Reproductive Outcome and Pesticide Exposure

Summary of Selected Studies

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Some Notes on the Table

This table is a selective summary of studies of long term effects on the reproductive system associated with potential occupational and environmental exposure to pesticides . Most are from articles published in English in peer-reviewed journals. The studies are listed in chronological order by author – the most recent first.

The source of pesticide exposure could be occupation as a farmer, agricultural worker, sprayer, exterminator, factory worker, or other jobs. The exposure could also be from household, lawn, garden, pet, or other use. Living on a farm, in an agricultural spray area, near a pesticide factory, or other environmental exposures are other potential sources of exposure.

How The Studies Are Done

Epidemiology is the study of diseases and their causes in human populations. It compares groups of people with an exposure or a disease to those without it.

In the studies in this table, groups of people with adverse reproductive outcomes, or with exposure to pesticides are the *"cases"*. Groups of people without adverse reproductive outcomes or without exposure to pesticides are the *"controls"*.

The aim is to find out if groups of people with adverse reproductive outcomes (the cases) are more likely to have exposure to pesticides than the groups without adverse reproductive outcomes (the controls). Or to find out if groups of people with pesticide exposure (the cases) are more likely to have adverse reproductive outcomes groups without pesticide exposure (the controls).

How Study Results are Reported

Study results are reported as risk ratios. These ratios indicate whether the people with adverse reproductive outcomes were ***more*** likely to have pesticide exposure (at increased risk), ***equally*** likely to have pesticide exposure (no difference in risk), or ***less*** likely to have pesticide exposure (at decreased risk) than the people without adverse reproductive outcomes.

Or whether the people with pesticide exposure were ***more*** likely to have adverse reproductive outcomes (at increased risk), ***equally*** likely to have adverse reproductive outcomes (no difference in risk), or ***less*** likely to have adverse reproductive outcomes (at decreased risk) than those without pesticide exposure.

For example: In a study of birth defects*, the cases would be mothers of infants with birth defects, and the controls mothers of infants without them. There are three possible outcomes. The mothers of infants with birth defects could be more likely, equally likely, or less likely to have pesticide exposure.

1. More likely: If the ratio is greater than 1 (> 1), this means that the mothers of infants with birth defects were more likely to have pesticide exposure – that pesticide exposure ***increases*** the risk of birth defects. The size of the ratio indicates how much the risk is increased. The larger the number the greater the risk. A ratio of 1.4 means a 40% increase in risk. A ratio of 2.0 means a doubling of the risk, or a 200% increase. At least a doubling of the risk is considered more important than ratios less than 2.

2. **Equally likely**: If the ratio is equal to one (= 1) this means that there was no difference in pesticide exposure found in the mothers of infants with or without birth defects – pesticides did ***not*** increase the risk of birth defects in the study.

3. **Less likely**: If the ratio is less than one (< 1), this means that mothers of infants with birth defects were less likely to have pesticide exposure than mothers of infants without them, or the risk was ***decreased.*** The smaller the number the lower the risk. A ratio of 0.80 means that mothers of infants with birth defects are 20% less likely to have been exposed to pesticides. A ratio of 0.40, that they are 60% less likely.

When studying humans, it is impossible to determine every factor that might influence the results of a study. It might have occurred anyway, by chance. It is possible that any increase in risk was not from

pesticides, but something else. This could be something the researcher didn't think of, or didn't even ask about. Or it could be from pesticide exposure in combination with other unknown or unstudied factors. Therefore, finding an increase in risk does not mean that pesticides "cause" birth defects.

This is why it is common to report increase in risk by stating that "pesticide exposure increases the risk of birth defects", or "pesticide exposure is a risk factor for birth defects", and not that pesticides "cause" birth defects.

Are the Study Results "Significant"?

There are methods to determine how strong the link or associations between neurlogical diseases and pesticides are, or if they occurred by chance. They are called tests of statistical significance. The statistical part is usually left out, and the results reported as "significant" or "not significant". The two most common tests are the "p" value, and confidence intervals.

1. "p" value: This tests whether the findings could have occurred by chance 5% of the time or less. The 5% is converted to a fraction and written as 0.05. For example, you will see the results as "p = 0.05" (read as p equals point 0 5), or "p < 0.05" (read as p less than point 0 5), or "p ≤ 0.05" (read as p less than or equal to point 0 5).

If the "p" value is less than or equal to 0.05, the findings are considered to be statistically significant; that is, they are unlikely to have occurred by chance. The smaller the "p" value the more significant the findings. For example" p ≤ 0.01" (read as p less than or equal to point 0 1) means that it could have occurred by chance 1% of the time or less.

2. Confidence intervals: Another widely used test is called the confidence interval. It shows how close the risk ratio found in the study is to the "true" or expected value. The chosen level is usually 95%. This means that 95% of the time the study results will lie within the calculated interval. Another way of saying this is that 5% of the time they will not.

Because it is an interval, there are two numbers, with the lower number written first. If the lower number of the confidence interval is less than or equal to one (≤ 1), than the increase in risk is "not significant" or "non-significant". If the lower number of the interval is greater than one (> 1) then the increase in risk is considered "significant".

If the number of cases is small, the confidence interval can be very wide. When there is a very wide interval between the lowest and the highest number, the less confidence you have in the findings. It usually means that the number of cases found were very small.

The larger the number of people in the study (the sample size), the narrower the confidence interval, and the more significant the findings.

Commonly Used Ratios

FR	Fecundability Ratio	SHR	Standardized Hospital Ratio
OR	Odds Ratio	SIR	Standardized Incidence Ratio
PMR	Proportionate Mortality Ratio	SMR	Standardized Mortality Ratio
PCMR	Proportionate Cancer Mortality Ratio	SMbR	Standardized Morbidity Ratio
PR	Prevalence Ratio	SPR	Standard Proportional Ratio
RR	Relative Risk (or Rate Ratio)	SRR	Standardized Rate Ratio
SFR	Standardized Fecundability Ratio		

* Birth defects is used as an example, but the discussion refers to all the reproductive outcomes listed in the table.

Birth Defects

Location	Exposure and Outcome	Findings (95% CI)	Ref.
Phillipines 1998-1999	Conventional pesticide vs IPM users[1] Birth defects	**RR** 4.56 sig	2002 Crisotomo
Red River Valley Minnesota 1997-1998	Farm family parent-reported birth defects. First year of life First 3 years of life Conceptions in spring Sex ratio of children with birth defects Applicator families Fungicide exposure Fungicide expos. male to female chldrn Neurolog/neurobehav.developmental effects Applicators fumigant phosphine Glyphosate herbicide users	**Rate - Prevalence** 31.3 / 1,000 births 47.0 / 1,000 births 7.6% vs. 3.7% other seasons 1.75 to 1 male predominance 1.25 to 1 female predominance 0.57 to 1 p = 0.02 **OR** 2.48 (1.2-5.1) 3.60 (1.3-9.6)	2002 Garry
Collaborative Perinatal Project[2]	Maternal serum DDE level ≥ 85.6 µg/liter Cryptorchidism Hypospadias Polythelia (extra nipples)	**OR** 1.3 (0.7-2.4) 1.2 (0.6-2.4) 1.9 (0.9-4.0)	2002 Longnecker
California	Birth defects Matern. residence pest. application[3] Halogenated hydrocarbons applications	**OR** 1.4 (0.8-2.4) 2.2 (1.3-3.9)	2001 Bell
US-Mexico border. 1995-2000	Neural tube defects - Mexican-Americans Parental pesticide exposure	**OR** No positive associations	2001 Brender
France	Male with ambiguous genitalia Mother exposed to pesticides	Case Report	2001 Jeandel
Baltimore Washington area. 1987-1989	Transposition great arteries Mother pest. exposed 1st trimester Mother herbicide exposed Mother rodenticide exposed Mother insecticide exposed	**OR** 2.0 (1.2-3.3) 2.8 (1.3-7.2) 4.7 (1.4-12.1) 1.5 (0.9-2.6)	2001 Loffredo
Europe 3 countries	Spina bifida Women in agriculture - Sweden Women in agriculture - Spain Women in agriculture - Hungary	**OR** 1.8 (0.8-4.2) 2.2 (0.8-5.9) 1.1 (0.7-1.7)	2000 Blatter
Washington 1980-1993	Limb defects[4] Mother occ. pest. exp. vs non-agric ctrls Mother occ. pest. exp. vs father agric ctrls	**Prevalence Ratio** 2.6 (1.1-5.8) 2.6 (0.7-9.5)	2000 Engel
Norway 1970-1993	Birth defects Agricultural workers - from census	**OR** No associations	2000 Irgens
Chile	Maternal pesticide exposure Congenital malformations	**Attributable Risk** 54.4%	2000 Rojas

Spain 1993-1994	Birth defects Mother agricultural work[5] Father agricultural work Father pesticide handler	**OR** 3.16 (1.11-9)[6] 1.5 (0.7-3.1) 1.49 (0.94-2.4)[7]	1999 Garcia
Sweden 1973-1991	Birth defects Fisher's wives East coast Fisher's wives West coast West coast vs general population	**Prevalence** 3.3 % 5.0 % **OR** = 0.78 (0.58-1.04)	1999 Rylander
California 1987-1989	Periconceptual Pesticide Exposure Home garden use Cleft lip/palate plus another defect Neural tube defect (mother applied) Neural tube defect (commercial.appl.) Cono-truncal heart defects Limb defects Home use Neural tube defects Insect repellent use (reported by mother) Cono-truncal heart defects Maternal residence ≤ 2.5 miles agric. area Neural tube defects Father occupational exposure Cleft lip and/or palate	**OR** 3.8 (1.5-9.7) 2.9 (1.3-6.7) 2.5 (0.9-6.9) 3.1 (1.3-7.3) 3.5 (1.2-9.9) 1.6 (1.1-2.5) 2.2 (1.3-3.9) 1.5 (1.1-2.1) 1.7 (0.9-3.4)	1999 Shaw
Texas 1980-1993	Down Syndrome mothers Pest. exp. 3 mon before/after LMP[8]	**OR** No significant differences	1998 Fixler
Spain 1993-1994	Birth defects Patern. agric. exposure glufosinate Patern. agric. exposure pyridils	**OR** 2.45 (0.78-7.7) 2.80 (1.19-6.4)	1998 Garcia
Denmark 1983-92	Cryptorchidism Female garden workers Male garden workers Hypospadias Female garden workers Male garden workers	**OR** 1.67 (1.14-2.47) No increase No increase No increase	1998 Weidner
US 1981-1989	Ventricular Septal Defect (isolated membr.) Pesticide exposure	**Attributable Risk** 5.5 %	1998 Wilson
Netherlands 1980-1992	Spina Bifida Father high exposure to pesticides	**OR** 1.7 (0.7-4.0)	1997 Blatter
Norway 1967-1991	Parent farmers with pesticide exposure Spina bifida Hydrocephalus Limb reduction Cryptorchidism Hypospadias/urinary system	**OR** 2.76 (1.07-7) 3.49 (1.34-9.1) 2.50 (1.06-5.9) 2.32 2.94	1997 Kristensen
Netherlands 1980-1992	Spina bifida Women in agricultural jobs[9]	**OR** 3.4 (1.3-9.0)	1996 Blatter

Sweden 1976-1991	Spina bifida Women in agricultural jobs Women who lived on a farm	**OR** 1.8 (0.8-4.2) 2.2 (1.3-3.8)	1996a Blatter
Netherlands 1980-92	Spina bifida Mother works in agriculture	**OR** 5.6 (1.8-17.8)	1996b Blatter
Hungary 1989-1990	Birth defects Trichlorfon contaminated farm fish[10]	**Prevalence** 11 of 15 births (73%)	1996 Czeizel 1995 Viragh
Canada 1952-1988	Eye, anencephaly, spina bifida, genital def. Fathers exposed wood preservatives[11]	**OR** Increased risk	1996 Dimich-W
England 1988-1994	Anophthalmia/microophthalmia (benomyl)[12] All cases Severe cases.	**OR Rural vs Urban areas** 1.8 (1.15-2.8) 2.4 (1.4-4.1)	1996 Dolk
Minnesota 1989-992	Birth defects Pesticide applicators (state licensed) General population Low pest. use vs. high pest. use area Circulatory/respiratory Urogenital Musculoskeletal / integumentary All births with anomalies	**OR** 1.96 (1.5-2.7) 1.86 (1.68-2.1) 1.66 (1.08-2.05) 1.7 (1.04-2.8) 1.7 (1.06-2.64) 1.5 (1.03-2.14) 1.4 (1.15-1.64)	1996 Garry
Colorado 1986-1989	Craniosynostosis Father in agriculture/ forestry[13]	**OR** 2.3 (1.0-5.2)	1995 Bradley
Finland	Maternal agricultural work All birth defects[14] Orofacial defects	**OR** 1.5 (0.9-2.0) 1.9 (1.1-3.5)	1995 Nurminen
Metropolitan Atlanta 1968-1980	Cleft lip and palate Farmer as occupation[15]	**OR** 3.3 (0.9-11.9)	1995 Schnitzer
New York State 1977-1983	Limb reduction defects Parent exposed to pesticides Farming occupation.	**OR** 0.9 (0.6-1.4 1.1 (0.5-2.7)	1994 Lin
China 1988-1989	Birth defects Rural pesticide use during gestation	Risk increased with increased num. pest. used	1994 Pan
Italy 1986-1990	Anophthalmia & microophthalmia Parental occup. agriculture (benomyl)[12]	**OR** 0.63 (0.07-2.52)	1994 Spagnolo
Finland 1982-1983	Hypoplastic left heart syndrome Pesticide exposure	**OR** No association	1994 Tikkanen
India 1984-1990	Birth defects MIC[16] exposure Bhopal	**Affected vs Control Areas** No significant difference	1993 Bajaj
Austria 1989-1991	Orofacial clefts Mother agricultural occupation Father agricultural occupation	**OR** 1.9 (1.1-3.5) 1.9 (0.4-8.3)	1993 Strohmer

Case Report	Multiple severe defects Deet applied daily by mother during entire pregnancy (also took chloroquine)	Craniofacial dysmorphology, mental retardation, sensorimotor impairment	1992 Schaefer
San Francisco Bay	GI[17] anomalies 2nd trimester exposure Pregnant aerial spraying malathion	**OR** 2.6 (13 cases) not sig.	1992 Thomas
Finland 1982-1983	Atrial septal defect (secundum) Mother exposed pesticides/wood preserv.	**OR** No association	1992 Tikkanen
China 1986-1987	Matern.occup. pesticide expos.1st trimester All birth defects Central nervous system defects.	**OR** 1.8 (0.3-10.5) 7.8 $p < .01$	1992 Zhang
Baltimore Washington area	Total anomalous pulmonary venous return Pesticide exposure	**OR** 2.74 (1.17-6.44)	1991 Correa-V
Canada 1952-1973	Forestry / logging Congenital cataracts Arial septal defect Syndactyly	**OR** 2.28 2.03 2.03	1991 Olshan
India	Birth defects ♂ cotton workers exposed pesticides[18] Unexposed workers	**Prevalence** 3.0 % 0.7% $p <.05$	1991 Rupa
Finland 1982-1983	Ventricular septal defect Mother exposed pesticides/wood preserv.	**OR** No association	1991 Tikkanen
Texas 1981-1986	Anencephaly - parent's occupation Exposed to pesticides[19] Farmers and ranchers Hired farm and ranch workers Gardeners and landscapers Farm and ranch work - father Farm and ranch work - mother	**OR** 1.28 (0.77-2.13) 1.05 (0.40-2.76) 1.73 (0.8-3.55) 0.91 (0.3-2.6) 1.77 χ^2 $p< .001$ 1.30 χ^2 $p< .05$	1990 Brender
Colombia 1981	Birth defects Pesticide exposed female workers[20] Wives of pest. exposed male workers[21]	**RR** 1.3 (1.07-1.7) 1.5 (1.04-2.3)	1990 Restrepo
Colombia 1982-83	Birth defects - Flower workers High pesticide exposure jobs All pesticide exposed jobs Employed more than 1 year Employed less than 1 year Low pesticide exposure jobs	**RR** 2.1 1.8 1.9 1.3 0.6	1990 Restrepo
California Case Report	Pesticide poisoned[22] pregnant farm worker 4 weeks post fertilization. (Took bendectin for nausea 11 weeks after LMP)	Chromosomally normal female with multiple defects[23] Died 14 days after birth	1989 Romero
Quebec 1982-1984	Tracheo-esopageal. fistula (2 cases) ♀ agric/hort ≥15 hr/wk at conception	**OR** 2.61 $p< .05$ (1.32 expected)	1988 McDonald

California 1982-84	Limb reduction defects only [24] Either parent in agriculture Mother resides high agric. prodxn area Mother resides high pesticide use area Limb reduction plus additional defects Either parent in agriculture Mother resides high agric. prodxn area Mother resides high pesticide use area	**RR** 0.9 (0.4-1.7) 1.7 (1.1-2.7) 1.9 (1.2-3.1) 1.6 (0.7-3.6) 2.4 (1.2-4.7) 3.1 (1.5-6.5)	1988 Schwartz
Canada 1973-1979	Birth defects[25] Residence high vs low pest. use areas[26]	**SRR** 2.49 $p < .05$	1988 White
California 1981-1982	Tracheo-esophageal fistula (N=9) Malathion spraying (SF Bay area)	**Results** 2.66 (0.55-12.78)	1987 Grether
Netherlands Case Report	Severe malformations Malathion lice rx wks 11,12 gestation	Cytogenically normal Died after birth	1987 Lindhout
Finland	Agric/hortic. pesticide expos. 1st trimester Central nervous system defects Orofacial clefts Cardiovascular defects Skeletal defects	**OR** 1.0 3.3 0.3 None in exposed	1987 Rantala
Australia 1970-81	Parental personal/household pest. expos[27] Limb reduction - one exposure Limb reduction - more than 1exposure	**RR** 3.1 (1.8-5.3) 7.0 (2.8-17.5)	1986 Kricker
Hawaii 1981-1983	Birth defects Heptachlor contaminated milk[28]	**Incidence** No major rate increase seen	1986 LeMarchand
China 1977-1983	Women exposed to rice pesticides Any pesticide exposure Pesticide exposure 1st trimester Direct pesticide exposure	**RR** 1.36 $p < .05$ 1.62 $p < .001$ 1.87 $p < .001$	1986 Li
Imperial County, California 1975-1978	Limb reduction defects One/both parents agricultural worker Neither parents agricultural worker All other major defects	**Rate** 5.05 / 1000 live births 2.19 / 1000 live births No differences	1986 Schwartz
Case report	Multiple facial/cranial defects, ment. retard. Both forest sprayers of 2,4-D[29]	20 year old primipara, 35 yr old father	1984 Casey
Antioch-Pittsburg, California 1979-1980	Spina bifida / Anencephaly Pesticide or chemical exposure	**Cluster Investigation** No associations found	1984 Hearey
US	Birth defects Crop duster pilots vs unexposed siblings	**OR** No differences	1984 Roan

England/Wales 1965-74	Father in agriculture, horticulture, forestry Anencephaly Spina bifida Cleft palate Anencephaly Farmers Gardeners	**RR** 1.2 not sig. 0.8 0.9 1.0 2.3 not sig.	1983 Golding
England/Wales 1974-1979	Spina bifida, facial clefts Female gardeners[30] Female agricultural workers	**OR** Increased Increased	1983 Balarajan
New Zealand 1969-1980	Birth defects[31] 2,4,5-T Sprayers	**RR** 1.19 (0.58-2.45)	1982 Smith A
Iowa Michigan	Agricultural chemical exposure Cleft lip and/or palate	**OR** Iowa 2.85 (1.49-5.44) Michigan 1.68 (1.02-2.78)	1981 Gordon
New Zealand 1960-77	Aerial 2,4,5-T application Heart, hypo/epispadias, talipes All defects	**IR** > 1 not sig > 1 sig	1981 Hanify
New South Wales Australia	Anencephaly and meningomyelocele. Annual use of 2,4,5-T	**Results** Linear correlation[32]	1979 Field
Arkansas 1948-1974	Cleft lip and/or palate (N=1,201) 2,4,5-T Herbicide use[33]	**Results** Increase high, low exposure grps	1979 Nelson

Spontaneous Abortion, Stillbirth, Preterm, Low Birth Weight

Location	Source of Exposure	Findings (95% CI)	Ref.
Phillipines 1998-1999	Conventional pesticide vs IPM users[1] Spontaneous abortion	**RR** 6.17 sig	2002 Crisotomo
Minnesota	Spouses fungicide applicators Miscarriages and/or fetal loss Spouses herbicide applicators 1st trimester miscarriage in spring[34] Sulfonylurea use Imidizolinone use Cheyenne combination[35] Spouses of pesticide applicators Changes in menarche, menopause Endometriosis Women appliers of pesticides Miscarriage/fetal loss	**OR** 1.6 to 2.0 More frequent 2.1 2.6 2.9 No associations found No associations found 1.8	2002 Garry
Bangladesh	Arsenic contaminated well water Spontaneous abortion Stillbirth Preterm births	**RR** Increased p = 0.008 Increased p = 0.046 Increased p = 0.018.	2001 Ahmad

Canada	Early[36] spontaneous abortion	**OR**	2001
	Phenoxy herbicide exposure[37]	1.5 (1.1-2.1)	Arbuckle
	Ttriazine herbicide exposure[37]	1.4 (1-2.0)	
	Any herbicide exposure[37]	1.4 (1.1-1.9)	
	Late[38] spontaneous abortion		
	Glyphosate exposure[37]	1.7 (1-2.9)	
	Thiocarbamate exposure[37]	1.8 (1.1-3.0)	
	Miscellaneous pesticide expo[37]	1.5 (1.0-2.4)	
California	Late fetal death	**OR**	2001
	Matern. residence pest. application[39]		Bell
	Carbamate exposure	1.3 (1.0-1.8)	
	Halogenated hydrocarb. exposure	1.3 (1.0-1.8)	
	Estrogenic pesticide exposure	1.4 (0.8-2.5)	
Atoya River basin, Nicaragua	76 mothers urban and rural areas	**Venous Blood** / **Cord Blood**	2001
	Cord, venous blood 13 pesticides[40]	DDE 100% / 100%	Dorea
	at time of delivery	DDT 1.92% / 3.84%	
		Dieldrin 15.38% / 19.23%	
		Heptachlor 15.38% / 9.16%	
		gamma-HCH 7.69%	
		beta-HCH 11.53%	
		delta-HCH 1.92%	
Sweden	Fisher's wives	**OR**	2000
	Spontaneous abortion	0.48 (0.26-0.92)	Axmon
	Stillbirth	No difference	
Rome, Italy	Spontaneous abortion	**OR**	2000
	Wives pest. applicators vs controls	3.8[41] 7.6[42]	Petrelli
	Spontaneous abortion/preg.ratio		
	Applicator wives vs control wives	0.27 0.07	
Canada	Spontaneous abortion	**OR**	1999
	Preconception exposure 2,4-D	1.1 (0.6-1.9)	Arbuckle
	Spouse use 2,4-D	2.5 (1.0-6.4)	
	Spouse use 2,4 -no protec. equip.	5.0 (0.7-36)	
Germany	Exposure to PCP[43] wood preservative	**Blood Levels**	1999
	Gynecological problems	20.7 to 133 ug/l	Gerhard
	Women without problems	< 20 ug/l	
Sweden 1973-91	Stillbirth		1999
	Fisher's wives vs controls	No difference	Rylander
Germany 1989-1993	Chlorinated hydrocarbons[44]	**Blood Levels**	1998
	Repeated miscarriages	No significant associations found	Gerhard
Texas 1983-1993	GIS link agricultural arsenic plant	**Prevalence OR**	1998
	Stillbirth - Hispanics hi-exposure	8.4 (1.4- 50.1) >100 ng/m3	Ihrig
Turkey	♀ 40 y post exp. hexachlorobenzene[45]	**Serum HCB**	1998
	Spontaneous abortion	Strong relation	Jarrell
	Stillbirth	No relationship	

Norway 1967-91	Late-term spontaneous abortion[46] Farmer parents Grain vs non-grain farmers Poor grain harvest[47]	**OR** 1.9 (1.6-2.3) 1.8 (1.1-2.8) 2.4 (1.5-3.8)	1997 Kristensen
Iowa 1984-1990	Intrauterine Growth Retardation Herbicide contaminated wells[48]	**OR** 1.8 (1.3, 2.7)	1997 Munger
California 1984	Fetal death[49] Occupational exposure pesticides Home exposure pesticides	**RR** 2.4 (1.0-5.9) 1.7 (1.0 to 2.9)	1997 Pastore
Canada 1986	Spontaneous abortion Male farmer pesticide users[50]	**OR** Increased risk	1997 Savitz
Spain	Spontaneous abortion Female greenhouse pest. sprayers	**Prevalence** Increased	1996 Parron
California 1987	Spontaneous abortion Ethylene oxide exposure	**OR** 2.5 (1.0-6.3)	1996 Rowland
Germany 1987-88	Daycare teachers wood preserv. exp.[51] Birth weight Birth length	**Results** 175 g lower p = 0.04 2 cm lower p = 0.02	1995 Karmaus
China 1988-1989	Spontaneous abortion Mother pest. work while pregnant	Increased risk Increased further with no. pesticides used	1994 Pan
Bhopal India	MIC[16] exposure survivors Spontaneous abortion Perinatal mortality Neonatal mortality Stillbirth	**Affected vs Control Area** 24 % vs 5.6 % p < 0.0001 6.9% vs 5.0% 6.1% vs 4.5% No differences	1993 Bajaj 1990 Bhandari
Sudan 1989-90	Stillbirth Women farmers - hospital group Women farmers - community group Women not farmers - community grp	**Attributable Risk** 34.5 % 22.6 % 15.7%	1993 Taha
Bhopal India	Spontaneous abortion Women preg. time of MIC[16] accident	**Prevalence** Increased	1993 Varma
California 1987-89	Spontaneous abortion Occup./environ. pesticide expos.	No associations	1993 Willis
San Francisco Bay Area	Spontaneous abortion / Stillbirth Malathion residential spraying	**OR** No increase	1992 Thomas
China 1986-1987	Threatened abortion Maternal occup. pesticide expos	**OR** 3.9 (1.2-12.6)	1992 Zhang
Quebec 1982-1986	Sillbirth[52] ♀ low-level pesticide/germicide exp.	**OR** 3.1 (1.1-8.6)	1991 Goulet

India	Spontaneous abortion ♀ cotton field wrkrs pest. exp. Unexposed workers Stillbirths Wives of exposed workers Wives unexposed workers	**Prevalence** 26.0 % 14.9 % difference sig 8.73% 2.65% difference signif.	1991 Rupa
Colombia 1981	Spontaneous abortion Female flower workers Wives of male workers[53] Stillbirth Female flower workers Wives of male workers[53]	**RR** 2.20 (1.82-2.66) 1.79 (1.16-2.77) 0.99 (0.66-1.48) 0.89 (0.42-1.83)	1990 Restrepo
Boston 1977-80	Stillbirth Chlorinated water exposure	**OR** 2.6 (0.9-7.5)	1989 Aschengrau
Quebec	Women working in agriculture Pesticide/germicide exposure Potentially fetotoxic chem. exposure	**OR** 2.06 (1.15-3.68 12.07 (1.22-119.9)	1989 Goulet
Italy	Women hospitalized for miscarriage Hexachlorobenzene DDT compounds.	**Blood Levels vs Controls** No significant differences No significant differences	1989 Leoni
US 1980	Stillbirth Maternal home pesticide exposure Maternal work pesticide exposure Paternal home pesticide exposure Paternal work pesticide exposure	**OR** 1.5 (1.3-1.7) 1.6 (1.3-2.1) 1.3 (1.1-1.5) 1.2 (1.0-1.5)	1989 Savitz
Quebec 1982-84	Female agric. / horticul.workers[54] Spontaneous abortion Stillbirth	**OR** 2.40 p <.05 5.55 p <.01	1988 McDonald
New Brunswick, Canada 1973-79	Stillbirth Resid. high vs low forest/ag pest	**SRR** 2.5 p< .05 trend p = .03	1988 White
India	Spontaneous abortion Pesticide exposed vineyard workers Non-exposed workers	**Prevalence** 43.75 % 7.5 % signif.	1987 Rita
Italy	Hexachlorobenzene Spontaneous abortion group Normal comparison group	**Blood Levels** 0.2 to 6.0 ppb (mean 1.6) 1.6 to 4.6 ppb (mean 1.5)	1986 Leoni
Denmark 1980	Spontaneous abortion Female indoor garden workers[55] Female outdoor garden workers[55] Fem. indoor pest. use vs non-use[55]	**OR** 0.9 (0.4-2.2) 1.3 (0.2-7.1) 2.0 (0.3-11.8)	1984 Heidam
Washington State 1980-1981	Stillbirth Farm workers	**OR** 1.5 (1.2-1.9)	1984 Vaughan
US	Spontaneous abortion Crop duster pilots vs unexp. sibs	**OR** No difference	1984 Roan

Italy		**Serum level - parts per billion (ppb)**	1983
	Chlorinated hydrocarbon pesticides	**Recent** SAB[56] **Past** SAB[56] **Norm**.preg	Bercovici
	DDT isomers	38 - 44 61 36	
	Lindane	6.4 -8.5 4.9 8.0	
	Dieldrin	1.3 - 2.9 2.6 1.6	
	Heptachlor epoxide	4.0 - 3.8 2.5 4.5	
Finland1980	Spontaneous abortion	**Prevalence**	1982
	Hospital sterilization workers	11.3% vs 10.6% non-exposed	Hemminki
	Sterilizing procedures during preg	16.7% vs 5.6% non-exposed	
	Ethylene oxide exposure	Positive correlation	
	Glutaraldehyde/formaldehyde exp	No correlation	
New Zealand	Spontaneous abortion	**RR**	1982
1969-80	Wives of 2,4,5-T sprayers	0.89 (0.61-1.30)	Smith A
India	Pesticides in Premature delivery (PD)/	**Blood mean ppb** **Placenta mean ppb**	1980
	spontaneous abortion (SAB), normal	**PD/SAB Normal** **PD/SAB Normal**	Saxena
	BHC	149 53 73.57 28	
	Lindane	56 18.5 25 8.56	
	Aldrin	32 10 18.5 3	
	DDE	103 12 52 11.79	
	DDD (TDE)	39.6 6.5 16.7 4.85	
	DDT	90.55 4 90.55 3.66	
	DDTR	250.6 25 250 22	
Bulgaria	Pesticide exposed female farm workers	**Prevalence Exposed vs Controls**	1973
	Spontaneous abortions	No differences	Marinova
Florida	DDT and DDE serum levels	**Compared to normal pregnancies**	1970
	Spontaneous abortion	No significant differences	O'Leary

Fertility, Infertility, Sterility

Location	Exposure and Outcome	Findings (95% CI)	Ref.
Turkey	Hexachlorobenzene exposure 1950s[45]		2002
	Sex ratio progeny of survivors	No difference from controls	Jarrell
	Exposed peak of episode (1955-57)	Lower lifetime proportion males[57] - sig	
North Carolina	137 Black farmers[58]		2002
	Median plasma DDE level	7.7 ug/L (1,213 ug/ kg lipid)	Martin
	DDE and androgens relationship	Overall were unrelated[59]	
	If DDE level in top 10th percentile		
	Total testosterone	lower by 23% (-40% - 1%)	
	Free androgen index	lower by 22% (-41% - 4%)	
Argentina	Primary infertility - males	**Compared to Unexposed**	2001
Litoral Sur region	Exposure to pesticides	Oligospermia	Oliva
1995-1998		Higher estradiol levels	
Italy	Male occupational pesticide exposure[60]	**OR - Delay in Conception**	2001
	Greenhouse workers heavy expos.	2.4 (1.2-5.1)	Petrelli
	Greenhouse workers moderate expos.	1.6 (0.8-3.1)	

Mexico	Agricultural workers exposed to OPs[61] . All aneuploidies Lack sex chromosome, sex null XY18 XY18-18 Samples before/after pesticide season OP metabolite concentrations DEP and sex null	**Aneuploidies /Total Sperm Nuclei** 0.67 % 0.19 % 0.15 % 0.06 % No difference Increased frequency Strong assoc., increased spray season	2001 Recio
Denmark Greenhouse workers	Sperm characteristics[62] % normal sperm - high pest. exp % normal sperm - low pest. exp Conc. >10 yrs expos. vs < 5 yrs Testosterone / SHBG ratio[63]	**Prevalence** 60% lower - signif. 14% lower - signif. 40% lower Declined 1.9% per year of work	2000 Abell
Denmark Female greenhouse workers	Fecundability[64] female workers All workers Handling cultivars many hrs/wk Spraying of pesticides Not using gloves	**FR[65]** 1.11 (0.9-1.46) 0.69 (0.47-1.03) 0.78 (0.59-1.06) 0.67 (0.46-0.9)	2000 Abell
NewYork State 1991-1994	Fecundability[64] Maternal fish consumption[66] 3-6 yrs More than one 1 meal per month	**FR[65]** 0.75 (0.59-0.9) 0.73 (0.54-0.98)	2000 Buck
U.S. Navy	Preterm birth Mother, self-reported pesticide expos. Father, occupational pesticide expos.	**OR** Increased risk Increased risk	2000 Hourani
Italy	Time to Pregnancy Pesticide exposed greenhouse wrkrs Non-exposed controls Conception delay beyond 3 months Greenhouse workers high exposure	**Results** 5.4 months ±SD 5.6 3.9 months ±SD 5.6 **OR** 2.4 (1.2-5.1)	2000 Petrelli
Weld County, Colorado 199 -1993	Maternal residence agric. areas[67] Total crop area Sugar beet production Corn production	**Low Birth Weight** Sig. association p=0.058 Sig. association p=0.05 Sig. association p=0.1	2000 Xiang
Canada 1991-92	Fecundability[65] 6 of 13 pesticide exposure categories Farm pesticide - wife not exposed	**FR[66]** 0.51 - 0.80 0.75 - 1.50	1999 Curtis
Minnesota	Pesticide applicators pre and post season Herbicide users only Free testosterone levels FSH[68] FSH[68] Herbicide/insecticide users Herb/insect/fumigant users	**Blood Levels** Post season elevated p = 0.032 Height season decreased p =0.016 Post season decreased p = 0.010 No differences found No differences found	1999 Garry
Finland	Farmers exposed to fungicides Sperm aneuploidy[69]	**Results** No associations found	1999 Harkonen

Denmark 1993-1998	Sperm count[62] Farmer pre-pesticide exposure Farmer post-pesticide exposure	**Cases** **Controls** 197 m/ml 223 m/ml not sig 153 m/ml 178 m/ml not sig	1999 Larsen
Denmark 1995-1996	Sperm count[62] Traditional farmers Organic farmers Inhibin B[70] concentration Testosterone / SHBG[63] ratio	**Mean** 58 million/ml 64 million/ml Slightly higher organic farmers Slightly higher organic farmers	1999 Larsen
China	Sperm aneuploidy[71] Pest. exposed factory workers[72] Sperm aneuploidy[71] Pesticide exposed Non-exposed	**RR** 1.51 (1. 04-2.20) **Median Count** 3.03 / 1,000 sperm 1.94 / 1,000 sperm	1999 Padungtod
China	Pesticide exposed factory workers PON1 allele Arg192 homozygotes / heterozygotes[73]	Lower sperm count χ^2 9.0, $p < 0.01$ Lower % normal sperm χ^2 4.2, $p < .05$ Higher LH[74] levels χ^2 7.9, $p < 0.01$	1999 Padungtod
12 countries[75]	Sperm count All DBCP[76] exposed Philippines only	**Prevalence** 64 % azoospermia[77] 90 % azoospermia/oligospermia[78]	1999 Slutsky
Germany	One day after acute pesticide exposure Testosterone and estradiol T4- and T8-lymphocytes Chronic occupational pesticide expos. Testosterone T4-/T8-lymphocytes LH in exposed men	**Compared to Controls** Decreased level Slightly increased Increased level Increased Higher after exposure than before[79]	1999 Straube
Denmark, France 1995-1996	Fecundability[65] Pesticide exposed farmers Greenhouse workers France - vineyard workers	**FR**[66] 1.09 (0.8-1.4) 0.83 (0.69-1.18) 1.17 (0.89-1.55)	1999 Thonneau
Netherlands	Infertility clinic couples Paternal pesticide exposure	**Fertilization Rate** Decreased sig.	1999 Tielemans
US	Molinate exposed workers[80] Sperm counts Serum hormone levels Observed vs expected births	**Findings** No associations No associations No associations	1999 Tomensen
Canada 1955-88	Fertility sawmill workers Chlorophenol/chlorophenate expos.	**SFR** Decrease - not signif.[81]	1998 Heacock
Denmark 1995-96	Fecundability[65] Traditional farmer vs organic farmer Pesticide user vs non-user Tradition pesticide user 6-10 yrs Tradition pesticide user 11-15 yrs	**FR**[66] 1.03 (0.75-1.4) 1.18 (0.8-1.7) 1.30 (0.9-1.8) 1.61 (1.1-2.4)	1998 Larsen

China[9]	Male pesticide factory workers Serum LH[74] level increase Amt. pest. exp. incr. LH[74] level Serum FSH[74] level sl. increase Serum testosterone decreased	**Findings** beta[82] = 0.79 (0.42, 1.16) signif. 1.1 mIU/mL (0.34, 1.82) beta = 1.38 (-0.09, 2.85) not signif. beta = -55.13 (-147.24, 37) not signif.	1998 Padungtod
Turkey	Villages with high vs low boron levels[83] Work in borate mining/processing Birth of at least one living child Primary infertility (estimated) Gender ratio (M:F) offspring	**Region I - High** **Region II - Low** 28.3% 11.7% 96% 96% 2.34% 2.62% 0.89 1.04 diff not sig.	1998 Sayli
California 1981-1985	DBCP[76] chemical worker[84] (prior1977) Azoospermia[77] Oligospermia[78] Non-azoospermics	**Results** 6% DBCP, 22% voluntary, 4%unkn 15% Sperm count 73.8 million (mean)	1998 Schenker
Iowa 1991-1992	Infertility[85] - females[86] Ever work in agriculture Agric. work prior to infertility Residing on a farm	**OR** 7.0 (2.3-20.8) 11.3 (2.6-48.8) 1.8 (1.2-2.7)	1997 Fuortes
Quebec	Female infertility[87] Pesticide exposure Ovulatory effect	**OR** 3.02 (1.10-8.29) 3.82 (1.28-11.4)	1997 Smith E
Israel 17 year follow-up	DBCP[76] production workers Azoospermics[77] sperm count recovery Oligospermics[78] sperm count recovery Most severely affected individuals	**Results** 36 to 45 months in 33% 36 to 45 months in 50% Sig. increase plasma FSH[68], LH[74] Non-sig. decrease testosterone	1995 Potashnik
California Boron mine	Males sodium borate mining/production Excess offspring fathered Excess female offspring fathered	**SBR[88]** Significant Not significant	1995, 1994 Whorton
Germany 1992	Vinclozolin exposed workers[89] Serum testosterone ng/ml Serum LH[74] IU/ml FSH[68] mU/ml	**Findings** 5.6 ± 1.9 no sig diff 9.0 ± 1.2 no sig diff 4.9 ± 2.6 no sig diff	1995 Zober
Netherlands 1978-1990	Fecundability[65] Fruit growers during spray season Fruit growers not spray season	**FR[66]** 0.42 (0.20-0.92) 0.82 (0.33-2.02	1994 DeCock
Austria 1989-91	Male factor infertility Agricultural occupation	**OR** 11.34 p<0.01	1993 Strohmer
Armenia	Pregnancies Women areas high pesticide use Women areas moderate pest. use	**Prevalence** 31 % 22 %	1991 Airiian

Argentina.	32 Farm sprayers exposed 2,4-D Sperm count (millions/ml) Motility (percent) Dead sperm (percent) Abnormal sperm[90]	**Exposed** **Unexposed** **Signif.** 49.0 101.6 p<0.01 34.8 70.4 p<0.01 82.9 37.1 p<0.01 72.9 33.4 p<0.01	1991 Lerda
Michigan 11 year follow-up	DBCP[76] exposed workers 1976-1977[91] 50% azoospermics[77] recovered All oligospermics[78] recovered 1977 FSH[68] level in azoospermics	**Sperm Count** 44.4 million/mL 88.8 million/mL difference sig. p <.01 Predictive of return normospermia	1990 Olsen
California Fresno County 1978-1982	DBCP[76] in drinking water[92] From 14,861 laboratory reports Births outcomes Sex ratio Highest exposure category (> 3 ppb) Lowest exposure category (< 0.010 ppb)	**Results** Mean 0.0041 - 5.7543 ppb No correlation No associations **SBR**[88] 113 **SBR**[88] 74	1989, 1988 Whorton
Iowa 1977-1980	Farmers vs non-farmers Semen parameters	**Results** No associations found	1988 Gerber
Hawaii	EDB[93] exposed papaya fumigators Sperm count (mean /ejaculate) Viable sperm (mean) Sperm - tapered heads Sperm - absent heads Sperm - abnormal tails YFF bodies[94]	**% Exposed** **% Unexposed** **Signif.** 80.99 million 139.76 million p <0.01 67.1 67.1 p <0.01 4.21 ±6.22 2.49 ±3.17 p< 0.001 2.08 ±1.76 1.43 ±1.29 p< 0.001 6.54 ±10.7 5.71 ±4.45 p< 0.001 1.28 ±0.68 1.33 ±0.62 No assoc.	1987 Ratcliffe
California 1977-1984 5-8 yr follow-up	Azoospermia[77] / oligospermia[78] DBCP[76] exposed workers 2 yrs later DBCP[76] exposed workers 8 yrs later	**Follow-up Data**[95] 2 cases full recovery 6 cases still azoospermic[77]	1986 Eaton
Israel 1977-1982	Azoospermia[86] DBCP[85] exposed workers 5 yrs later	**Follow-up Data** 4 of 13 (31%) recovered	1984 Goldsmith
Israel	DBCP[76] production workers Pre-exposure period During exposure Azoospermic[77]/oligozoospermic[78]	**Male Infants Conceived** 52.9% 35.2% 16.6% p < 0.025	1984 Potashnik
14 studies	DBCP[76] exposed workers Mean sperm counts Median sperm count Men with sperm counts < 20 m/ml	**Results** 107.1 m/ml 83.0 m/ml 8.7 %	1984 Whorton
France Case Report	Infertile farm couple -heavy lindane user Without protective equipment After protective measures Successful pregnancy	**Motility** **Necrospermia** **Teratospermia** 5% 60% 60% 20% 0% Persistent Several months after protections	1981 Cranz
Texas	14 Oligospermic[78] DBCP[76] workers[96] Serum testosterone Testicular biopsy Sperm count	**Results** Within normal range Patchy tubular hyalinization Improved 18-21 mo after last exposure	1981 Lantz

	Lindane factory workers Serum LH[74] geometric mean Serum FSH[68] Serum testosterone	**Exposed Workers Controls** 8.8 mIU/ml 5.7 mIU/ml Higher, not significant Lower, not significant	1981 Tomczak
Michigan	92 Dow DBCP[76] production workers Sperm counts FSH[68] and LH[74] levels Testicular size	**Exposed vs Unexposed** Lower Higher Smaller volume	1980 Egnatz
	Y-Chromosomal nondisjunction Healthy males Tumor pts. treated with radiation DBCP[76] exposed workers	**YFF[94] Mean Incidence Sperm** 1.1 % Significant increase Significant increase	1980 Kapp
Israel Jordan Valley 1977	DBCP exposed kibbutzim banana wrkrs Spontaneous abortions In sub-sample of 16[97]	**Before After Expos. Signif.** 6.6% 19.8% $p < 0.01$ (χ^2=5.52) 5.9% 27.5% $p < .05$ (χ^2=4.60)	1980 Kharrazi
California 1978	1 yr post termination DBCP[76] exposure 9 oligospermic[78] 12 azoospermics[77] (11 exposed > 4 yrs) Serum FSH[68] azoospermics	**Results** 8 of 9 improved, 6 normospermic No improvement Increased significantly	1980 Whorton
California	DBCP[76] pesticide applicators Infertility Azoospermia[77] Decreased sperm count Serum FSH[68] Serum LH[74]	**Results** Not found Not found Equipment calibrators, irrigators only Increased longer duration exposure No increase found	1979, 1978 Glass
U.S. Six states	Workers exposed to DBCP[76] Formulators Custom Applicators Farmers Farm workers Researchers Salesmen	**Sperm Count FSH[77] LH[83]** 12(.8-371) 10.7 (5-29) 14.2 (6-29) 2.7(1.6-3.8) 45.7 (29-62) 16.3 (11-22) 17.8(1.4-171 23.3 (2-61) 12.0 (6-20) 37.8(0-159) 12.9 (5-86) 12.6 (6-60) 101(41-188) 4.9 (3-13) 6.7 (4-29) 73(32-166) 7.2 (2-12) 6.8 (5-17)	1979 Sandifer
California 1969-19877	DBCP[76] exposed factory workers[98] Azoospermia[77,99] Oligospermia, severe <20 m/ml Oligospermia, mild 20-39 m/ml Sperm count (median) Exposure, FSH[68] correlation Biopsy results	**Exposed Non-exposed** 13.1 % 2.9 % 16.8 % None 15.8 % 5.7 % 46 million/mL 79 million/mL r = .770 Seminiferous tubules site of damage[100]	1979 Whorton
U.S.	Carbaryl production workers Sperm count Fathering children	**Compared to Unexposed** Small excess oligospermia not sig. No associations	1979 Whorton
Bulgaria	Pesticide exposed female farm workers Menorrhagia and hypermenorrhea Oligomenorrhea Sterility	**Prevalence Exposed vs Controls** 12.9% vs 3.2% 18.1% vs 6.7% No differences	1973 Marinova

England Case Report	Farm workers pesticide spraying[101] Impotence	4 of crew of 5 affected All recovered (3 months to 13 months)	1970 Espir

Maternal-Fetal Blood, Reproductive Tissue Contaminants

Location	Exposure and Outcome	Findings (95% CI)	Ref.
Spain 1997-1999	Residence near factory Maternal serum hexachlorobenzene Cord blood Hexachlorobenzene Neonatal urinary porphyrin[102]	**Results** 3.31 ng/mL 1.08 ng/mL 37.87 umol/mol creatinine	2002 Ozalla
Canada	In vitro fertilization couples Follicular fluids: p,p'-DDE, mirex Serum samples: p,p'-DDE, endosulfan Seminal plasma: Mirex Serum and follicular fluid p,p'-DDE	**Prevalence of Detection** 50% or more of samples 50% or more of samples 33.3% of samples Associated with failed fertilization	2002 Younglai
U.S.	9 Pregnant migrant farm workers Maternal urine, cord blood, placenta	7 of 51 analytes[103] found ≥ 1 woman DDE, DDT, endosulfan in cord blood 2,4-D in urine	2001 Cooper
Belgium	Girls with precious puberty Foreign adopted Foreign non-adopted 13 of 15 native Belgian girls	**Median Plasma p,p'-DDE** 1.20 ng/ml 1.04 ng/ml < 0.1 ng/ml	2001 Krstevsk-
Mexico	Term placenta examination. Parathion exposure during pregnancy	**Compared to Controls** Increased atypical characteristics[104]	2001 Levario-C
U.S. Collaborative Perinatal Project 1959-1966	Median maternal DDE Preterm births - increases in DDE Small-for-gest-age - increases in DDE	25ug/L range 3-178 (stored samples)[105] OR 1.5 to 3.1 trend sig $p < 0.0001$ OR 1.9 to 2.6 trend sig $p = 0.04$	2001 Longnecker
Thailand	Deet use 2nd, 3rd trimester pregnancy[106] Crosses the placenta	**Detection in Cord Blood** 8% of samples (2.6-18.2)	2001 McGready
Spain 1977-1999	Cord blood Hexachlorobenzene p,p ´DDE, β-HCH	**Geometric Mean** 1.1 ng/ml Range 0.3-5.7 ng/ml. Detectable levels	2001 Sala
New York Presbyterian Hospital	Normal deliveries Meconium from 20 newborns DEP DETP DMP DEDTP DMTP and DMDTP	**Organophosphate Urine Metabolites**[107] 19 of 20 samples (0.8-3.2 ug/g) 20 of 20 samples (2.0-5.6 ug/g) 1 of 20 samples 16 ug/g 1 of 20 samples 1.8 ug/g Not detected.	2001 Whyatt
Faroe Islands 1986-1987	Umbilical cords (N=316) Hexachlorobenzene (HCB) DDE	**Pooled Sample** 0.17 ng/g whole weight 1.19 ng/g whole weight	2000 Burse

U.S.	Human amniotic fluid[108] 2nd trimester p,p'-DDE alpha-Hexachlorocyclohexane	**Mean Levels** 0.21 ± 0.18 ng/ml 0.15 ± 0.06 ng/m	2000 Foster
Germany	Children with undescended testes Chlorinated hydrocarbons in fat[109]	Significant increased levels heptachlor epoxide and hexachlorobenzene	2000 Hosie
New Bedford Massachusetts 1993-1998	Cord blood (N=751 infants) pp'-DDE Hexachlorobenzene	**Mean in ng/g Serum** 0.48 ± 0.94 0.03 ± 0.04	2000 Korrick
Mexico 1997-1998	Maternal-infant pairs Maternal adipose tissue Maternal serum Cord blood	**p,p'- DDE** **p,p'- DDT** 4.51 mg/kg 1.27 mg/kg 4.45 mg/kg 0.78 mg/kg 4.70 mg/kg 0.88 mg/kg	2000 Waliszewski
Ontario, Canada Farmers	Semen Samples Recent use of herbicide 2,4-D	**Prevalence of 2,4-D Detection** 50% contained ≥ 5.0 ng/mL	1999 Arbuckle
U.S.	DDT levels during pregnancy Specimens collected 1st, 3rd trimester	**Correlation Coefficient** r = 0.86	1999 Longnecker
Quebec 1994	New diagnosis of endometriosis[110] Organochlorine pesticides	**Mean plasma levels** No significant differences	1998 Lebel
Poland 1986-1996 4 Case Reports	Suicidal pesticide pois. in pregnancy Carbofuran 17yr-old (18 weeks) Carbofuran 20yr-old (12 weeks) Attempts to provoke abortion Formothion 30yr-old (10 weeks) Endosulfan 21-yr-old (5 months)	**Outcome** Fetus died - blood level same as mother Spontaneous abortion 27 days later[111] Inserted into vagina, fetus survived Ingested, relatively quick fetal death	1997 Sancewicz-Pach
Germany	Fetal fat tissue (N=34) DDT HCH Heptachlor	**Mean in Fat mg/kg** 0.7 0.14 0.03	1996 Bosse
India	Normal delivery vs premature labor Maternal blood Cord blood and placenta	**Organochlorine Pesticides**[112] No significant difference No significant difference	1996 Sharma
Canada Halifax, Hamilton, Vancouver	Ovarian follicular fluid and serum[113] Chlorin. hydrocarbon pesticides Rate/time to cleavage first egg	**Trace Amounts** Chlordane, DDE, heptachlor epoxide, HCB, oxychlordane No association with contaminant levels	1993 Jarrell
Germany	Wood preservative exposure[114] Habitual abortion Unexplained infertility Women with infertility Menstrual dysfunction	**Blood Levels** PCP[115] >25 µg/l &/or lindane >100 ng/l PCP >25 µg/l &/or lindane >100 ng/l PCP mean = 73 µg/l PCP mean = 42 µg/l	1991 Gerhard
India	Chlorinated pesticides in uterine tissue Total DDT	**Leiomyomas**[116] **Normal** 0.245-1.982 ppm 0.030-0.282 ppm (mean 0.845) (mean 0.103)	1987 Saxena

India	Stillborn (SB) vs Live born (LB) Mean in parts per billion Lindane Aldrin p,p'-DDT Total DDT	**Mat. Blood** **Placenta** **Cord Blood** **SB LB** **SB LB** **SB LB** 17.3 18.3 13.4 17.1 14.8 13.6 33.3 5.6[a] 31.7[a] 8.0 19.1[b] 16.7 62.9[a] 9.2 38.5[a] 13.8 22.9[b] 11.6 96.8[a] 26.2 60.8[a] 39.8 33.6 30.9 **a** sig. p <.01 **b** sig. p <.05	1983 Saxena
	Premature delivery (PD)[117] versus normal births DDT Lindane Dieldrin Heptachlor epoxide	**Serum - Mean in ppb** **PD low PD high PD all Normal** 50.80 119.60 71.10 26.51 11.00 22.1 15.0 4.30 5.50 15.20 8.40 1.10 6.20 16.00 9.10 3.00	1982 Wasserman
India 1978	Women from general population Lindane DDT Aldrin	**Mean in Parts per Billion** Placenta Placental Fluid 389.64 27.12 200.91 23.83 (geometric) 158.7 20.76	1980 Saxena
U.S.	Pregnant women rural agricultural area Recent DDT exposure evidence Mothers Black newborns White newborns	**Serum DDT levels** Comparable occup. expos. ♂ (>blacks) **Prevalence** 90% 84% 45%	1976 D'Ercole
Nigeria	Fetal adipose tissue taken at autopsy Total DDT Total BHC Dieldrin Heptachlor epoxide Age group from 0 to 11 mo Total DDT	**Findings** 0.96 ppm 0.19 ppm 0.002 ppm 0.006 ppm 2.8 ppm (45% of residues found)	1972 Day
U.S.	DDE blood levels White premies weighing <2,500 g Black premies weighing <2,500 g White normal mature infants Black normal mature infants DDE blood levels White premies Black premies White normal mature infants Black normal mature infants	**Mean in parts per billion (range)** 22.1 (18.7- 26.8) 19.0 (6.6-34.4) 4.9 (2- 3) 6.1 (3-12) **Median in parts per billion** 21 17 5 5	1972 O'Leary
U.S.	Mean DDT, DDE in pregnancy (ppb) DDE maternal blood DDE cord blood DDT maternal blood DDT cord blood DDT amniotic fluid	**Whites** **Blacks** **Range** 10.8 15.2 3 - 92 4.8 5.9 17.0 32.0 5.0 9.0 6.0 14.0	1970 O'Leary

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Footnotes

1. 345 conventional pesticide user households (applied pesticides routinely and regularly), and 331 IPM (integrated pest management) used pesticides as necessary, and on economically injured crop areas only.
2. US birth cohort study begun in 1959–1966.
3. In week 3 to 8 of pregnancy, in the square mile of maternal residence, or in one of adjacent 8 sq mi. to organophosphate, N–methyl carbamate, and endocrine disruptor types of pesticides.
4. Syndactyly, polydactyly, adactyly, and "other limb reductions" (as listed in the birth record).
5. During the month before conception and the first trimester of pregnancy.
6. Primarily nervous system defects, oral clefts, and multiple anomalies.
7. Primarily nervous system and musculoskeletal defects.
8. Last menstrual period.
9. Pesticide exposure during period just after conception.
10. Concentration in fish was very high (100 ppm). The cluster ceased when the chemical treatment of farmed fish with

trichlorfon was banned in March 1991.

11. Children of fathers who were saw mill workers exposed for at least one year.
12. 1993 media reports alleged clusters might be linked to exposure to the pesticide (fungicide) Benomyl. Overall prevalence of anophthalmia and microophthalmia was 1 / 10,000 births.
13. Each job of either parent during pregnancy; any job of father 3 months before the last menstrual period before conception.
14. 581 orofacial clefts, 365 central nervous system defects, 360 skeletal defects.
15. Six months before until one month after the estimated date of conception.
16. Methylisocyanate, toxic chemical released from explosion at factory manufacturing carbaryl (Sevin) in Dec.1984 .
17. Gastrointestinal.
18. 80% of males in the exposed group had health effects such as severe giddiness, nervous, skin, and eye disorders consistent with mild to moderate pesticide poisoning.
19. Based on birth certificate: farmers, ranchers, farm workers, landscapers, gardeners, pest control operators considered exposed, all other groups considered non-exposed to pesticides.
20. After exposure to pesticides vs before exposure.
21. The interval between the exposure and the interview ranged from 1 to 15 years.
22. By metasystox-R, Phosdrin, and Lannate while tying cauliflower leaves in a field sprayed 20 hours prior to entry.
23. Patent ductus, ventricular/atrial septal defects, pulmonary stenosis, ocular hypertelorism, microopthalmia left eye, bilateral optic nerve colobomas, low set ears, micrognathia, diffuse cerebellar and cerebral atrophy.
24. 158 had only this single defect, 79 had additional defects. Those with additional defects showed a trend of increasing risk with increasing exposure to agricultural production.
25. Neural tube defects (n=103), facial clefts (n=127), bilateral renal agenesis (n=30), combination of the above three defects, and a combined category of 40 major birth defects.
26. Forest / agricultural use, with focus on fenitrothion, aminocarb, phenoxy herbicides, non-chlorinated herbicides.
27. Case mothers and controls divided into 2 groups – those with first trimester pesticide exposure and those without.
28. During 1980-1982 pineapple waste contaminated with heptachlor was used in feed for dairy cows.
29. Used an often leaky spray aerosol bottle 6 days a week, 7 hours a day from 6 months prior to conception until 5 weeks after last menstrual period; severe chemical burn from spill on lower leg treated with topical corticosteroids during this time.
30. Increased ratios also found for anencephaly.
31. 3 hip dislocations, 2 heart defects, one each club foot, other limb deformity, anencephaly, spina bifida, other vertebral defects, ureter defects. Cleft palate, hypospadias not found.
32. Except for 1975 and 1976.
33. Estimated levels of exposure determined by categorizing 75 Arkansas counties into high, medium, or low exposure groups based on rice acreage during 6 or 7 year intervals beginning in 1943.
34. During the time when herbicides are applied.
35. Thifensulfuron-methyl plus tribenuron-methyl, and fenoxaprop-P-ethyl plus MCPA.
36. 12 weeks gestation.
37. Periconception exposure - 3 months before conception to the month of conception.
38. 12 to 19 weeks gestation.
39. Pesticide exposure week 3 to 8 of pregnancy, in the sq mi of maternal residence, or in one of adjacent 8 sq mi. areas.
40. DDT, DDE, DDD, alpha/beta/gamma/delta-HCH, toxaphene, dieldrin, endrin, aldrin, heptachlor/heptachlor epoxide.
41. Multiple logistic regression model.
42. Interaction effects model.
43. Pentachlorophenol.
44. Pentachlorophenol, hexachlorocyclohexane, hexachlorobenzene, DDT group, PCBs.
45. Women with acquired porphyria cutanea tarda after eating fungicide treated seed wheat (not meant for human consumption).
46. 16 to 27 weeks gestation.
47. After the harvest, authors hypothesize exposure to mycotoxins in grain induces early labor.
48. Levels of atrazine, metolachlor, and cyanazine each significant predictors of IUGR rates, being strongest for atrazine.
49. Within 24 hours of birth.
50. Thiocarbamates, carbaryl, and unclassified pesticides used on the farms.
51. Measured levels of pentachlorophenol (PCP) and lindane in wood panels, of PCP, lindane, polychlorinated dibenzo-p-dioxins and dibenzofurans in indoor air.
52. After 28 weeks gestation.
53. Who had worked at least 6 months for one of 58 floriculture companies.
54. Fetal death after 27 weeks, single pregnancies in women employed $\geq$30 hrs/wk for $\geq$2 wks any time during pregnancy.

55. Union members exposed to pesticides in greenhouses. Skilled gardeners authorized to spray only 9% of the group.
56. Spontaneous abortion (20 weeks or less).
57. Lifetime reported spontaneous abortion rate of the women significantly predicted the percent males per subject.
58. Age 30 to 88 (mean 62). Most had farmed for about 30 years and 27% reported having used DDT.
59. Total testosterone decreased 2% per increase interquartile level DDE; percent change other hormones also negligible.
60. 322 agricultural workers licensed to handle pesticides and 127 greenhouse workers.
61. Organophosphate pesticides.
62. Sperm concentration (density) measured in millions sperm / ml semen. Normal ≥ 20 m/ml, or > 80 m/ejaculation.
63. Sex hormone binding globulin; indicator of available unbound testosterone. An increase in SHBG lowers free biologically active testosterone.
64. Fecundability is the ability to conceive a child; also called time to pregnancy . It is the number of menstrual cycles or months it takes for a couple to conceive when not using birth control.
65. Fecundability ratio. The likelihood of pregnancy during a month for the exposed couples vs controls. The lower the ratio the less fecund (fertile) the couple.
66. Sports fish from Lake Ontario. Women were participants in the New York State Angler Cohort Study.
67. GIS used to create maps of crop types within 300- and 500-m circular zones around mothers' homes.
68. Follicle-stimulating hormone. High FSH levels indicate testicular failure.
69. Disomy and diploidy frequencies for chromosomes 1 and 7.
70. Inhibin B is a protein in sperm that correlates to sperm count. The higher the sperm count the higher the inhibin B levels.
71. Having an abnormal number of chromosomes.
72. OP insecticides methidathion and parathion manufactured. Controls textile factory workers at another location.
73. Enzymes associated with organophosphate pesticide metabolism. Human paraoxonase gene (PON1) Arg192 homozygotes have greater detoxifying capability than Gln192 homozygotes.
74. Luteinizing hormone. High LH levels indicate testicular failure.
75. 26,400 male banana and pineapple plantations workers with median DBCP exposure of 3 years.
76. Dibromochloropropane, a soil and post harvest fumigant banned by EPA in 1979, except in Hawaii where banned in 1989.
77. Azoospermia - a sperm count of 0 (zero). Failure to produce any sperm.
78. Oligospermia - less than 20 million sperm per milliliter of semen.
79. Authors assume an inhibition of the aromatase system by testosterone metabolites.
80. 272 formulation and production workers at three US plants. Mean exposures ranged from 12.7 to 210.9 ug/m^3
81. Controlling for time since first hire, no inverse relation between cumulative exposure and fertility was found.
82. Coefficient of exposure effect.
83. 2 villages high boron levels in drinking water (8.5-29mg/l, 2.05-2.5mg/l); 3 with low levels (0.03-0.40 mg/l).
84. All men ≥ 25% time: 6 supervisors, 86 production workers, 5 maintenance workers, median age 36 (22-62); 68% white, 26% Hispanic, 6% black or Asian. 50% had 9 or more years of employment.
85. Self-reported inability to conceive after 12 months of unprotected intercourse; or the failure to deliver a live-born child.
86. All male partners were diagnosed as fertile.
87. Study of risk of medically diagnosed infertility in 281 women compared with 216 fertile women.
88. Standardized birth ratio.
89. Exposed for 1 to 13 years during synthesis and formulation operations.
90. Over time percent motility and dead sperm decreased but abnormal sperm did not.
91. Maximum 18 months exposure.
92. County had 532 drinking water systems (49 large, 483 small), plus an additional 14,000 private wells. Census tracts categorized into 7 DBCP levels: < 0.010 ppb, 0.01-.1 ppb, 0.1-.2 ppb, 0.2-.5 ppb, 0 .5-1 ppb, 1-3 ppb, >3 ppb.
93. Ethylene dibromide. Mean duration exposure 5 yrs; geometric mean breathing zone 8 ppb (8 hr TWA), below NIOSH recommended limit of 45 ppb 8 hr TWA, and OSHA of 20 ppm. Peak exposures of up to 262 ppb.
94. YFF is the number of spermatozoa with two fluorescent bodies (per 1000 sperm counted). It is a measure of Y chromosomal nondisjunction observed directly in the male gamete.
95. 44 men still at plant in 1984; 9 of 32 with testicular dysfunction in 1977, 17 normal counts, 10 unexposed, 8 vasectomies.
96. Production workers - total exposure ranged from less than 50 to 700 hours.
97. Whose wives conceived both before and after exposure to DBCP.
98. 1½ to 3 million pounds DBCP formulated yearly between 1969-77. No data available on DBCP use prior to 1968.
99. 2 with azoospermic had had no exposure to DBCP for 9 and 13 years respectively; the first exposed for 4 years, the second for 2, and both had fathered children prior to DBCP exposure.

100. In worst cases no spermatogenic activity or spermatogonia, resembling Sertoli cell only syndrome. Less severe cases a decrease in amount of cellularity within the seminiferous tubules. No evidence of inflammation.

101. A large number of pesticides used including: 5 organophosphates, dinoseb, paraquat, dieldrin, 3 phenoxy herbicides, simazine, linuron, and mancozeb.

102. Primarily coproporphyrin I and III. No positive association urinary porphyrin excretion and HCB levels.

103. Obtained at delivery; 51 compounds including 6 phenoxy acid/triazine herbicides and 21 organochlorine insecticides.

104. In some recent microinfarctions, microcalcifications, increased deposition fibrinoid material; more atypical villi (bullous, balloon-like formations, nonhomogeneous surfaces); areas devoid of microvilli.

105. Several fold higher than current US concentrations.

106. Mean of 214.2 g deet per pregnancy (range 0 - 345.1 g).

107. Diethylphosphate (DEP), diethylthiophosphate (DETP), diethyldithiophosphate (DEDTP), dimethylphosphate (DMP), dimethylthiophosphate (DMTP), and dimethyldithiophosphate (DMDTP).

108. One in three amniotic fluid samples tested positive for at least one environmental contaminant.

109. 18 cases 30 controls tested for DDT and metabolites, PCBs, toxaphene, hexachlorocyclohexane, chlorinated cyclodienes, chlorinated benzenes.

110. 86 cases, 70 controls from women undergoing laparoscopy for chronic pelvic pain, infertility, or tubal fulguration.

111. Highest level carbofuran in mother's blood 9.71 ug/g.

112. Tested for aldrin, isomers of HCH, metabolites of DDT and heptachlor.

113. In 74 women undergoing in-vitro fertilization

114. Exposure duration 4.6 to10 years via off gassing from wooden ceiling, wall panels, carpet, leather upholstery treated with wood preservatives as well as dermal contact with these treated materials.

115. Pentachlorophenol.

116. Fibroids.

117. Fetus of more than 500 and less than 2500 grams after the 20th and before the 37th week of gestation.