

Table 2.8.1: Cohort studies on relationship of endocrine disruptors with hypospadias

Region and subjects	Number of subjects	Follow-up period	Compound	Relative risk	Confounders considered
Mau, 1981					
Germany Course of Pregnancy and Child Development Women treated/not treated with progesterone preparations during gestation in 1965-72	7625 (556 exposed, 3043 unexposed)	Until delivery	Hormone preparations used during gestation (prevention of miscarriage, pregnancy test)	1.75 (0.5-4.4)	Drug use, medical history, smoking and drinking habits, caffeine intake (coffee, etc.), chemical exposure
Shapiro, 1982					
U.S. Collaborative Perinatal Project Pregnant women who used/did not use transvaginal contraceptive in 1958-65	50,282 (462 exposed/ 49,820 unexposed)	Until delivery	nonoxynol octoxynol	0.6(0-3.4)	Number of visits after delivery, mother's age, week of pregnancy, newborn body weight, times of pregnancy, mother's medical history (diabetes mellitus, etc.), eclampsia, smoking, malformation of siblings
Correy, 1991					
Tasmania, Australia Drug exposure during gestation in 1982-89	56,027		Aspirin	3.5(1.4-8.8)	Drinking, smoking, details on drug use
North, 2000					
U.K. Avon Longitudinal Study of Pregnancy and Childhood Pregnant women expected to deliver in 1991-92	7,928	Until delivery	Vegetarian (vs. omnivorous) Vegetarian (vs. omnivorous + iron preparation)	3.88(1.69-8.92) 4.99(2.10-11.88)	Drinking and smoking habits, times of pregnancy, times of miscarriage or premature birth, contraceptives, age of pregnancy, age of menarche, diet, infection during gestation
Klip, 2002					
Holland Pregnant women participating in OMEGA project	8,934 male infants (205 exposed, 8,729 unexposed)	Until delivery	DES-prevalence ratio	21.3%(95%CI=6.5-70.1)	

Table 2.8.2: Nested case-control study on relationship of endocrine disruptors with hypospadias

Region and subjects (case/control)	Compound and exposure	Odds ratio (95% CI)
Longnecker, 2002 U.S. Case-control study in the Collaborative Perinatal Project cohort Hypospadias patient/control = 166/552	The highest quartile of mother's serum DDE level: 1.2 (0.6-2.4) (The lowest quartile as reference)	

Table 2.8.3: Case-control studies on relationship of endocrine disruptors with hypospadias

Region and subjects (case/control)	Compound and exposure	Odds ratio	(95% CI)
Bjerkedal, 1975 Norway, born in 1967-74 Population-based All malformations/hypospadias/control = 265/10/265		With pill use	Not associated (no numeric data reported)
Källén, 1979 Sweden, born in 1965-77 Population-based (congenital malformations registry, birth registry) Hypospadias/control (combined malformation, with month and place of birth and mother's age matched) = 48/48		With hormone preparation use during gestation	Not associated (no numeric data reported)
Angerpointner, 1984 Bavaria, Germany, born in 1970-79 Hospital-based Hypospadias/control = 515/515		Association of living in rural village with scrotal type Association of farmer's wife with scrotal type	p <0.05 p <0.05
Calzolari, 1986 Emilia-Romagna, Italy, born in 1978-83 Population-based (congenital malformation registry) Case/control (with time of birth matched) = 167/378		Progesterone preparations during gestation Oral contraceptives	1.65 (p <0.05) Not associated (no numeric data reported)
Louik, 1987 U.S., born in 1983-86 Hospital-based Hypospadias/control (other malformations) = 396/3442		Use of transvaginal contraceptives in unspecified period Use of transvaginal contraceptives around time of conception Use of transvaginal contraceptives in the first trimester	1.2 (1.0-1.6) 1.2 (0.8-1.7) 1.2 (0.7-1.7)
Czeizel, 1988 Hungary Population-based (Hungarian Congenital Malformation Registry, Hungarian Case-Control Study Surveillance System for Congenital Malformations) Hypospadias/control = 877/10962		Alyllesterenol use during gestation	p <0.05
Stroll, 1990 Alsace, France, born in 1979-87 Population-based (congenital malformation registry) Hypospadias/control (with time of birth and hospital matched) = 176/176		Oral contraceptives	0.49 (0.20-1.20)

Region and subjects (case/control)	Compound and exposure	Odds ratio	(95% CI)
Källén, 1992 ICBDMS Denmark, Hungary, Sweden: population-based Italy, Mexico, South America, Spain: hospital-based Hypospadias/control (next child without congenital malformation) = 846/846 (born in 1986-89)	19 Use of hormone preparation in 8-16th week of pregnancy Use of progesterone or its derivative in 8-16th week of pregnancy Use of hormone preparation in 8-16th week of pregnancy (Adjusted for threatened miscarriage and premature birth, history of miscarriage or stillbirth, infertility and smoking habit)	2.3(1.2-4.4) 2.3(1.01-5.15) 2.8(1.2-6.9)	
Kristensen, 1997 Norway, born in 1967-91 Population-based (agriculture census, population statistics, birth registry) Congenital malformation/hypospadias/control = 4565/270/188085	Agriculture and stock raising Pesticide spraying with tractor Pesticide spraying with tractor + grain culture	1.00(0.75-1.34) 1.38(0.95-1.99) 1.51(1.00-2.26)	
Weidner, 1998 Denmark, born in 1983-92 Population-based (population registry, patient registry, malformation registry) Hypospadias/control = 1345/23273	Farming and gardening mother Farming mother Gardening mother Farming and gardening father Farming father Gardening father	1.27(0.81-1.99) 1.26(0.68-2.33) 0.85(0.34-2.11) 1.19(0.96-1.49) 1.16(0.88-1.53) 1.47(0.63-3.39)	
Dolk, 1998 EUROHAZACON Study Population-based (around industrial waste landfills) All malformations/hypospadias/control = 806/45/2326	Distance of mother's residence from landfill in all areas studied	1.00	Within 3 km 1.96 (0.98-3.92)
Bianca, 2003 Italy Population-based (malformation registry) Hypospadias/control (all malformations except neural tube defect, cardiac malformation, cleft palate, and kidney and urinary malformations) = 68/211	Father working in oil refinery (exposure to hydrocarbons) Father working in greenhouse (exposure to pesticides)	5.5(1.22-24.7) 2.9(1.01-8.55)	