of insect sprays and pesticides.

Bunin, G.R., et al. 1994. Cancer Epidemiology, Biomarkers and Prevention 3:197-204

Family pesticide use and childhood brain cancer

The relationship between family pesticide use and childhood brain cancer was examined in a case-control study. Telephone interviews were conducted from June 1989 through March 1990 with the natural mothers of 45 childhood brain cancer cases, 85 friend controls, and 108 cancer controls. In comparisons to friend controls, significant positive associations were observed for use of pesticides to control nuisance pests in the home, no-pest-strips in the home, pesticides to control termites, Kwell shampoo, flea collars on pets, diazinon in the garden or orchard, and herbicides to control weeds in the yard. In comparisons to cancer controls, significant positive associations were observed for use of pesticide bombs in the home, pesticides to control termites, flea collars on pets, insecticides in the garden or orchard, carbaryl in the garden or orchard, and herbicides to control weeds in the yard. In general, positive associations in comparisons to one control group were supported by elevated odds ratios in comparisons to the other control group. Several potentially important associations were identified in this study. However, small sample sizes, potential recall bias, multiple comparisons, and lack of detailed exposure verification require further research to confirm these findings.

Davis, J., et al. 1993. Family pesticide use and childhood brain cancer. Archives of Environmental Contamination and Toxicology 24:87-92

Parental occupation and intracranial neoplasms of childhood: results of a case-control interview study

A case-control study of childhood brain tumors finds paternal employment in agriculture is associated with excess risk.

Wilkins, J.R. and T. Sinks. 1990. Am J Epidemiol 132(2):275-292

Paternal occupation and brain cancer in offspring: a mortality-based case-control study

A mortality-based case-control study of Ohio-born children who died from brain cancer looking at paternal occupation finds that case fathers are more likely than control fathers to have been employed, at the time of the child's birth, in agriculture.

Wilkins, J.R. and Koutras, R.A. 1988. Am J Ind Med 14(3):299-318

Risk factors for brain tumors in children

An exploratory case-control study in Baltimore, Maryland, finds that more children with brain tumors and children with other cancers are found to have been exposed to insecticides than other children.

Gold, E., et al. 1979. American Journal of Epidemiology 109(3):309-319

Childhood Leukemia

Agricultural crop density in the municipalities of France and incidence of childhood leukemia: An ecological study

Pesticide exposure is suspected to play a role in the etiology of childhood leukemia (AL). Various sources of exposure have been explored, but few studies have investigated the risk of childhood AL in relation to residential exposure to agricultural pesticides. Since around 50% of France is agricultural land, with marked pesticide use, France is a suitable location to investigate for an association. We aimed to analyze the association between the agricultural crop density in the municipalities of France and the incidence of childhood AL between 1990 and 2014. 11,487 cases of AL diagnosed in children aged 0–14 years were registered by the French National Registry of Childhood Hematological Malignancies over 1990–2014. National agricultural census data for 1990, 2000 and 2010 were used to estimate the densities of the most common crops in France. The incidence of AL was estimated in the 35,512 municipalities, by age and gender, and 3 observation periods, and expressed as the standardized incidence ratio (SIR). We observed a moderate log-linear association between viticulture density and the incidence of AL, with a 3% increase in SIR for a 10% increase in viticulture density (SIRR = 1.03; 95%CI [1.00–1.06]). The association remained for lymphoblastic AL but not for myeloid AL. The association was stable after stratification by geographic area, age and period, and after adjustment on UV radiation and a French deprivation index. No consistent association was observed for other crop types. This nationwide study shows a moderate increase in incidence of childhood AL in municipalities where viticulture is common. Future individual studies are needed to know whether this observation is confirmed and related to particular use of pesticides.

Coste, A., Goujon, S., Faure, L., Hémon, D. and Clavel, J., 2020. Environmental Research, p.109517.

Prenatal pesticide exposure and childhood leukemia - A California statewide case-control study

A number of epidemiologic studies with a variety of exposure assessment approaches have implicated pesticides as risk factors for childhood cancers. Here we explore the association of pesticide exposure in pregnancy and early childhood with childhood acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) utilizing land use and pesticide use data in a sophisticated GIS tool. We identified cancer cases less than six years of age from the California Cancer Registry and cancer-free controls from birth certificates. Analyses were restricted to those living in rural areas and born 1998–2011, resulting in 162 cases of childhood leukemia and 9,805 controls. Possible carcinogens were selected from the Environmental Protection Agency's classifications and pesticide use was collected from the California Department of Pesticide Regulation's (CDPR) Pesticide Use Reporting (PUR) system and linked to land-use surveys. Exposures for subjects were assessed using a 4000m buffer around the geocoded residential addresses at birth. Unconditional logistic and hierarchical regression models were used to assess individual pesticide and pesticide class associations. We observed elevated risks for ALL with exposure to any carcinogenic pesticide (adjusted Odds Ratio (aOR): 2.83, 95% CI: 1.67-4.82), diuron (Single-pesticide model, adjusted (OR): 2.38, 95% CI: 1.57-3.60), phosmet (OR: 2.10, 95% CI: 1.46-3.02), kresoxim-methyl (OR: 1.77, 95% CI: 1.14-2.75), and propanil (OR: 2.58, 95% CI: 1.44-4.63). Analyses based on chemical classes showed elevated risks for the group of 2,6-dinitroanilines (OR: 2.50, 95% CI: 1.56-3.99), anilides (OR: 2.16, 95% CI: 1.38-3.36), and ureas (OR: 2.18, 95% CI: 1.42-3.34). Our findings suggest that in rural areas of California exposure to certain pesticides or pesticide classes during pregnancy due to residential proximity to agricultural applications may increase the risk of childhood ALL and AML. Future studies into the mechanisms of carcinogenicity of these pesticides may be beneficial.

Park, A.S., Ritz, B., Yu, F., Cockburn, M. and Heck, J.E., 2020. International journal of hygiene and environmental health, 226, p.113486.

Prenatal pesticide exposure and childhood leukemia – A California statewide case-control study

A number of epidemiologic studies with a variety of exposure assessment approaches have implicated pesticides as risk factors for childhood cancers. Here we explore the association of pesticide exposure in pregnancy and early childhood with childhood acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) utilizing land use and pesticide use data in a sophisticated GIS tool. We identified cancer cases less than six years of age from the California Cancer Registry and cancer-free controls from birth certificates. Analyses were restricted to those living in rural areas and born 1998–2011, resulting in 162 cases of childhood leukemia and 9,805 controls. Possible carcinogens were selected from the Environmental Protection Agency's classifications and pesticide use was collected from the California Department of Pesticide Regulation's (CDPR) Pesticide Use Reporting (PUR) system and linked to land-use surveys. Exposures for subjects were assessed using a 4000m buffer around the geocoded residential addresses at birth. Unconditional logistic and hierarchical regression models were used to assess individual pesticide and pesticide class associations. We observed elevated risks for ALL with exposure to any carcinogenic pesticide (adjusted Odds Ratio (aOR): 2.83, 95% CI: 1.67–4.82), diuron (Single-pesticide model, adjusted (OR): 2.38, 95% CI: 1.57–3.60), phosmet (OR: 2.10, 95% CI: 1.46–3.02), kresoxim-methyl (OR: 1.77, 95% CI: 1.14–2.75), and propanil (OR: 2.58, 95% CI: 1.44–4.63). Analyses based on chemical classes showed elevated risks for the group of 2,6-dinitroanilines (OR: 2.50, 95% CI: 1.56–3.99), anilides (OR: 2.16, 95% CI: 1.38–3.36), and ureas (OR: 2.18, 95% CI: 1.42–3.34). Our findings suggest that in rural areas of California exposure to certain pesticides or pesticide classes during pregnancy due to residential proximity to agricultural applications may increase the risk of childhood ALL and AML. Future studies into the mechanisms of carcinogenicity of these pesticides may be beneficial.

Park, A.S., Ritz, B., Yu, F., Cockburn, M. and Heck, J.E., 2020. International journal of hygiene and environmental health, 226, p.113486.

A task-based assessment of parental occupational exposure to pesticides and childhood acute lymphoblastic leukemia

Associations between parental occupational pesticide exposure and childhood acute lymphoblastic leukemia (ALL) vary across studies, likely due to different exposure assessment methodologies. This study assessed parental occupational pesticide exposure from the year before pregnancy to the child's third year of life for 669 children diagnosed with ALL and 1021 controls. Authors conducted expert rating using task-based job modules (JM) to estimate exposure to pesticides among farmer workers, gardeners, agricultural packers, and pesticide applicators. Compared to complete JMs, partial JMs and JEM led to 3.1% and 9.4% of parents with pesticide exposure misclassified, respectively. Misclassification was similar in cases and controls. Using complete JMs, we observed an increased risk of ALL for paternal occupational exposure to any pesticides (OR=1.7; 95% CI=1.2, 2.5), with higher risks reported for pesticides to treat nut crops (OR=4.5; 95% CI=0.9, 23.0), and for children diagnosed before five years of age (OR=2.3; 95% CI: 1.3, 4.1). Exposure misclassification from JEM attenuated these associations by about 57%. Maternal occupational pesticide exposure before and after birth was not associated with ALL. The risk of ALL was elevated in young children with paternal occupational pesticide exposure during the perinatal period, using more detailed occupational information for exposure classification.

Gunier RB, Kang A, Hammond SK, Reinier K, et al. 2017. Environ Res. 156:57-62.

Chemical exposure and infant leukaemia: development of an adverse outcome pathway (AOP) for aetiology and risk assessment research

Infant leukaemia (less 1 year old) is a rare disease of an in utero origin at an early phase of foetal development. Rearrangements of the mixed-lineage leukaemia (MLL) gene producing abnormal fusion proteins are the most frequent genetic/molecular findings in infant B cell-acute lymphoblastic leukaemia. In small epidemiological studies, mother/foetus exposures to some chemicals including pesticides have been associated with infant leukaemia; however, the strength of evidence and power of these studies are weak at best. Experimental in vitro or in vivo models do not sufficiently recapitulate the human disease and regulatory toxicology studies are unlikely to capture this kind of hazard. Here, we develop an adverse outcome pathway (AOP) based substantially on an analogous disease-secondary acute leukaemia caused by the topoisomerase II (topo II) poison etoposide-and on cellular and animal models. The hallmark of the AOP is the formation of MLL gene rearrangements via topo II poisoning, leading to fusion genes and ultimately acute leukaemia by global (epi) genetic dysregulation. The AOP condenses molecular, pathological, regulatory and clinical knowledge in a pragmatic, transparent and weight of evidence-based framework. This facilitates the interpretation and integration of epidemiological studies in the process of risk assessment by defining the biologically plausible causative mechanism(s). The AOP identified important gaps in the knowledge relevant to aetiology and risk assessment, including the specific embryonic target cell during the short and spatially restricted period of susceptibility, and the role of (epi) genetic features modifying the initiation and progression of the disease. Furthermore, the suggested AOP informs on a potential Integrated Approach to Testing and Assessment to address the risk caused by environmental chemicals in the future.

Pelkonen O, Terron A, Hernandez AF, et al. 2017. Arch Toxicol. 91(8):2763-2780.

Spatial clustering of childhood leukaemia with the integration of the Paediatric Environmental History

Leukaemia remains the most common type of paediatric cancer and its aetiology remains unknown, but considered to be multifactorial. It is suggested that the initiation in utero by relevant exposures and/or inherited genetic variants and, other promotional postnatal exposures are probably required to develop leukaemia. This study aimed to map the incidence and analyse possible clusters in the geographical distribution of childhood acute leukaemia during the critical periods and to evaluate the factors that may be involved in the aetiology by conducting community and individual risk assessments. Researchers analysed all incident cases of acute childhood leukaemia diagnosed in a Spanish region during the period 1998-2013. At diagnosis, the addresses during pregnancy, early childhood and diagnosis were collected and codified to analyse the spatial distribution of acute leukaemia. A total of 158 cases of acute leukaemia were analysed. The crude rate for the period was 42.7 cases per million children. Among subtypes, acute lymphoblastic leukaemia had the highest incidence (31.9 per million children). A spatial cluster of acute lymphoblastic leukaemia was detected using the pregnancy address ($p<0.05$). The most common environmental risk factors related with the aetiology of acute lymphoblastic leukaemia, identified by the Paediatric Environmental History were: prenatal exposure to tobacco (75%) and alcohol (50%); residential and community exposure to pesticides (62.5%); prenatal or neonatal ionizing radiation (42.8%); and parental workplace exposure (37.5%). Study suggests that environmental exposures in utero may be important in the development of childhood leukaemia. Due to the presence of high-incidence clusters using pregnancy address, it is necessary to introduce this address into the childhood cancer registers. The Paediatric

Environmental History which includes pregnancy address and a careful and comprehensive evaluation of the environmental exposures will allow us to build the knowledge of the causes of childhood leukaemia.

Cárceles-Álvarez A, Ortega-García JA, López-Hernández FA, et al. 2017. Environ Res. 156:605-612

A review of risk factors for childhood leukemia

Leukemia is the most common cancer of childhood, with AML, CML, ALL and CLL being the most common. Environmental and genetic factors have been studied extensively in children with childhood leukemia. Other factors, such as the prenatal parental use of controlled substances, have not been investigated to the same degree. We review what is currently known about environmental and parental factors and the occurrence of leukemia in children.Electronic databases were searched for studies correlated pediatric leukemia with (1) ionizing radiation; (2) benzene; (3) parental drug use (4) parental alcohol use; (5) genetic factors.The two known significant environment risk factors for the occurrence leukemia are ionizing radiation and benzene. However, at least four studies have been published over the last century have looked at other environmental factors such as pesticides and drug and alcohol use as well as genetic factors such as gene fusions and translocations. We determined the risk of environmental and genetic factors that could be the cause of childhood leukemia in an effort to reduce the incidence of this disease.

Jin MW, Xu SM, An Q, Wang P. 2016. Eur Rev Med Pharmacol Sci. 20(18):3760-3764.

Childhood Leukemia and Primary Prevention

Leukemia is the most common pediatric cancer, affecting 3800 children per year in the United States. Its annual incidence has increased over the last decades, especially among Latinos. Although most children diagnosed with leukemia are now cured, many suffer long-term complications, and primary prevention efforts are urgently needed. The early onset of leukemia — usually before five years of age — and the presence at birth of "pre-leukemic" genetic signatures indicate that pre- and postnatal events are critical to the development of the disease. In contrast to most pediatric cancers, there is a growing body of literature — in the United States and internationally — that has implicated several environmental, infectious, and dietary risk factors in the etiology of childhood leukemia, mainly for acute lymphoblastic leukemia, the most common subtype. For example, exposures to pesticides, tobacco smoke, solvents, and traffic emissions have consistently demonstrated positive associations with the risk of developing childhood leukemia. In contrast, intake of vitamins and folate supplementation during the preconception period or pregnancy, breastfeeding, and exposure to routine childhood infections have been shown to reduce the risk of childhood leukemia. Some children may be especially vulnerable to these risk factors, as demonstrated by a disproportionate burden of childhood leukemia in the Latino population of California. The evidence supporting the associations between childhood leukemia and its risk factors — including pooled analyses from around the world and systematic reviews — is strong; however, the dissemination of this knowledge to clinicians has been limited. To protect children's health, it is prudent to initiate programs designed to alter exposure to well-established leukemia risk factors rather than to suspend judgment until no uncertainty remains. Primary prevention programs for childhood leukemia would also result in the significant co-benefits of reductions in other adverse health outcomes that are common in children, such as detriments to neurocognitive development.

Whitehead TP, Metayer C, Wiemels JL, et al. 2016. Curr Probl Pediatr Adolesc Health Care. 46(10):317-352.

Childhood Leukemia: A Preventable Disease

In contrast to most pediatric cancers, there is a growing body of literature, nationally and internationally, that has implicated the role of several environmental indoor and outdoor hazards in the etiology of childhood leukemia. For example, exposures to solvents, traffic, pesticides, and tobacco smoke have consistently demonstrated positive associations with the risk of developing childhood leukemia. Intake of vitamins and folate supplementation during the preconception period or pregnancy has been demonstrated to have a protective effect. Despite the strength of these findings, the dissemination of this knowledge to clinicians has been limited. Some children may be more vulnerable than others as documented by the high and increasing incidence of childhood leukemia in Hispanics. To protect children's health, it is prudent to establish programs to alter exposure to those factors with well-established associations with leukemia risk rather than to suspend judgment until no uncertainty remains. This is particularly true because other serious health outcomes (both negative and positive) have been associated with the same exposures. Study draws from historical examples to put in perspective the arguments of association versus causation, as well as to discuss benefits versus risks of immediate and long-term preventive actions.

Metayer C, Dahl G, Wiemels J, Miller M. 2016. Pediatrics. 138(Suppl 1):S45-S55.

Linking Pesticide Exposure with Pediatric Leukemia: Potential Underlying Mechanisms

Leukemia is the most common cancer in children, representing 30% of all childhood cancers. The disease arises from recurrent genetic insults that block differentiation of hematopoietic stem and/or progenitor cells (HSPCs) and drives uncontrolled proliferation and survival of the differentiation-blocked clone. Pediatric leukemia is phenotypically and genetically heterogeneous with an obscure etiology. The interaction between genetic factors and environmental agents represents a potential etiological driver. Although information is limited, the principal toxic mechanisms of potential leukemogenic agents (e.g., etoposide, benzene metabolites, bioflavonoids and some pesticides) include topoisomerase II inhibition and/or excessive generation of free radicals, which may induce DNA single- and double-strand breaks (DNA-DSBs) in early HSPCs. Chromosomal rearrangements (duplications, deletions and translocations) may occur if these lesions are not properly repaired. The initiating hit usually occurs in utero and commonly leads to the expression of oncogenic fusion proteins. Subsequent cooperating hits define the disease latency and occur after birth and may be of a genetic, epigenetic or immune nature (i.e., delayed infection-mediated immune deregulation). Here, we review the available experimental and epidemiological evidence linking pesticide exposure to infant and childhood leukemia and provide a mechanistic basis to support the association, focusing on early initiating molecular events.

Hernández AF, Menéndez P. 2016. Int J Mol Sci. 17(4):461.

Passive exposure to agricultural pesticides and risk of childhood leukemia in an Italian community

Exposure to pesticides has been suggested as a risk factor for childhood leukemia, but definitive evidence on this relation and the specific pesticides involved is still not clear.We carried out a population-based case-control study in a Northern Italy community to assess the possible relation between passive exposure to agricultural pesticides and risk of acute childhood leukemia.We assessed passive pesticide exposure of 111 childhood leukemia cases and 444 matched controls by determining density and type of agricultural land use within a 100-m radius buffer around children's homes. We

focused on four common crop types, arable, orchard, vineyard and vegetable, characterized by the use of specific pesticides that are potentially involved in childhood induced leukemia. The use of these pesticides was validated within the present study. We computed the odds ratios (OR) of the disease and their 95% confidence intervals (CI) according to type and density of crops around the children's homes, also taking into account traffic pollution and high-voltage power line magnetic field exposure. Childhood leukemia risk did not increase in relation with any of the crop types with the exception of arable crops, characterized by the use of 2.4-D, MCPA, glyphosate, dicamba, triazine and cypermethrin. The very few children (n=11) residing close to arable crops had an OR for childhood leukemia of 2.04 (95% CI 0.50-8.35), and such excess risk was further enhanced among children aged

Malagoli C, Costanzini S, Heck JE, Malavolti M, et al. 2016. Int J Hyg Environ Health. 219(8):742-748.

Agricultural crop density and risk of childhood cancer in the midwestern United States: an ecologic study

This study examined the association of county level agricultural land use and the incidence of specific childhood cancers.Authors linked county-level agricultural census data (2002 and 2007) and cancer incidence data for children ages 0–4 diagnosed between 2004 and 2008 from cancer registries in six Midwestern states. Crop density (percent of county area that was harvested) was estimated for total agricultural land, barley, dry beans, corn, hay, oats, sorghum, soybeans, sugar beets, and wheat. Results found statistically significant exposure-response relationships for dry beans and total leukemias and acute lymphoid leukemias (ALL); oats and acute myeloid leukemias (AML); and sugar beets and total leukemias and ALL. State-level analyses revealed some additional positive associations for total leukemia and CNS tumors and differences among states for several crop density-cancer associations. However, some of these analyses were limited by low crop prevalence and low cancer incidence.The associations observed in this study need to be confirmed by analytic epidemiologic studies using individual level exposure data and accounting for potential confounders that could not be taken into account in this ecologic study.

Booth BJ, Ward MH, Turyk ME, Stayner LT. 2015. Environ Health. 14(1):82

Home pesticide exposures and risk of childhood leukemia: Findings from the childhood leukemia international consortium

Some previous studies have suggested that home pesticide exposure before birth and during a child's early years may increase the risk of childhood leukemia. To further investigate this, authors pooled individual level data from 12 case-control studies in the Childhood Leukemia International Consortium. Exposure data were harmonized into compatible formats. The odds ratio (ORs) for acute lymphoblastic leukemia (ALL) associated with any pesticide exposure shortly before conception, during pregnancy and after birth were 1.39, 1.43 and 1.36, respectively. Corresponding ORs for risk of acute myeloid leukemia (AML) were 1.49, 1.55 and 1.08, respectively. There was little difference by type of pesticide used. The relative similarity in ORs between leukemia types, time periods and pesticide types may be explained by similar exposure patterns and effects across the time periods in ALL and AML, participants' exposure to multiple pesticides, or recall bias.

Bailey HD, Infante-Rivard C, Metayer C, Clavel J, Lightfoot T, et al. 2015. Int J Cancer. 137(11):2644-63.

Household pesticide exposure and the risk of childhood acute leukemia in Shanghai, China

Childhood acute leukemia (AL) is the most common malignant tumor in children, but its etiology remains largely unknown. Study investigated the relationship between household exposure to pesticides and childhood AL. Between 2009 and 2010 in Shanghai, a total of 248 newly diagnosed cases of AL and 111 gender-, age-, and hospital-matched controls were included. Five nonspecific dialkyl phosphate (DAP) metabolites of organophosphate pesticides (OPPs) [including dimethyl phosphate (DMP), diethyl phosphate (DEP), dimethyl thiophosphate (DMTP), diethyl thiophosphate (DETP), and diethyl dithiophosphate (DEDTP)] in the urine were analyzed by gas chromatography. The results showed that the median DMP, DEP, DMTP, DETP, and DEDEP levels adjusted for creatinine (Cr) in cases were all significantly elevated compared with those in controls. The household use of mosquito repellent was significantly associated with an increased risk of childhood AL. Moreover, higher exposures were significantly associated with an elevated risk of childhood AL for DMs, DEs, and DAPs. Findings support the notion that the household use of pesticides may play a role in the etiology of childhood AL and provide some evidence to warrant further investigation of the link between household pesticide exposures and childhood AL in Shanghai.

Zhang Y, Gao Y, Shi R, Chen D, Wang X, et al. 2015. Environ Sci Pollut Res Int. 22(15):11755-63.

Relationship between exposure to pesticides and occurrence of acute leukemia in Iran

One of the causes of acute leukemia can be exposure to certain chemicals such as pesticides. This study determined the relationship between exposure to pesticides and the occurrence of acute leukemia in Fars province, south of Iran. Between April 2011 and April 2013 in a case-control study conducted in Nemazee Hospital in Shiraz, Southern Iran; 314 subjects diagnosed with acute leukemia (94 pediatric cases and 220 adults) were enrolled to determine any correlation between exposure to pesticides and the occurrence.There was a history of exposure to pesticides among 85% of pediatric cases an d 69% of their controls and 83% of adult cases and 75% of their controls while 87.5% of pediatric cases and 90% of adult cases reported exposure to intermediate and high doses of pesticides and among the controls, the exposure to low doses of pesticides was 70.5% and 65%, respectively. Exposure to indoor pesticides was seen among most of cases and controls. Being a farmer was at a significantly more increased risk of developing acute leukemia in comparison to other jobs, especially for their children. Exposure to pesticides was shown to be one of the most important causes of acute leukemia.

Maryam Z, Sajad A, Maral N, Zahra L, et al. 2015. Asian Pac J Cancer Prev. 16(1):239-44.

Residential Exposure to Pesticide During Childhood and Childhood Cancers: A Meta-Analysis

In this meta-analysis, authors aimed to examine associations between residential childhood pesticide exposures and childhood cancers. The literature search yielded 277 studies that met inclusion criteria.Sixteen studies were included in the meta-analysis, and authors found that childhood exposure to indoor but not outdoor residential insecticides was associated with a significant increase in risk of childhood leukemia (odds ratio [OR] = 1.47; 95% CI, 1.26-1.72; I(2) = 30%) and childhood lymphomas (OR = 1.43; 95% CI, 1.15-1.78; I(2) = 0%). A significant increase in risk of leukemia was also associated with herbicide exposure (OR = 1.26; 95% CI, 1.10-1.44; I(2) = 0%). Results from this meta-analysis indicated that children exposed to indoor insecticides would have a higher risk of childhood hematopoietic cancers. Additional research is needed to confirm the association between residential indoor pesticide exposures and childhood cancers. Meanwhile, preventive

measures should be considered to reduce children's exposure to pesticides at home.

Chen M, Chang CH, Tao L, Lu C. 2015. Pediatrics. 136(4):719-29.

Maternal factors and risk of childhood leukemia

The aim of this study was to examine association of childhood leukemia with maternal factors especially during pregnancy, to help in avoiding risk factors.This case-control study included children younger than 18 years diagnosed with leukemia from 2008 to 2012. Statistically significant associations between risk of childhood leukemia with mother's education , occupation and pesticides exposure during pregnancy were found. However, there were no significant links with maternal age, history of fetal loss, history of radiography during pregnancy, history of drug intake and infection during pregnancy. The results showed increased risk of leukemia in children whose mothers were working in agriculture and were exposed to pesticides during pregnancy. The further study needs to be investigated to know association of various maternal risk factors with leukemia which remained unknown in this study.

Kumar A, Vashist M, Rathee R. 2014. Asian Pac J Cancer Prev. 15(2):781-4.

Parental occupational pesticide exposure and the risk of childhood leukemia in the offspring: findings from the childhood leukemia international consortium

Maternal occupational pesticide exposure during pregnancy and/or paternal occupational pesticide exposure around conception have been suggested to increase risk of leukemia in the offspring. Authors pooled individual level data from 13 case-control studies participating in the Childhood Leukemia International Consortium (CLIC). Using exposure data from mothers of 8,236 cases, and 14,850 controls, and from fathers of 8,169 cases and 14,201 controls the odds ratio (OR) for maternal exposure during pregnancy and the risk of acute lymphoblastic leukemia (ALL) was 1.01 and for paternal exposure around conception 1.20. For acute myeloid leukemia (AML), the OR for maternal exposure during pregnancy was 1.94 and for paternal exposure around conception 0.91. Finding of a significantly increased risk of AML in the offspring with maternal exposure to pesticides during pregnancy is consistent with previous reports. Study also found a slight increase in risk of ALL with paternal exposure around conception which appeared to be more evident in children diagnosed at the age of 5 years or more and those with T cell ALL which raises interesting questions on possible mechanisms.

Bailey HD, Fritschi L, Infante-Rivard C, Glass DC, et al. 2014. Int J Cancer. 135(9):2157-72.

Exposure to herbicides in house dust and risk of childhood acute lymphoblastic leukemia

Study examines the association between exposure to herbicides and childhood acute lymphoblastic leukemia (ALL). Dust samples were collected from homes of 269 ALL cases and 333 healthy controls (<8 years of age at diagnosis/reference date and residing in same home since diagnosis/reference date) in California, using a high-volume surface sampler or household vacuum bags. Amounts of agricultural or professional herbicides (alachlor, metolachlor, bromoxynil, bromoxynil octanoate, pebulate, butylate, prometryn, simazine, ethalfluralin, and pendimethalin) and residential herbicides (cyanazine, trifluralin, 2-methyl-4-chlorophenoxyacetic acid (MCPA), mecoprop, 2,4-dichlorophenoxyacetic acid (2,4-D), chlorthal, and dicamba) were measured. The risk of childhood ALL was associated with dust levels of chlorthal; compared to homes with no detections, ORs for the first, second, and third tertiles were 1.49, 1.49, and 1.57, respectively. The magnitude of this association appeared to be higher in the presence of alachlor. No other herbicides were identified as risk factors of childhood ALL. The data suggest that home dust levels of chlorthal, and possibly alachlor, are associated with increased risks of childhood ALL.

Metayer C, Colt JS, Buffler PA, Reed HD, et al. 2013. J Expo Sci Environ Epidemiol. 23(4):363-70.

Pyrethroid pesticide exposure and risk of childhood acute lymphocytic leukemia in Shanghai

Significant amounts of pyrethroid pesticides are used throughout China. Previous studies have suggested that exposure to pesticides may increase the risk of childhood cancer; however, few studies have focused on pyrethroid metabolites. This study investigated five nonspecific metabolites of pyrethroid pesticides found in children's urine and examined the correlation with childhood leukemia. A hospital-based case-control study of childhood acute lymphocytic leukemia (ALL) in Shanghai between 2010 and 2011 was carried out and included 176 children aged 0–14 years and 180 controls matched for age and sex. Compared with those in the lowest quartiles of total and individual metabolites, the highest quartiles were associated with an approximate two-fold increased risk of ALL [total metabolites: odds ratio (OR) = 2.75, 1.43-5.29; cis-DCCA: OR = 2.21; trans-DCCA: OR = 2.33; and 3-PBA: OR = 1.84], and most of the positive trends were significant. Findings suggest that urinary levels of pyrethroid metabolites may be associated with an elevated risk of childhood ALL and represent a previously unreported quantitative exposure assessment for childhood leukemia.

Ding G, Shi R, Gao Y, Zhang Y, Kamijima M, et al. 2012. Environ Sci Technol. 46(24):13480-7

Risk of childhood acute lymphoblastic leukaemia following parental occupational exposure to pesticides

Study was performed to ascertain whether there was an association between parental occupational exposure to pesticides and increased risk of acute lymphoblastic leukaemia (ALL) in the offspring. A population-based case-control study of childhood ALL was conducted in Australia. Information about the occupational pesticide exposure of mothers and fathers was collected using job-specific modules. Information on the types and extent of pesticide exposure was collected for mothers and fathers before and around the time of conception, and also for mothers during pregnancy for the index case or control and for 1 year after birth. Paternal occupational exposure to pesticides before or around conception was not related to increased risk of childhood ALL. There was a low prevalence of occupational exposure to pesticides among women that reduced after birth. Paternal occupational exposure to pesticides was not found to be associated with an increased risk of acute lymphoblastic leukaemia in the offspring. The study was underpowered with respect to maternal exposure to pesticides.

Glass DC, Reid A, Bailey HD, et al. 2012. Occup Environ Med. 69(11):846-9.

Exposure to pesticides and risk of childhood cancer: a meta-analysis of recent epidemiological studies

The authors performed a meta-analysis of case-control and cohort studies to clarify the possible relationship between exposure to pesticides and childhood cancers. Two cohort and 38 case-control studies were selected for the first meta-analysis. Meta-analysis of the three cohort studies did not show any positive links between parental pesticide exposure and childhood cancer incidence. However, the meta-analysis of the 40 studies with OR values showed that the risk of lymphoma and leukemia increased significantly in exposed children when their mother was exposed during the prenatal period (OR=1.53; 95% CI 1.22 to 1.91 and OR=1.48; 95% CI 1.26

to 1.75). The risk of brain cancer was correlated with paternal exposure either before or after birth (OR=1.49; 95% CI 1.23 to 1.79 and OR=1.66; 95% CI 1.11 to 2.49). The OR of leukemia and lymphoma was higher when the mother was exposed to pesticides. Despite some limitations in this study, the incidence of childhood cancer does appear to be associated with parental exposure during the prenatal period.

Vinson F, Merhi M, Baldi I, Raynal H, Gamet-Payrastre L. 2011. Occup Environ Med. 68(9):694-702.

Exposure to professional pest control treatments and the risk of childhood acute lymphoblastic leukemia

Previous studies suggest that exposure to pesticides increases the risk of childhood acute lymphoblastic leukemia (ALL). The aim of this analysis was to investigate whether professional pest treatments in or around the home before birth or during childhood increased the risk of childhood ALL. Data from 388 cases and 870 frequency-matched controls were analyzed using unconditional logistic regression, adjusting for study matching variables and potential confounders, to calculate odds ratios (ORs). The ORs for any professional pest control treatments were 1.19 in the year before pregnancy, 1.30 during pregnancy and 1.24 for those done after the child's birth. The ORs for exposure after birth were highest when it occurred between the ages of two and three years. ORs were elevated for termite treatments before birth. ORs were higher for pre-B than T cell ALL and for t(12;21) (ETV6-Runx-1) than other cytogenetic subtypes. Results provide some evidence of a modestly increased risk of ALL for professional pest control treatments done during the index pregnancy and possibly in the child's early years.

Bailey HD, Armstrong BK, de Klerk NH, et al. 2011. Int J Cancer. 129(7):1678-88

Residential exposures to pesticides and childhood leukemia

The aim of this study was to conduct a systematic review of published studies on the association between residential/household/domestic exposure to pesticides and childhood leukaemia, and to provide a quantitative estimate of the risk. Publications in English were searched in MEDLINE (1966-31 December 2009) and from the reference list of identified publications. Separate analyses were conducted after stratification for exposure time windows, residential exposure location, biocide category and type of leukaemia. Statistically significant associations with childhood leukaemia were observed when combining all studies. Exposure during and after pregnancy was positively associated with childhood leukaemia, with the strongest risk for exposure during pregnancy. Other stratifications showed the greatest risk estimates for indoor exposure, for exposure to insecticides as well as for acute non-lymphocytic leukaemia (ANLL). Outdoor exposure and exposure of children to herbicides (after pregnancy) were not significantly associated with childhood leukaemia. Findings support the assumption that residential pesticide exposure may be a contributing risk factor for childhood leukaemia but available data were too scarce for causality ascertainment. It may be opportune to consider preventive actions, including educational measures, to decrease the use of pesticides for residential purposes and particularly the use of indoor insecticides during pregnancy.

Van Maele-Fabry G, Lantin AC, Hoet P, Lison D. 2011. Environ Int. 37(1):280-91.

Residential pesticides and childhood leukemia: a systematic review and meta-analysis

Study is a systematic review and meta-analysis of previous observational epidemiologic studies examining the relationship between residential pesticide exposures during critical exposure time windows (preconception, pregnancy, and childhood) and childhood leukemia. Exposures during pregnancy to unspecified residential pesticides insecticides, and herbicides were positively associated with childhood leukemia. Exposures during childhood to unspecified residential pesticides and insecticides were also positively associated with childhood leukemia, but there was no association with herbicides. Positive associations were observed between childhood leukemia and residential pesticide exposures. Further work is needed to confirm previous findings based on self-report, to examine potential exposure-response relationships, and to assess specific pesticides and toxicologically related subgroups of pesticides in more detail.

Turner MC, Wigle DT, Krewski D. 2011. Cien Saude Colet. 16(3):1915-31.

A systematic review and meta-analysis of childhood leukemia and parental occupational pesticide exposure

Authors conducted a systematic review and meta-analysis of childhood leukemia and parental occupational pesticide exposure. They found no overall association between childhood leukemia and any paternal occupational pesticide exposure; there were slightly elevated risks in subgroups of studies with low total-quality scores, ill-defined exposure time windows, and exposure information collected after offspring leukemia diagnosis. Childhood leukemia was associated with prenatal maternal occupational pesticide exposure (OR = 2.09; 95% CI, 1.51-2.88); this association was slightly stronger for studies with high exposure-measurement-quality scores (OR = 2.45; 95% CI, 1.68-3.58), higher confounder control scores (OR = 2.38; 95% CI, 1.56-3.62), and farm-related exposures (OR = 2.44; 95% CI, 1.53-3.89). Childhood leukemia risk was also elevated for prenatal maternal occupational exposure to insecticides (OR = 2.72; 95% CI, 1.47-5.04) and herbicides (OR = 3.62; 95% CI, 1.28-10.3). Childhood leukemia was associated with prenatal maternal occupational pesticide exposure in analyses of all studies combined and in several subgroups.

Wigle DT, Turner MC, Krewski D. 2009. Environ Health Perspect. 117(10):1505-13

Pediatric acute lymphoblastic leukemia and exposure to pesticides

A case-control study of children diagnosed with ALL and their mothers in the Washington, DC, area finds an association between the development of childhood ALL and common household pesticides, as ALL child-mother pairs have elevated levels for the organophosphate metabolites diethylthiophosphate and diethyldithiophosphate and more case mothers (33%) than controls (14%) reported using insecticides in the home.

Soldin, O.P., et al. 2009. Therapeutic Drug Monitoring 31(4):495-501

Residential proximity to agricultural pesticide applications and childhood acute lymphoblastic leukemia

A population based, case control study in California using residential histories and proximity to agricultural pesticide use shows an elevated risk of childhood ALL associated with moderate exposure, but not high exposure, to pesticides classified as organophosphates, chlorophenoxy herbicides, and triazines, and with agricultural pesticides used as insecticides or fumigants.

Rull, R.P., et al. 2009. Environ Res 109(7):891-9

Risk of childhood cancers associated with residence in agriculturally intense areas in the United States

An ecological study analyzing incidence data from U.S. children ages 0–14 years diagnosed with cancer between 1995 and 2001 and residence in a county with agricultural activity finds an elevated risk for AML at high agricultural activity (greater than 60% of county acreage devoted to farming).

Carrozza, S.E., et al. 2008. Environ Health Perspect 116(4):559-565.

Association between prenatal pesticide exposures and the generation of leukemia-associated T(8;21)

A study analyzing umbilical cord blood samples of infants whose meconium sample detected the pesticide propoxur, finds a two-fold increase incidence of t(8;21)(a22;a22), one of the most common cytogenetic abnormalities in childhood acute myeloid leukemia, suggesting that prenatal pesticide exposure is a factor in the generation of leukemia-associated chromosomal translocations.

Lafiura, K.M., et al. 2007. Pediatr Blood Cancer 48(5):624-628

Household exposure to pesticides and risk of childhood hematopoietic malignancies: The ESCALE study (SFCE)

We investigated the role of household exposure to pesticides in the etiology of childhood hematopoietic malignancies. The national registry-based case-control study ESCALE (Etude sur les cancers de l'enfant) was carried out in France over the period 2003-2004. Population controls were frequency matched with the cases on age and sex. Maternal household use of pesticides during pregnancy and paternal use during pregnancy or childhood were reported by the mothers in a structured telephone questionnaire. Insecticides (used at home, on pets, or for garden crops), herbicides, and fungicides were distinguished. We estimated odds ratios (ORs) using unconditional regression models closely adjusting for age, sex, degree of urbanization, and type of housing (flat or house). We included a total of 764 cases of acute leukemia (AL), 130 of Hodgkin lymphoma (HL), 166 of non-Hodgkin lymphoma (NHL), and 1,681 controls. Insecticide use during pregnancy was significantly associated with childhood AL [OR = 2.1; 95% confidence interval (CI), 1.7-2.5], both lymphoblastic and myeloblastic, NHL (OR = 1.8; 95% CI, 1.3-2.6), mainly for Burkitt lymphoma (OR = 2.7; 95% CI, 1.6-4.5), and mixed-cell HL (OR = 4.1; 95% CI, 1.4-11.8), but not nodular sclerosis HL (OR = 1.1; 95% CI, 0.6-1.9). Paternal household use of pesticides was also related to AL (OR = 1.5; 95% CI, 1.2-1.8) and NHL (OR = 1.7; 95% CI, 1.2-2.6); but for AL the relationships did not remain after adjustment for maternal pesticide use during pregnancy. The study findings strengthen the hypothesis that domestic use of pesticides may play a role in the etiology of childhood hematopoietic malignancies. The consistency of the findings with those of previous studies on AL raises the question of the advisability of preventing pesticide use by pregnant women.

Rudant, J., et al. 2007. Environmental Health Perspectives 115(12):1787-1793

Parental occupational exposure to pesticides and the risk of childhood leukemia in Costa Rica

In a Costa Rica population-based, case-control study, researchers find parental occupational exposure to pesticides increases the risk of childhood leukemia. Maternal pesticide exposure doubles offspring leukemia risk, whether before conception (OR 2.4), or during the first (OR 22) or second trimesters (OR 4.5) the risk is significant. Paternal pesticide exposure during the second trimester also increases risk (1.5 OR) in offspring. In regards to organophosphates, maternal exposure during the first trimester is three and a half times higher (OR 3.5). Exposure to benzimidazole pesticides during pregnancy also has twice the risk for childhood leukemia (OR 2.2)

Monge, P., et al. 2007. Scandinavian Journal of Work, Environment and Health 33(4):293-303

Child and maternal household chemical exposure and the risk of acute leukemia in children with Down's syndrome: a report from the Children's Oncology Group

Compared with the general pediatric population, children with Down's syndrome have a much higher risk of acute leukemia. This case-control study was designed to explore potential risk factors for acute lymphoblastic leukemia and acute myeloid leukemia in children with Down's syndrome living in the United States or Canada. Mothers of 158 children with Down's syndrome and acute leukemia (97 acute lymphoblastic leukemia, 61 acute myeloid leukemia) diagnosed between January 1997 and October 2002 and mothers of 173 children with Down's syndrome but without leukemia were interviewed by telephone. Positive associations were found between acute lymphoblastic leukemia and maternal exposure to professional pest exterminations (odds ratio = 2.25, 95% confidence interval: 1.13, 4.49), to any pesticide (odds ratio = 2.18, 95% confidence interval: 1.08, 4.39), and to any chemical (odds ratio = 2.72, 95% confidence interval: 1.17, 6.35). Most of the associations with acute myeloid leukemia were nonsignificant, and odds ratios were generally near or below 1.0. This exploratory study suggests that household chemical exposure may play a role in the development of acute lymphoblastic leukemia in children with Down's syndrome.

Alderton, L.E., et al. 2006. American Journal of Epidemiology 164(3):212-221

Household exposure to pesticides and risk of childhood acute leukaemia

The study included 280 incident cases of acute leukemia and 288 controls frequency-matched on gender, age, hospital, and ethnic origin. The data were obtained from standardized face-to-face interviews of the mothers with detailed questions on parental occupational history, home and garden insecticide use, and insecticidal treatment of pediculosis. Odds ratios were estimated using unconditional regression models including the stratification variables parental socioeconomic status and housing characteristics. Acute leukemia was observed to be significantly associated with maternal home insecticide use during pregnancy (OR = 1.8, 95% CI 1.2 to 2.8) and during childhood (OR = 1.7, 95% CI 1.1 to 2.4), with garden insecticide use (OR = 2.4, 95% CI 1.3 to 4.3), and fungicide use (OR = 2.5, 95% CI 1.0 to 6.2) during childhood. Insecticidal shampoo treatment of pediculosis was also associated with childhood acute leukemia (OR = 1.9, 95% CI 1.2 to 3.3). The results reported herein support the hypothesis that various types of insecticide exposure may be a risk factor for childhood acute leukemia. The observed association with insecticidal shampoo treatment of pediculosis, which has never been investigated before, requires further study.

Menegaux, F., et al. 2006. Occup Environ Med 63(2):131-134

Agricultural pesticide use and childhood cancer in California

Looking at residential proximity to agricultural pesticides, a population-based case-control study of early childhood cancer, ages 0–4 years, in California finds an elevated risk for leukemia associated with probable and possible carcinogen use and with nearby agricultural applications of organochlorines and organophosphates during pregnancy (metam sodium OR 2.05 and dicofol OR 1.83)

Reynolds, P, et al. 2005. Epidemiology 16(1):93-100

Childhood cancer and agricultural pesticide use: an ecologic study in California

We analyzed population-based childhood cancer incidence rates throughout California in relation to agricultural pesticide use. During 1988–1994, a total of 7,143 cases of invasive cancer were diagnosed among children under 15 years of age in California. Building on the availability of high-quality population-based cancer incidence information from the Cali-

fornia Cancer Registry, population data from the U.S. Census, and uniquely comprehensive agricultural pesticide use information from California's Department of Pesticide Regulation, we used a geographic information system to assign summary population, exposure, and outcome attributes at the block group level. We used Poisson regression to estimate rate ratios (RRs) by pesticide use density adjusted for race/ethnicity, age, and sex for all types of childhood cancer combined and separately for the leukemias and central nervous system cancers. We generally found no association between pesticide use density and childhood cancer incidence rates. The RR for all cancers was 0.95 [95% confidence interval (CI), 0.80-1.13] for block groups in the 90th percentile and above for use of pesticides classified as probable carcinogens, compared to the block groups with use of <1 lb/mi(2). The RRs were similar for leukemia and central nervous system cancers. Childhood leukemia rates were significantly elevated (RR = 1.48; 95% CI, 1.03-2.13) in block groups with the highest use of propargite, although we saw no dose-response trend with increasing exposure categories. Results were unchanged by further adjustment for socioeconomic status and urbanization.

Reynolds, P., et al. 2002. Environmental Health Perspectives 110(3):319-324

Critical windows of exposure to household pesticides and risk of childhood leukemia

The potential etiologic role of household pesticide exposures was examined in the Northern California Childhood Leukemia Study. A total of 162 patients (0–14 years old) with newly diagnosed leukemia were rapidly ascertained during 1995–1999, and 162 matched control subjects were randomly selected from the birth registry. The use of professional pest control services at any time from 1 year before birth to three years after was associated with a significantly increased risk of childhood leukemia [odds ratio (OR) = 2.8; 95% confidence interval (CI), 1.4-5.7], and the exposure during year 2 was associated with the highest risk (OR = 3.6; 95% CI, 1.6-8.3). The ORs for exposure to insecticides during the three months before pregnancy, pregnancy, and years 1, 2, and 3 were 1.8 (95% CI, 1.1-3.1), 2.1 (95% CI, 1.3-3.5), 1.7 (95% CI, 1.0-2.9), 1.6 (95% CI, 1.0-2.7), and 1.2 (95% CI, 0.7-2.1), respectively. Insecticide exposures early in life appear to be more significant than later exposures, and the highest risk was observed for exposure during pregnancy. Additionally, more frequent exposure to insecticides was associated with a higher risk. In contrast to insecticides, the association between herbicides and leukemia was weak and nonsignificant. Pesticides were also grouped based on where they were applied. Exposure to indoor pesticides was associated with an increased risk, whereas no significant association was observed for exposure to outdoor pesticides. The findings suggest that exposure to household pesticides is associated with an elevated risk of childhood leukemia and further indicate the importance of the timing and location of exposure.

Ma, X., et al. 2002. Critical windows of exposure to household pesticides and risk of childhood leukemia. Environmental Health Perspectives 110:955-960

Transplacental chemical exposure and risk of infant leukemia with MLL gene fusion

A small case-control, population-based study finds a significant increase risk for infant acute leukemia for maternal exposure to insecticides (OR 9.68) during pregnancy, including the carbamate propoxur.

Alexander, F.E., et al. 2001. Cancer Res 61(6):2542-2546

Risk of childhood leukemia associated with exposure to pesticides and with gene polymorphisms

A population-based case-control study of childhood ALL finds an increased risk for homeowner use of indoor insecticides and garden and interior plant pesticides, in particular with use during pregnancy and among carriers of the CYP1A1m1 and CYP1a1m2 gene mutations.

Infante-Rivard, C., et al. 1999. Epidemiology 10(5):481-487

Childhood leukaemia and exposure to pesticides: results of a case-control study in northern Germany

The association between childhood leukaemia and exposure to pesticides was examined in a population-based case-control study conducted in Lower Saxony, Northern Germany. Between July 1988 and June 1992, 219 newly diagnosed cases were identified, of whom 173 participated in the study. Two sex- and age-matched control groups were recruited: local controls from the same communities as the newly diagnosed cases of leukaemia and state controls from other randomly selected communities in Lower Saxony. An additional study group consisted of 175 cases of solid tumours. When the leukaemia cases were compared with the local controls, positive associations with parental occupational exposure, particularly agriculture-related exposure, were observed, which were statistically non-significant. A significant association was found for pesticide use in gardens (odds ratio = 2.52, 95% confidence interval: 1.0-6.1). No positive associations were seen when the leukaemia cases were compared to the state controls, but this finding could be explained by a higher proportion of state controls living in rural areas. In communities with a significantly elevated standardised incidence ratio of childhood leukaemia over the last decade (1984–1993), the prevalence of pesticide use in the garden was 21%, compared with the 10% in other communities. None of the examined risk factors were more common among cases of solid tumours. Our findings add some evidence to the hypothesis that pesticides are a risk factor for childhood leukaemia, and there are good reasons to consider abundant pesticide use in rural areas as a possible cause for clustering of childhood leukaemia.

Meinert, E., et al. 1996. Eur J Cancer 32A(11):1943-1948

Home pesticide use and childhood cancer: A case-control study

The association between childhood cancer and home pesticide use was examined in a case-control study of children under 15 years of age. Parents of 252 children diagnosed with cancer in the Denver area between 1976 and 1983 and of 222 control subjects were interviewed regarding use of home pest extermination, yard treatment, and pest strips. The strongest associations were found for yard treatments and soft tissue sarcomas (odds ratios [ORs] around 4.0) and for use of pest strips and leukemias (ORs between 1.7 and 3.0). These results suggest that use of home pesticides may be associated with some types of childhood cancer.

Leiss, J., et al. 1995. American Journal of Public Health 85:249-252

Case-control study on the association between a cluster of childhood haematopoietic malignancies and local environmental factors in Aalsmeer, The Netherlands.

In Aalsmeer, a horticultural community near the main international airport in The Netherlands, a more than fourfold increase in the incidence of haematopoietic malignancies in young people was observed between 1980 and 1985. In a population based case-control study, the association with local environmental factors was investigated. For each patient younger than 40 years of age (n = 14) diagnosed between 1975 and 1989, four age and sex-matched controls were selected via local general practitioners. All parents of patients and controls completed

a questionnaire on their lifestyle, living conditions, and health, for several years preceding each individual diagnosis. Odds ratios (ORs) with 95% confidence intervals (CI) were calculated, matched, and, if necessary, stratified for neighbourhood. Increased ORs were recorded for intensive use of petroleum products and pesticides by the patients themselves and their fathers: OR petroleum products: 8.0 (95% CI 2.2, 129.9) and 9.0 (1.0, 66.1) respectively; OR pesticides: 6.0 (0.6, 49.3) and 3.2 (1.0, 10.1) respectively. Swimming in a local pond was also significantly associated with the disease: OR = 5.3 (1.3, 17.4). In the 1970s this pond had been polluted by petroleum products and pesticides. The increased incidence of childhood haematopoietic malignancies in Aalsmeer may have been associated with several specific local environmental factors. Interpretation of the results, however, should take into account the fact that confidence intervals were wide because of the limited number of case

Mulder, Y.M., et al. 1994. Journal of Epidemiology and Community Health 48:161-165

Epidemiological characteristics of childhood acute lymphocytic leukemia. Analysis by immunophenotype. The Childrens Cancer Group

While a number of epidemiological studies of childhood acute lymphocytic leukemia (ALL) have been conducted, separate analysis of risk factors for ALL subtypes has generally not been possible. We report the results of an analysis of data obtained from parents of children with ALL (and a control group of children without cancer), linked to a clinical database. Cases were classified into four ALL subtypes, and odds ratios (OR) were determined for each subtype for a broad range of factors. Numerous significant associations were found, some across all subtypes and others that were subtype-specific. Factors with elevated and/or significant ORs included: (i) for common ALL (n = 286): Down syndrome; family history (FH) of bone/joint diseases; postnatal jaundice; birthweight; MMR vaccination; exposure to gases and insecticides; and parental occupational exposure to insecticides. (ii) for pre-B ALL (n = 38): FH of gastrointestinal, hematological or bone/joint diseases, or allergy; cat ownership; exposure to solvents, fumes, petroleum products, cleaning agents and farm animals; and parental exposure to farm animals, fumes and solvents; (iii) for T-cell ALL (n = 158): FH of gastrointestinal disorders, maternal age, male gender, and parental occupational exposure to metals; (iv) for null-cell ALL (n = 65): FH of congenital heart disorders; measles; and parental occupational exposure to fumes, metals or solvents. This analysis should be considered as a hypothesis-generating process for future case-control interview studies.

Buckley, J.D., et al. 1994. Leukemia 8(5):856-864

Parental occupation and other environmental factors in the etiology of leukemias and non-Hodgkin's lymphomas in childhood: a case-control study

A hospital-based case-control study in Italy finds a positive association with paternal work as a farmer and childhood ALL

Magnani, C., et al. 1990. Tumori 76(5):413-419

Occupational Exposures of Parents of Children with Acute Nonlymphocytic Leukemia: A Report from the Childrens Cancer Study Group

A case-control study finds a consistent pattern of association of AML, also known as acute nonlymphoblastic leukemia (ANLL), risk with paternal exposure to pesticides for jobs held longer than three years, which is substantially increased for children under age 6 at diagnosis. An elevated risk is also found for a child's direct exposure to pesticides in the home and for maternal exposure to home pesticides at the time of pregnancy.

Buckley, J.D., et al. 1989. Cancer Research 49:4030-4037

A population-based case-control study of childhood leukemia in Shanghai

A population based case-control study in China of childhood leukemia cases finds an association between ALL with maternal occupational exposure to pesticides.

Shu, X.O., et al. 1988. Cancer 62(3):635-644

Environmental factors in childhood leukaemia

Various factors have been suspected of influencing childhood leukaemia; this in itself indicates how limited and uncertain is our understanding to date of the epidemiology of the disease. In this case-control study an attempt was made to examine the various hypotheses that have been proposed... The small French case-control study finds paternal occupational exposures to pesticides as a risk factor for leukemia (12 cases versus three controls)

Laval, G. and Tuyns, A.J. 1988. British Journal of Industrial Medicine 45:843-844

Childhood leukemia and parents' occupational and home exposures

A case-control study in California finds household pesticide use can more than triple the risk of childhood leukemia and that garden pesticides increase the risk to over six-fold.

Lowengart, R., et al. 1987. Journal of the National Cancer Institute 79(1):39-46

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