In the name of God

ENVIRONMENTAL AND INDIVIDUAL EXPOSURE AND THE RISK OF CONGENITAL ANOMALIES

Nasrin Asadi.MD

Perinatologist

Associated professor of SUMS

- Industries
- Mines
- Landfills
- Socioeconamic status
- Air pollution
- Beauty products

INDUSTRIES

- Soaps
- Insecticides
- Oils
- Grease
- Freon refrigerants
- Dry cleaning agent
- Fire extinguisher
- Waxes
- In making nylons

Natural gas wells

- Retrospective cohort study Investigate the maternal exposure to emissions from natural gas wells based on both the number of wells within the 10 miles radius and the proximity to the mother's residence

Environ Health Perspect. 2014 Apr;122(4):412-7. doi: 10.1289/ehp.1306722. Epub 2014 Jan 28.

Birth outcomes and maternal residential proximity to natural gas development in rural Colorado.

McKenzie LM[1], Guo R, Witter RZ, Savitz DA, Newman LS, Adgate JL.

⊕ Author information

Abstract

BACKGROUND: Birth defects are a leading cause of neonatal mortality. Natural gas development (NGD) emits several potential teratogens, and U.S. production of natural gas is expanding.

OBJECTIVES: We examined associations between maternal residential proximity to NGD and birth outcomes in a retrospective cohort study of 124,842 births between 1996 and 2009 in rural Colorado.

METHODS: We calculated inverse distance weighted natural gas well counts within a 10-mile radius of maternal residence to estimate maternal exposure to NGD. Logistic regression, adjusted for maternal and infant covariates, was used to estimate associations with exposure tertiles for congenital heart defects (CHDs), neural tube defects (NTDs), oral clefts, preterm birth, and term low birth weight. The association with term birth weight was investigated using multiple linear regression.

RESULTS: Prevalence of CHDs increased with exposure tertile, with an odds ratio (OR) of 1.3 for the highest tertile (95% CI: 1.2, 1.5); NTD prevalence was associated with the highest tertile of exposure (OR = 2.0; 95% CI: 1.0, 3.9, based on 59 cases), compared with the absence of any gas wells within a 10-mile radius. Exposure was negatively associated with preterm birth and positively associated with fetal growth, although the magnitude of association was small. No association was found between exposure and oral clefts.

CONCLUSIONS: In this large cohort, we observed an association between density and proximity of natural gas wells within a 10-mile radius of maternal residence and prevalence of CHDs and possibly NTDs. Greater specificity in exposure estimates is needed to further explore these associations.

Colorado (USA)	Cohort LB	124,842 live births (1996-2009)	aOR: 1.2 (1.0-1.3) aOR: 1.3 (1.2-1.5) aOR: 1.5 (1.1-2.1) aOR: 1.5 (1.1-2.1) aOR: 1.6 (1.1-2.2) aOR: 3.9 (1.3-11) aOR: 4.2 (1.3-13) aOR: 2.0 (1.0-3.9)	CHD CHD VSD PVS PVS Tricuspid valve defects Tricuspid valve defects NTD	Average High High Average High Average High High	Newborn gender, maternal age, active smoking, educational level, smoking, alcohol consumption, number of births	McKenzie 2014

Solvents


SPECTRUM
Ethyl Alcohol
Acetonitrile
HPLC Grade
Sulfuric Acid

chlorinated solvents

- The study investigated effects linked to the maternal residential distance from industrial areas or linked to the amount of solvents released from each source on a yearly basis which is higher with mothers aged 35 years or older

Environ Health. 2014 Nov 19;13:96. doi: 10.1186/1476-069X-13-96.

Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: a case-control study.

Brender JD[1], Shinde MU, Zhan FB, Gong X, Langlois PH.

⊕ Author information

Abstract

BACKGROUND: Some studies have noted an association between maternal occupational exposures to chlorinated solvents and birth defects in offspring, but data are lacking on the potential impact of industrial air emissions of these solvents on birth defects.

METHODS: With data from the Texas Birth Defects Registry for births occurring in 1996-2008, we examined the relation between maternal residential proximity to industrial air releases of chlorinated solvents and birth defects in offspring of 60,613 case-mothers and 244,927 control-mothers. Maternal residential exposures to solvent emissions were estimated with metrics that took into account residential distances to industrial sources and annual amounts of chemicals released. Logistic regression was used to generate odds ratios and 95% confidence intervals for the associations between residential proximity to emissions of 14 chlorinated solvents and selected birth defects, including neural tube, oral cleft, limb deficiency, and congenital heart defects. All risk estimates were adjusted for year of delivery and maternal age, education, race/ethnicity, and public health region of residence.

RESULTS: Relative to exposure risk values of 0, neural tube defects were associated with maternal residential exposures (exposure risk values >0) to several types of chlorinated solvents, most notably carbon tetrachloride (adjusted odds ratio [aOR] 1.42, 95% confidence interval [CI] 1.09, 1.86); chloroform (aOR 1.40, 95% CI 1.04, 1.87); ethyl chloride (aOR 1.39, 95% CI 1.08, 1.79); 1,1,2-trichloroethane (aOR 1.56, 95% CI 1.11, 2.18); and 1,2,3-trichloropropane (aOR 1.49, 95% CI 1.08, 2.06). Significant associations were also noted between a few chlorinated solvents and oral cleft, limb deficiency, and congenital heart defects. We observed stronger associations between some emissions and neural tube, oral cleft, and heart defects in offspring of mothers 35 years or older, such as spina bifida with carbon tetrachloride (aOR 2.49, 95% CI 1.09, 5.72), cleft palate with 1,2-dichloroethane (aOR 1.93, 95% 1.05, 3.54), cleft lip with or without cleft palate with ethyl chloride (aOR 1.81, 95% CI 1.06, 3.07), and obstructive heart defects with trichloroethylene (aOR 1.43, 95% CI 1.08, 1.88).

CONCLUSIONS: These findings suggest that maternal residential proximity to industrial emissions of chlorinated solvents might be associated with selected birth defects in offspring, especially among older mothers.

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carbon tetrachloride

- Refrigerants
- Dry cleaning agent
- Fire extinguisher
- Nylons
- Rubber cement
- Soaps
- Insecticides

Texas (USA)	Case-control LB; FD; ET	60,613 cases 244,927 controls (1996-2008)	aOR: 1.13 (1.04-1.22)	CSD	Carbon tetrachloride
			aOR: 1.23 (1.10-1.37)	CSD	1,1-etylene dichloride
			aOR: 1.21 (1.07-1.38)	CSD	Propylene dichloride
			aOR: 1.19 (1.06-1.32)	CSD	1,2-dichloroethylene
			aOR: 1.14 (1.02-1.28)	CSD	Tetrachlororethane
			aOR: 1.13 (1.05-1.21)	CSD	Ethylchloride
			aOR: 1.13 (1.02-1.24)	CSD	1,2,3-trichloropropane
			aOR: 1.12 (1.01-1.24)	CSD	1,1,2-trichloroethane
			aOR: 1.10 (1.01-1.19)	CSD	Chloroform
			aOR: 1.06 (1.02-1.10)	CSD	Trichloroethylene
			aOR: 1.06 (1.04-1.09)	CSD	Any type of solvent
			aOR: 1.56 (1.11-2.18)	NTD	1,1,2- trichloroethane
			aOR: 1.49 (1.08-2.06)	NTD	1,2,3-trichloropropane
			aOR: 1.42 (1.09-1.86)	NTD	Carbon tetrachloride
			aOR: 1.40 (1.04-1.87)	NTD	Cloroformium
			aOR: 1.39 (1.08-1.79)	NTD	Ethylchloride
			aOR: 1.29 (1.01-1.63)	NTD	Metilchloroform
			aOR: 1.28 (1.01-1.62)	NTD	1,2-etylene diclhoride
			aOR: 1.94 (1.32-2.84)	Spina bifida	1,1,2- trichloroethane
			aOR: 1.78 (1.22-2.59)	Spina bifida	1,2,3-trichloropropane
			aOR: 1.78 (1.12-2.82)	Spina bifida	Tetrachlororethane
			aOR: 1.70 (1.06-2.71)	Spina bifida	1,1-ethylene dichloride
			aOR: 1.64 (1.24-2.16)	Spina bifida	1,2-ethylene dichloride
Texas (USA)	Case-control LB; FD; ET	60,613 cases 244,927 controls (1996-2008)	aOR: 1.60 (1.01-2.53)	Spina bifida	1,2-dichloroethylene
			aOR: 1.59 (1.18-2.14)	Spina bifida	Ethylchloride
			aOR: 1.58 (1.15-2.19)	Spina bifida	Carbon tetrachloride
			aOR: 1.56 (1.18-2.07)	Spina bifida	Methylchloroform
			aOR: 1.55 (1.10-2.20)	Spina bifida	Chloroform
			aOR: 1.77 (1.05-2.9)	Cleft palate	Propylene dichloride

chloroethane

- In foamed plastics

Texas (USA)	Case-control LB; FD; ET	60,613 cases 244,927 controls (1996-2008)	aOR: 1.13 (1.04-1.22)	CSD	Carbon tetrachloride
			aOR: 1.23 (1.10-1.37)	CSD	1,1-etylene dichloride
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			aOR: 1.19 (1.06-1.32)	CSD	1,2-dichloroethylene
			aOR: 1.14 (1.02-1.28)	CSD	Tetrachlororethane
			aOR: 1.13 (1.05-1.21)	CSD	Ethylchloride
			aOR: 1.13 (1.02-1.24)	CSD	1,2,3-trichloropropane
			aOR: 1.12 (1.01-1.24)	CSD	1,1,2-trichloroethane
			aOR: 1.10 (1.01-1.19)	CSD	Chloroform
			aOR: 1.06 (1.02-1.10)	CSD	Trichloroethylene
			aOR: 1.06 (1.04-1.09)	CSD	Any type of solvent
			aOR: 1.56 (1.11-2.18)	NTD	1,1,2- trichloroethane
			aOR: 1.49 (1.08-2.06)	NTD	1,2,3-trichloropropane
			aOR: 1.42 (1.09-1.86)	NTD	Carbon tetrachloride
			aOR: 1.40 (1.04-1.87)	NTD	Cloroformium
			aOR: 1.39 (1.08-1.79)	NTD	Ethylchloride
			aOR: 1.29 (1.01-1.63)	NTD	Metilchloroform
			aOR: 1.28 (1.01-1.62)	NTD	1,2-etylene dichloride
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			aOR: 1.56 (1.18-2.07)	Spina bifida	Methylchloroform
			aOR: 1.55 (1.10-2.20)	Spina bifida	Chloroform
			aOR: 1.77 (1.05-2.9)	Cleft palate	Propylene dichloride

Chloroform

- A clear, volatile liquid with a strong smell similar to that of ether

- Anesthesia
- Given to relieve pain
- Used as a remedy for cough

Texas (USA)	Case-control LB; FD; ET	60,613 cases 244,927 controls (1996-2008)	aOR: 1.13 (1.04-1.22)	CSD	Carbon tetrachloride
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			aOR: 1.10 (1.01-1.19)	CSD	Chloroform
			aOR: 1.06 (1.02-1.10)	CSD	Trichloroethylene
			aOR: 1.06 (1.04-1.09)	CSD	Any type of solvent
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			aOR: 1.55 (1.10-2.20)	Spina bifida	Chloroform
			aOR: 1.77 (1.05-2.9)	Cleft palate	Propylene dichloride

Propylene dichloride

- A liquid with a chloroform-like odor
- Production of chlorinated organic chemicals
- In **photographic film** manufacture
- For **paper coating**

Texas (USA)	Case-control LB; FD; ET	60,613 cases 244,927 controls (1996-2008)	aOR: 1.13 (1.04-1.22)	CSD	Carbon tetrachloride
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			aOR: 1.77 (1.05-2.9)	Cleft palate	Propylene dichloride

Hum Reprod. 2019 Mar 30. pii: dez033. doi: 10.1093/humrep/dez033. [Epub ahead of print]

Congenital anomalies in the offspring of occupationally exposed mothers: a systematic review and meta-analysis of studies using expert assessment for occupational exposures.

Spinder N[1,2], Prins JR[3], Bergman JEH[2], Smidt N[1], Kromhout H[4], Boezen HM[1,5], de Walle HEK[2].

⊕ Author information

Abstract

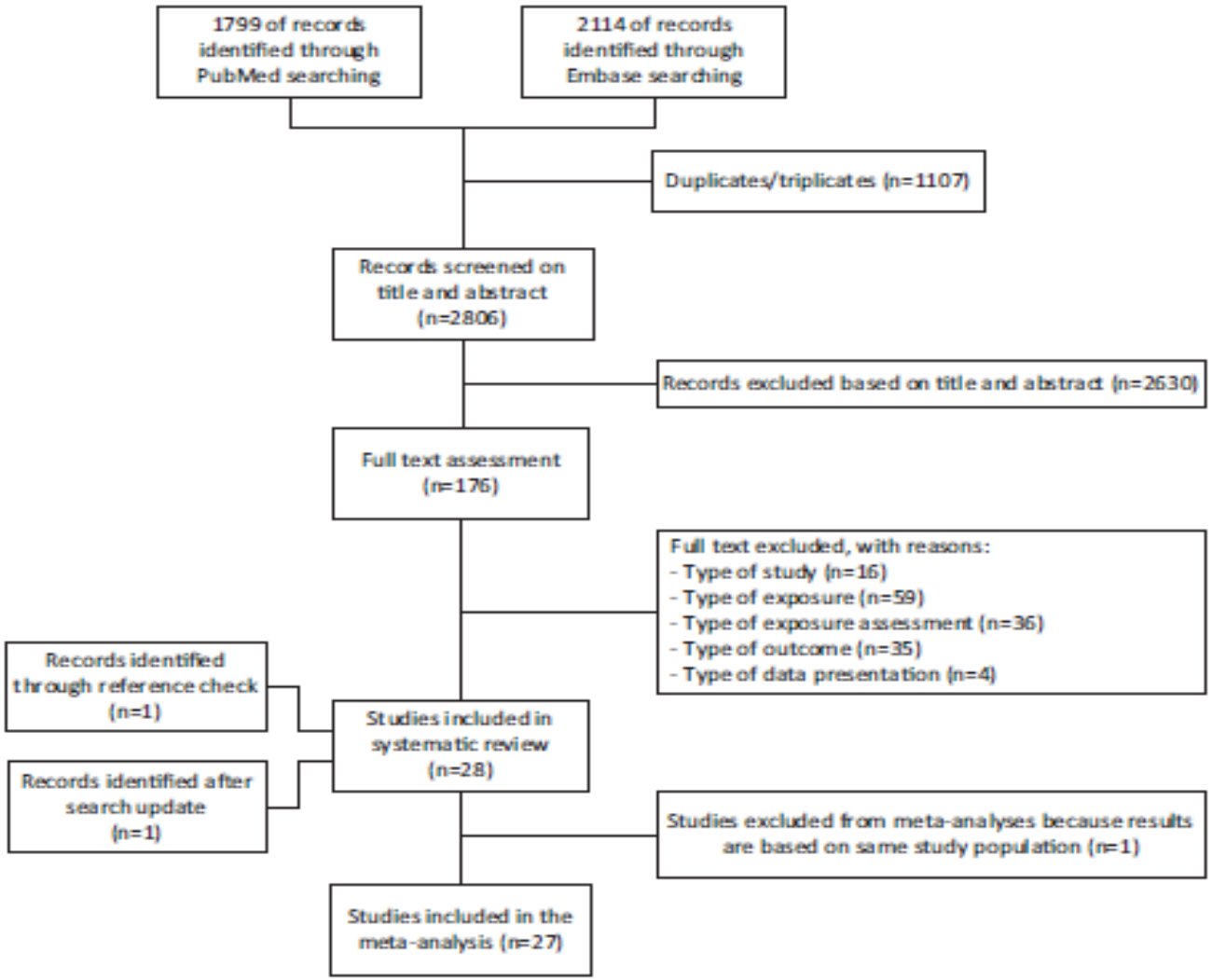
STUDY QUESTION: Is there an association between maternal occupational exposure to solvents, pesticides and metals as assessed by expert-based assessment and congenital anomalies in the offspring?

SUMMARY ANSWER: There is an association between maternal occupational exposure to solvents and congenital anomalies in the offspring, including neural tube defects, congenital heart defects and orofacial clefts.

WHAT IS KNOWN ALREADY: One important environmental risk factor for development of congenital anomalies is maternal occupational exposure to chemicals in the workplace prior to and during pregnancy. A number of studies have assessed the association with often conflicting results, possibly due to different occupational exposure assessing methods.

STUDY DESIGN, SIZE, DURATION: For this systematic review with meta-analysis, the search terms included maternal occupation, exposure, congenital anomalies and offspring. Electronic databases MEDLINE and EMBASE were searched for English studies up to October 2017.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Two reviewers independently screened all citations identified by the search. Case-control studies and cohort studies were included if (I) they reported on the association between maternal occupational exposure to solvents, pesticides or metals and congenital anomalies, and (II) assessment of occupational exposure was performed by experts. Data on study characteristics, confounders and odds ratios (ORs) were extracted from the included studies for four subgroups of congenital anomalies. Methodological quality was assessed using the Newcastle-Ottawa Scale. In the meta-analysis, random effects models were used to pool estimates.


1799 of records identified through PubMed searching
2114 of records identified through Embase searching
Duplicates/triplicates (n=1107)
Records screened on title and abstract (n=2806)
Records excluded based on title and abstract (n=2630)
Full text assessment (n=176)
Full text excluded, with reasons:
- Type of study (n=16)
- Type of exposure (n=59)
- Type of exposure assessment (n=36)
- Type of outcome (n=35)
- Type of data presentation (n=4)
Records identified through reference check (n=1)
Records identified after search update (n=1)
Studies included in systematic review (n=28)
Studies excluded from meta-analyses because results are based on same study population (n=1)
Studies included in the meta-analysis (n=27)

Congenital anomaly	Maternal occupational exposure	Studies	Exposed/total cases	Exposed/total controls	Pooled OR	95% CI	Heterogeneity (%)
Neural tube defects							
	Solvents	4	124/888	419/4145	**1.51**	**1.09–2.09**	35
	Glycol ethers	2	29/110	142/882	**1.93**	**1.17–3.18**	0
	Pesticides	4*	183/1097	918/3734	0.93	0.76–1.15	0
	Metals	2	12/458	18/539	NA	NA	82
Congenital heart defects							
	Solvents	6	185/2526	848/6744	**1.31**	**1.06–1.63**	0
	Glycol ethers	2	61/291	142/882	1.63	0.94–2.84	18
	Pesticides	5*	1088/4742	970/4477	0.81	0.54–1.21	38
	Metals	3	27/1185	48/1595	1.83	0.65–5.20	49.8
Orofacial clefts							
	Solvents	7*	354/1854	2111/11 120	NA	NA	65
	Glycol ethers	3	91/256	183/1037	**1.95**	**1.38–2.75**	0
	Pesticides	2	39/644	131/4773	NA	NA	57
	Metals	2	15/487	89/5107	1.62	0.91–2.86	0

Cleft lip with or without cleft palate							
	Solvents	5	198/866	1532/8371	**1.35**	**1.10–1.66**	8
	Glycol ethers	3	61/167	183/1037	**1.95**	**1.38–2.75**	0
	Pesticides	2	30/449	131/4773	1.30	0.84–2.01	0
	Metals	2	9/327	89/5107	1.45	0.70–3.01	0
Cleft palate							
	Solvents	5	142/966	1532/8371	1.25	0.94–1.65	26
	Glycol ethers	3*	30/89	183/1037	**1.85**	**1.10–3.09**	0
	Pesticides	2	9/195	131/4773	NA	NA	70
	Metals	2	6/160	89/5107	2.06	0.63–6.75	26
Hypospadias							
	Solvents	1	7/300	5/302	**3.63**[a]	**1.94–7.17**	
	Pesticides	7	227/5748	1190/82 120	0.97	0.75–1.24	24
	Metals	4	89/4870	1303/79 939	NA	NA	67

Glycol ethers

- A group of solvents based on alkyl *ethers* of ethylene *glycol* or propylene *glycol* commonly used in **paints and cleaners**

- Maternal occupational exposure to solvents :

  - Neural tube defects
  - Congenital heart anomalies
  - Orofacial clefts

Environ Res. 2014 Jan;128:9-14. doi: 10.1016/j.envres.2013.11.002. Epub 2013 Dec 17.

Congenital anomalies among live births in a high environmental risk area--a case-control study in Brindisi (southern Italy).

Gianicolo EA[1], Mangia C[2], Cervino M[3], Bruni A[4], Andreassi MG[5], Latini G[6].

⊕ Author information

Abstract

Maternal exposure to ambient pollution has been increasingly linked to the risk of congenital anomalies (CAs) in the fetus and newborns. Recently, a descriptive study in the high environmental risk city of Brindisi (Italy) revealed an increased prevalence of total CAs, especially congenital heart disease (CHD) and ventricular septal defects (VSDs), both at the local level and in comparison with the pool of EUROCAT registries. This paper concerns a population-based case control study to investigate the association between maternal exposure to air pollutants - sulfur dioxide (SO2) and total suspended particulate (TSP) matter - and the risk of CA. Cases were newborns up to 28 days of age, born to mothers resident in Brindisi between 2001 and 2010, and discharged with a diagnosis of CA. Cases and controls were individually matched according to sex, socio-economic status of the census area of residence of the mother, and year of beginning of pregnancy. Up to four controls were extracted for each case. Concentration data from monitoring stations were used to estimate air pollution exposure. Each case and control was assigned pollutant concentration values as mean and 90th percentile of the daily average values during weeks 3-8 of pregnancy. Exposure as both continuous and categorical variables was considered and a conditional logistic regression model was constructed to quantify the odds ratios of exposure to air pollutants and the occurrence of total CAs, CHDs and VSDs. We found exposure to the 90th percentile of SO2 to be associated with CHDs (p for trend =0.01) and VSDs (p for trend <0.05). Findings for TSP were less consistent. In conclusion, in the studied area, maternal exposure to sulfur dioxide increased risk of CHD.

- Power plants and a port in the city of Brindisi (Apulia Region, Southern Italy) reported a higher prevalence rate of total CAs, in particular of CHD

Brindisi (Italy)	Ecological LB	8,503 live births 194 cases (2001-2010)	RR: 1.42 (1.07-1.89) RR: 2.68 (1.33-5.33) RR: 1.80 (1.34-2.41) RR: 1.49 (1.20-1.85) ***vs.* outlying municipalities** aOR: 1.85 (1.36-2.50)	CAs PVS VSD CHD CHD		Maternal age, deprivation index

MINES

- Seepage of many metals into the groundwater via coal mining activities

Congenital anomaly	Maternal occupational exposure	Studies	Exposed/total cases	Exposed/total controls	Pooled OR	95% CI	Heterogeneity (%)
Neural tube defects							
	Solvents	4	124/888	419/4145	**1.51**	**1.09–2.09**	35
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Congenital heart defects							
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	Pesticides	5*	1088/4742	970/4477	0.81	0.54–1.21	38
	Metals	3	27/1185	48/1595	1.83	0.65–5.20	49.8
Orofacial clefts							
	Solvents	7*	354/1854	2111/11 120	NA	NA	65
	Glycol ethers	3*	91/256	183/1037	**1.95**	**1.38–2.75**	0
	Pesticides	2	39/644	131/4773	NA	NA	57
	Metals	2	15/487	89/5107	1.62	0.91–2.86	0

Cleft lip with or without cleft palate							
	Solvents	5	198/866	1532/8371	**1.35**	**1.10–1.66**	8
	Glycol ethers	3	61/167	183/1037	**1.95**	**1.38–2.75**	0
	Pesticides	2	30/449	131/4773	1.30	0.84–2.01	0
	Metals	2	9/327	89/5107	1.45	0.70–3.01	0
Cleft palate							
	Solvents	5	142/966	1532/8371	1.25	0.94–1.65	26
	Glycol ethers	3[c]	30/89	183/1037	**1.85**	**1.10–3.09**	0
	Pesticides	2	9/195	131/4773	NA	NA	70
	Metals	2	6/160	89/5107	2.06	0.63–6.75	26
Hypospadias							
	Solvents	1	7/300	5/302	**3.63**[a]	**1.94–7.17**	
	Pesticides	7	227/5748	1190/82 120	0.97	0.75–1.24	24
	Metals	4	89/4870	1303/79 939	NA	NA	67

heavy metal

- Mercury
- Cadmium
- Arsenic
- Chromium
- Thallium
- Lead

Landfills

- Evidence on associations between both total CA and selected subtypes, such as CHDs, NTDs, hypospadias, and skin disorders, and the maternal residential proximity to industrial or hazardous waste landfill sites ***are still to be considered limited***

- **CONCLUSIONS:**

In a review of 7 published studies conducted between 1998 and 2010(2014) :

- ✓ The current evidence-base is inconclusive
- ✓ Often limited by problems of exposure assessment
- ✓ Confounding
- ✓ lack of statistical power with variability in study design and outcomes

- For emissions of dioxins :

Slight associations for urogenital system and CNS defects

SOCIOECONOMIC STATUS

- Evidence of associations between SES and CAs are **still limited**
- The evidence of an association with socioeconomic factors was inadequate due to an insufficient number of studies selected during the period under consideration
- Findings suggest that the risk of CAs increases in the most disadvantaged classes

Am J Public Health. 2015 Dec;105(12):2518-25. doi: 10.2105/AJPH.2015.302804. Epub 2015 Oct 15.

Neighborhood-Based Socioeconomic Position and Risk of Oral Clefts Among Offspring.

Lupo PJ[1], Danysh HE[1], Symanski E[1], Langlois PH[1], Cai Y[1], Swartz MD[1].

Author information

Abstract

OBJECTIVES: We determined the association between maternal neighborhood socioeconomic position (SEP) and the risk of cleft lip with or without cleft palate (CL±P) or cleft palate alone (CP) in offspring.

METHODS: We obtained information on CL±P (n = 2555) and CP (n = 1112) cases and unaffected controls (n = 14 735) among infants delivered during 1999 to 2008 from the Texas Birth Defects Registry. Neighborhood SEP variables, drawn from the 2000 US Census, included census tract-level poverty, education, unemployment, occupation, housing, and crowding, from which we created a composite neighborhood deprivation index (NDI). We used mixed-effects logistic regression to evaluate neighborhood SEP and oral clefts.

RESULTS: Mothers with CL±P-affected offspring were more likely to live in high-NDI (adverse) areas than mothers with unaffected offspring (odds ratio [OR] = 1.20, 95% confidence interval [CI] = 1.05, 1.37). This association was strongest among Hispanic mothers (OR = 1.32, 95% CI = 1.07, 1.62). No associations were observed with CP.

CONCLUSIONS: Using data from one of the world's largest active surveillance birth defects registries, we found that adverse neighborhood SEP is modestly associated with CL±P, especially among Hispanics. These findings may have important implications for health disparities prevention.

PMID: 26469673 PMCID: PMC4638238 DOI: 10.2105/AJPH.2015.302804

Texas (USA)	Case-control LB	3,367 cases 14,735 controls (1999-2008)	aOR 1.20 (1.05-1.37) aOR: 1.32 (1.07-1.62) aOR: 0.95 (0.64-1.42)	Hispanics	CL±CP CL±CP CP	Newborn's year of birth, gender of newborn, mother's age, smoking, education level	Lupo 2015

Soc Sci Med. 2011 Feb;72(4):625-33. doi: 10.1016/j.socscimed.2010.11.025. Epub 2010 Dec 10.

Socioeconomic context and gastroschisis: exploring associations at various geographic scales.

Root ED[1], Meyer RE, Emch M.

Author information

Abstract

This study examines associations between area-level socioeconomic factors and the birth defect gastroschisis in order to further our understanding of the etiology of this condition. Specifically, this study explores how measuring socioeconomic conditions at different geographic scales affect the results of statistical models. A population-based case-control study of resident live births was conducted using data from the North Carolina Birth Defect Monitoring Program and the North Carolina composite linked birth files from 1998 through 2004. Neighborhood conditions potentially related to gastroschisis (poverty, unemployment, education, and racial composition) were measured using Census 2000 data and aggregated to several geographic scales. The Brown-Forsythe test of homogeneity of variance was used to select the neighborhood size by examining the effect of neighborhood size on variation in gastroschisis rates. To examine our assumptions about neighborhood size and neighborhood effects on gastroschisis, we estimated a series of logistic regression and multilevel logistic regression models. The Brown-Forsythe test suggested an optimal neighborhood size with a circular radius of approximately 2500 m, which was supported by the statistical analysis. Results indicate a weak association between living in a neighborhood characterized by high poverty and unemployment and an elevated risk of a gastroschisis-affected pregnancy after adjusting for individual-level risk factors. Cross-level interactions indicate that women in low poverty neighborhoods who do not rely on Medicaid have a significantly lower risk of gastroschisis. The choice of neighborhood scale influences model results suggesting that socioeconomic processes may influence health outcomes variably at different scales.

PMID: 21216059 DOI: 10.1016/j.socscimed.2010.11.025

North Carolina (USA)	Case-control LB	264 cases 12,488 controls (1998-2004)	aOR: 1.85 (1.19-2.83) 3rd quartiles of poverty aOR: 1.89 (1.25-2.94) 2nd and 3rd quartiles of unemployment	Gastroschisis Gastroschisis	Mother's age, marital status, race/ethnicity, smoking, parity, Medicaid status	Root 2011

AIR POLLUTION

- Maternal residence ranged from a minimum of 10 km to a maximum of 50 km
- **Single association between exposure to NO_2 and CoA**
- **No association between exposure to air pollutants and the risk of oro-facial clefts**

Int J Environ Res Public Health. 2014 Jul 31;11(8):7642-68. doi: 10.3390/ijerph110807642.

Effects of air pollution on the risk of congenital anomalies: a systematic review and meta-analysis.

Chen EK[1], Zmirou-Navier D[2], Padilla C[3], Deguen S[4].

Author information

Abstract

Congenital anomalies are the main causes of preterm and neonatal mortality and morbidity. We investigated the association between congenital anomalies and mothers' exposure to air pollution during pregnancy by combining risk estimates for a variety of air pollutants (SO2, NO2, PM10, PM2.5, CO and O3) and anomaly defect outcomes. Seventeen articles were included in the systematic review and thirteen studies were taken into account in the meta-analysis. Combined estimated were calculated separately according to whether the exposure metric was continuous or categorical. Only one significant combination was; NO2 concentrations were significantly associated with coarctation of the aorta (OR = 1.20 per 10 ppb, 95% CI, (1.02, 1.41)). This finding could stem from strong heterogeneity in study designs. Improved exposure assessment methods, in particular more accurate spatial measurements or modeling, standardized definition of cases and of better control of confounders are highly recommended for future congenital anomalies research in this area.

PMID: 25089772 PMCID: PMC4143824 DOI: 10.3390/ijerph110807642

USA (No. 13) Europe (No. 2) Taiwan (No. 1) Australia (No. 1)	Systematic review and metanalysis: • case-control (No. 15) • cohort (No. 2)	17 studies (2005-2013)	OR pooled: 1.08 (0.94-1.24) OR pooled: 0.92 (0.76-1.14) OR pooled: 1.04 (0.80-1.35) OR pooled: 1.17 (0.98-1.41) OR pooled: 1.06 (0.89-1.27) aOR pooled: 1.20 (1.02-1.41)	CL CL CL CL CL CoA	PM_{10}: high vs. low quartile NO_2: high vs. low quartile CO: high vs. low quartile O_3: high vs. low quartile NO_2/10 ppb NO_2/10 ppb	Mother's age, smoking, season of conception, folic acid intake, SES, alcohol consumption, marital status, sex of newborn, newborn's year of birth	Chen 2014

Environ Health Perspect. 2011 May;119(5):598-606. doi: 10.1289/ehp.1002946. Epub 2010 Dec 3.

Ambient air pollution and risk of congenital anomalies: a systematic review and meta-analysis.

Vrijheid M[1], Martinez D, Manzanares S, Dadvand P, Schembari A, Rankin J, Nieuwenhuijsen M.

Author information

Erratum in
Environ Health Perspect. 2011 Aug;119(8):A335.

Abstract

OBJECTIVE: We systematically reviewed epidemiologic studies on ambient air pollution and congenital anomalies and conducted meta-analyses for a number of air pollutant-anomaly combinations.

DATA SOURCES AND EXTRACTION: From bibliographic searches we extracted 10 original epidemiologic studies that examined the association between congenital anomaly risk and concentrations of air pollutants. Meta-analyses were conducted if at least four studies published risk estimates for the same pollutant and anomaly group. Summary risk estimates were calculated for a) risk at high versus low exposure level in each study and b) risk per unit increase in continuous pollutant concentration.

DATA SYNTHESIS: Each individual study reported statistically significantly increased risks for some combinations of air pollutants and congenital anomalies, among many combinations tested. In meta-analyses, nitrogen dioxide (NO_2) and sulfur dioxide (SO_2) exposures were related to increases in risk of coarctation of the aorta [odds ratio (OR) per 10 ppb NO_2 = 1.17; 95% confidence interval (CI), 1.00-1.36; OR per 1 ppb SO_2 = 1.07; 95% CI, 1.01-1.13] and tetralogy of Fallot (OR per 10 ppb NO_2 = 1.20; 95% CI, 1.02-1.42; OR per 1 ppb SO_2 = 1.03; 95% CI, 1.01-1.05), and PM_{10} (particulate matter ≤ 10 μm) exposure was related to an increased risk of atrial septal defects (OR per 10 μg/m³ = 1.14; 95% CI, 1.01-1.28). Meta-analyses found no statistically significant increase in risk of other cardiac anomalies and oral clefts.

CONCLUSIONS: We found some evidence for an effect of ambient air pollutants on congenital cardiac anomaly risk. Improvements in the areas of exposure assessment, outcome harmonization, assessment of other congenital anomalies, and mechanistic knowledge are needed to advance this field.

PMID: 21131253 PMCID: PMC3094408 DOI: 10.1289/ehp.1002946

- Slight increased risk of CoA and ToF with exposure to NO_2
- An increased risk of ASDs with exposure to PM_{10}
- Weak associations between CoA and ToF with SO_2

USA (No. 3) Europe (No. 4) Australia (No. 1)	Systematic review and metanalysis: • case-control (No. 6) • cohort (No. 2)	8 studies (2001-2011)	aOR pooled: 1.20 (1.02-1.44) aOR pooled: 1.17 (1.00-1.36) aOR pooled: 1.14 (1.01-1.28) aOR pooled: 1.07 (1.01-1.13) aOR pooled: 1.03 (1.01-1.05)	ToF CoA ASD CoA ToF	NO_2/10 ppb NO_2/10 ppb PM_{10}/10 µg/m^3 SO_2/1 ppb SO_2/1 ppb	Mother's age, smoking, season of conception, folic acid intake, marital status, SES, newborn's year of birth	Vrijheid 2011

- Most of these analytical epidemiological studies have focused on cardiac and oral cleft birth defects; **for cardiac defects, only a slight association was detected, for oral cleft defects no evidence was identified**

Beauty products

J Neurooncol. 2005 Apr;72(2):133-47.

Beauty product-related exposures and childhood brain tumors in seven countries: results from the SEARCH International Brain Tumor Study.

Efird JT[1], Holly EA, Cordier S, Mueller BA, Lubin F, Filippini G, Peris-Bonet R, McCredie M, Arslan A, Bracci P, Preston-Martin S.

Author information

Abstract

Data from 1218 cases of childhood brain tumors (CBT) diagnosed between 1976 and 1994 and 2223 matched controls from the general population were included in an analysis of maternal beauty product exposure and beauty-related employment in 9 centers in 7 countries. A 50% increased odds ratio (OR) [95% confidence interval (CI) = 1.0-2.1] for CBT was observed among children of mothers who were exposed via personal use of and/or possible ambient contact with beauty products during the 5 years preceding the index child's birth compared with children of mothers never exposed to beauty products during this time period. Overall maternal personal use of hair-coloring agents in the month before or during the pregnancy of the index child's birth was not associated with CBT (OR = 1.0, CI = 0.83-1.3) or with astroglial (OR = 1.1, CI = 0.85-1.4), PNET (OR = 1.0, CI = 0.71-1.5) and other glial subtypes (OR = 1.0, CI = 0.62-1.0). Similarly, no statistically increased ORs or discernable pattern of risk estimates were observed for period of use or for number of applications per year for maternal personal use of hair-coloring agents overall or by histologic type. Among children born on or after 1980, increased ORs for CBT were associated with maternal non-work-related exposure to any beauty products (OR = 2.6, CI = 1.2-5.9), hair-dyes (OR = 11, CI = 1.2-90), and hair sprays (OR = 3.4, CI = 1.0-11). No overall increased OR for CBT was observed among children of mothers employed in beauty-related jobs during the 5 years preceding the index child's birth compared with those who reported no beauty-related employment. In general, other specific beauty product-related exposures were not associated with increased ORs for CBT. Data from our study provide little evidence of an increased risk for CBT with mothers' exposures to beauty products.

Table 2. Adjusted odds ratios for CBT by maternal exposures to beauty products during the 5 years preceding the index child's birth: SEARCH International Brain Tumor Study, 1976–1994[a]

Maternal exposure to beauty products[b] during the 5 years preceding the index child's birth	Combined birth years		Birth year <1980		Birth year ≥1980	
	Cases/controls	OR [95% CI][c]	Cases/controls	OR [95% CI][c]	Cases/controls	OR [95% CI][c]
Never exposed[d]	1153/2143	1.0 Referent	574/1102	1.0 Referent	579/1041	1.0 Referent
Ever exposured	65/80	1.5 [1.0–2.1]	33/48	1.2 [0.77–2.0]	32/32	1.8 [1.0–2.9]
Work-related[e,g]	37/48	1.5 [0.99–2.4]	22/25	1.8 [1.0–3.3]	15/23	1.2 [0.64–2.4]
Non-work–related[f,g]	28/34	1.3 [0.77–2.2]	11/24	0.66 [0.31–1.4]	17/10	2.6 [1.2–5.9]
Hair dyes	38/47	1.6 [1.0–2.5]	22/28	1.5 [0.86–2.8]	16/19	1.6 [0.81–3.2]
Work-related[e,g]	26/38	1.3 [0.80–2.3]	16/20	1.6 [0.80–3.1]	10/18	1.1 [0.49–2.4]
Non-work-related[f,g]	12/10	2.3 [0.99–5.5]	6/9	1.3 [0.44–3.6]	6/1[h]	11 [1.2–90]
Hair sprays	46/58	1.4 [0.93–2.1]	25/34	1.2 [0.71–2.1]	21/24	1.5 [0.84–2.8]
Work-related[e,g]	29/40	1.4 [0.85–2.3]	17/20	1.6 [0.83–3.2]	12/20	1.1 [0.54–2.3]
Non-work-related[f,g]	17/19	1.3 [0.68–2.6]	8/15	0.70 [0.28–1.7]	9/4[i]	3.4 [1.0–11]
Permanent-wave chemicals	33/47	1.3 [0.81–2.0][j]	16/22	1.3 [0.69–2.6]	17/25	1.2 [0.64–2.3]
Work-related[e,g]	23/36	1.2 [0.71–2.1]	14/17	1.6 [0.76–3.3]	9/19	0.90 [0.40–2.0]
Non-work-related[f,g]	10/13	1.2 [0.52–2.8]	2/6	0.51 [0.10–2.6]	8/7	1.8 [0.64–5.1]

Table 3. Adjusted odds ratios for CBT by maternal exposures to beauty products during the 5 years preceding the index child's birth – Histology: SEARCH International Brain Tumor Study, 1976–1994[a]

Maternal exposure to beauty products[b] during the 5 years preceding the index child's birth	Astroglial		PNET		Other glial	
	Cases/controls	OR [95% CI][c]	Cases/controls	OR [95% CI][c]	Cases/controls	OR [95% CI][c]
Never exposed[d]	587/2143	1.0 Referent	246/2143	1.0 Referent	141/2143	1.0 Referent
Ever exposured	36/80	1.5 [1.0–2.3]	13/80	1.4 [0.75–2.6]	7/80	1.4 [0.61–3.1]
Work-related[e,g]	19/48	1.5 [0.89–2.7]	11/48	2.2 [1.1–4.4]	4/48	1.4 [0.50–4.1]
Non-work-related[f,g]	17/34	1.4 [0.78–2.6]	2/34	0.39 [0.09–1.7]	3/34	1.2 [0.35–4.1]
Hair dyes	18/47	1.5 [0.83–2.6]	9/47	1.9 [0.89–3.9]	6/47	2.2 [0.90–5.3]
Work-related[e,g]	13/38	1.4 [0.71–2.6]	8/38	2.0 [0.90–4.4]	3/38	1.3 [0.38–4.3]
Non-work-related[f,g]	5/10	1.7 [0.55–5.0]	1/10	1.2 [0.14–9.3]	3/10[h]	6.5 [1.6–26]
Hair sprays	21/58	1.2 [0.69–2.0]	12/58	1.8 [0.93–3.4]	7/58	1.9 [0.83–4.3]
Work-related[e,g]	12/40	1.1 [0.55–2.1]	11/40[i]	2.7 [1.3–5.4]	4/40	1.7 [0.60–5.0]
Non-work-related[f,g]	9/19	1.3 [0.56–2.9]	1/19	0.35 [0.05–2.6]	3/19	2.1 [0.59–7.7]
Permanent-wave chemicals	16/47	1.2 [0.66–2.1]	9/47	1.6 [0.77–3.4]	5/47	1.7 [0.65–4.4]
Work-related[e,g]	10/36	1.1 [0.51–2.2]	8/36	2.1 [0.93–4.6]	3/36	1.3 [0.39–4.4]
Non-work-related[f,g]	6/13	1.3 [0.48–3.4]	1/13	0.46 [0.06–3.7]	2/13	2.4 [0.50–12]

Table 4. Adjusted odds ratios for CBT by maternal personal use of hair dyes or coloring agents in the month before or during the pregnancy of the index child's birth: SEARCH International Brain Tumor Study, 1976–1994[a]

Maternal personal use of hair dyes or coloring agents in the month before or during the pregnancy of the index child's birth[b]	Combined birth years		Birth year < 1980		Birth year ≥ 1980	
	Cases/controls	OR [95% CI][c]	Cases/controls	OR [95% CI][c]	Cases/controls	OR [95% CI][c]
Never used[d]	1037/1913	1.0 Referent	510/993	1.0 Referent	527/920	1.0 Referent
Ever used	163/283	1.0 [0.83–1.3]	87/142	1.1 [0.83–1.5]	76/141	0.91 [0.67–1.2]
Applications per year						
1–2	45/97	0.81 [0.56–1.2]	15/39	0.90 [0.39–1.3]	30/58	0.86 [0.54–1.4]
3–6	63/93	1.2 [0.86–1.7]	39/49	1.5 [0.95–1.1]	24/44	0.92 [0.55–1.5]
>6	55/93	1.1 [0.75–1.5]	33/54	1.1 [0.68–1.7]	22/39	0.99 [0.58–1.7]
Period of use						
Month before pregnancy	107/170	1.1 [0.87–1.5]	65/91	1.3 [0.93–1.9]	42/79	0.91 [0.61–1.4]
1st trimester	113/198	1.0 [0.80–1.3]	73/107	1.2 [0.88–1.7]	40/91	0.77 [0.52–1.1]
2nd trimester	116/196	1.0 [0.81–1.3]	73/101	1.3 [0.93–1.8]	43/95	0.77 [0.52–1.1]
3rd trimester	118/191	1.1 [0.87–1.4]	71/102	1.2 [0.89–1.7]	47/89	0.93 [0.63–1.4]
Type of product used						
Temporary (washes out in 1 shampoo)	12/16	1.4 [0.65–3.0]	4/8	1.1 [0.31–3.6]	8/8	1.7 [0.61–4.6]
Semi-permanent (washes out in 6–10 shampoos)	28/42	1.2 [0.73–2.0]	15/18	1.5 [0.73–3.0]	13/24	0.98 [0.49–2.0]
Permanent (leaves a line as it grows in)	129/223	1.0 [0.81–1.3]	69/118	1.1 [0.77–1.5]	60/105	0.96 [0.68–1.4]
Hair darkener (used to blend grey with rest of hair)	7/7	1.8 [0.63–5.3]	4/2	4.5 [0.82–25]	3/5	0.94 [0.22–4.1]

Table 5. Adjusted odds ratios for CBT by maternal personal use of hair dyes or coloring agents in the month before or during the pregnancy of the index child's birth – Histology: SEARCH International Brain Tumor Study, 1976–1994[a]

Maternal personal use of hair dyes or coloring agents in the month before or during the pregnancy of the index child's birth[b]	Astroglial		PNET		Other glial	
	Cases/controls	OR [95% CI][c]	Cases/controls	OR [95% CI][c]	Cases/controls	OR [95% CI][c]
Never used[d]	524/1913	1.0 Referent	219/1913	1.0 Referent	129/1913	1.0 Referent
Ever used	90/283	1.1 [0.85–1.4]	35/283	1.0 [0.71–1.5]	19/283	1.0 [0.62–1.7]
Applications per year						
1–2	21/97	0.77 [0.47–1.3]	15/97	1.2 [0.70–2.2]	4/97	0.59 [0.21–1.6]
3–6	35/93	1.3 [0.89–2.0]	11/93	0.99 [0.51–1.9]	6/93	1.0 [0.42–2.4]
>6	34/93	1.3 [0.84–1.9]	9/93	0.87 [0.43–1.8]	9/93	1.6 [0.78–3.3]
Period of use						
Month before pregnancy	60/170	1.2 [0.91–1.7]	19/170	0.97 [0.59–1.6]	13/170	1.3 [0.71–2.4]
1st trimester	62/198	1.1 [0.81–1.5]	26/198	1.2 [0.74–1.8]	13/198	1.1 [0.58–1.9]
2nd trimester	69/196	1.2 [0.89–1.6]	20/196	0.87 [0.66–1.2]	15/196	1.2 [0.66–2.1]
3rd trimester	69/191	1.3 [0.95–1.7]	20/191	0.90 [0.55–1.5]	13/191	1.1 [0.60–2.0]
Type of product used						
Temporary (washes out in 1 shampoo)	7/16	1.7 [0.69–4.3]	4/16	2.1 [0.67–6.5]	1/16	0.84 [0.11–6.6]
Semi-permanent (washes out in 6–10 shampoos)	19/42	1.7 [0.96–3.0]	3/42	0.67 [0.20–2.2]	3/42	1.0 [0.31–3.5]
Permanent (leaves a line as it grows in)	71/223	1.1 [0.82–1.5]	28/223	1.0 [0.68–1.6]	14/223	1.0 [0.56–1.8]
Hair darkener (used to blend grey with rest of hair)	5/7	2.7 [0.85–8.8]	0/7	–	1/7	2.0 [0.22–17]