NCC/IBL aanvraagbon A100372112

Materiaal	Obx	PPN 277368685,830741089	
Titel	American journal of medical genetics		
Deel			
Auteur			
Corporatie			
Jaar/Editie	1999		
Uitgave	Hoboken, NJ Wiley-Liss		
Serie/Sectie			
ISBN/ISSN	1096-8628	ISBN-13	
Plaatscode	830741089 ; MG T 0014 ; ag ; 1983 V14 - 2001 V104		
Jaar	1993-00-00	Datum indienen	14-11-2014 13:36
Volume	47	Datum plaatsing	14-11-2014 13:36
Aflevering	6	Afhandelen voor	
Leenvorm	KOPIE	Datum rappel	28-11-2014
Leveringswijze	E	Aantal rappels	
Coöperatiecode(s)	F	Geplaatst bij	0036/0001
Aanvraagidentificatie		In bezit bij bibliotheek	
Auteur artikel	streissguth		
Artikel	Fetal alcohol syndrome in twins of alcoholic mothers: concor		
Bladzijden	857	PPN artikel	
Bron			
Opmerking	2015-01-08		
Componist			
Artiest			
Bewerker/Samensteller			
Bezetting			
Vorm uitgave			
Moeilijkheidsgraad			
Aanvrager	0036/7001	Bibliotheektype	UKB (U)
Aanvrageridentificatie	MW. S. ROOZEN	Particulier	N
Eindgebruiker	UM217555		
Klant			
Opmerkingen			
Afleveradres post	Mw. S.Roozen Universiteit Maastricht Work & Social Psychologye, Postbus616(UNS40) 6200 MD MAASTRICHT		
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Telefoon			
Opmerking m.b.t. kosten			
		Stuur rekening?	N
Factuuradres	Clearing House		

[1] origineel gestuurd
[2] kopie gestuurd
[3] overige
[4] nog niet aanwezig
[5] niet aanwezig
[6] niet beschikbaar
[7] uitgeleend
[8] wordt niet uitgeleend
[9] bibliografisch onjuist
[0] bij de binder

Aantal eenheden _____

Aanvraagnummer A100372112

American Journal of Medical Genetics 47:857–861 (1993)

Fetal Alcohol Syndrome in Twins of Alcoholic Mothers: Concordance of Diagnosis and IQ

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The effects of teratogens can be modified by genetic differences in fetal susceptibility and resistance. Twins of alcoholic mothers provide a unique opportunity to study this phenomenon with respect to alcohol teratogenesis. Sixteen pairs of twins, 5 MZ and 11 DZ, all heavily exposed to alcohol prenatally, were evaluated. They represented all available twins of alcohol-abusing mothers who were on the patient rolls of the authors. The rate of concordance for diagnosis was 5/5 for MZ and 7/11 for DZ twins. In two DZ pairs, one twin had fetal alcohol syndrome (FAS), while the other had fetal alcohol effects (FAE). In 2 other DZ pairs, one twin had no diagnosis while one had FAE. IQ scores were most similar within pairs of MZ twins and least similar within pairs of DZ twins discordant for diagnosis. Despite equivalent alcohol exposure within twin pairs, alcohol teratogenesis appears to be more uniformly expressed in MZ than in DZ twins. These data are interpreted as reflecting the modulating influence of genes in the expression of the teratogenic effects of alcohol. © 1993 Wiley-Liss, Inc.

KEY WORDS: genetics, teratology, alcoholism, fetal alcohol effects

INTRODUCTION

Genetic modulation of the effects of intra-uterine exposures is a well-recognized tenet of teratology [Wilson, 1977]. Multiple births involving a known teratogen provide a unique opportunity to examine these effects in humans. Alcohol has been clearly established as a human teratogen [Lemoine et al., 1968; Jones et al., 1973; Clarren and Smith, 1978]. Children of alcoholic mothers are diagnosed with fetal alcohol syndrome (FAS) when they have a recognizable pattern of malformation, including growth deficiency, a specific pattern of minor anomalies (particularly of the face), and some evidence of central nervous system (CNS) dysfunction (often borderline to retarded IQ). Children of alcoholic mothers with some of these characteristics but not enough for a full diagnosis are often designated as showing fetal alcohol effects (FAE) [Clarren and Smith, 1978]. Although most patients with FAS are diagnosed as infants or young children, the diagnosis can also be made in adolescence and adulthood, although the physical abnormalities may be less distinctive. Recent research indicates that this disorder has long-term consequences extending into adolescence and adulthood [Streissguth et al., 1991; Lemoine and Lemoine, 1992].

We present clinical data on 16 pairs of twins born to alcohol-abusing mothers from 2 countries, France and the United States. Several single case studies of twins with FAS have been reported [Palmer et al., 1974; Christoffel and Salafsky, 1975; Dehaene et al., 1977; Miller et al., 1981; Crain et al., 1983; Chasnoff, 1985; Riese, 1989; Lesure, 1988].

MATERIALS AND METHODS

This study began in 1981 when the co-authors developed a data collection system for collating information on twins who were registered in their clinical files or who might be referred in the future. Dr. Dehaene directs the Unité de Néonatologie, Centre Hospitalier de Roubaix, serving an area with approximately 6,000 births per year [Dehaene et al., 1991]. Dr. Streissguth directs the Fetal Alcohol Follow-up Project in Seattle, Washington, which involves a large cohort of patients from a variety of sources who have been referred for suspected fetal alcohol effects and seen for diagnostic and psychologic evaluations [Streissguth et al., 1991, 1978a,b, 1985]. All available twins in these 2 patient lists were included in this study if they had a history of maternal alcoholism or alcohol abuse during the target pregnancy. Presence of a diagnosis in the children was not a criterion for inclusion.

Eight pairs of twins came from 2 large industrial cities of Northern France, Roubaix and Tourcoing, where female alcoholism and its consequences to the fetus have been studied for 17 years [Dehaene et al., 1977, 1991, 1981]. Seven of these 8 pairs were ascer-

Received for publication March 4, 1993; revision received June 14, 1993.

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tained as infants or young children in the Unité de Néonatologie and/or the Pouponnière Boucicaut, a residence for the care of infants and young children from families with social or medical problems. One pair was ascertained in adulthood, as parents of infants at the Unité de Néonatologie.

Four pairs of U.S. twins came from an Indian reservation in the Southwestern United States where they were examined as part of a systematic community screening program for children with suspected FAS [May et al., 1983]. The other 4 pairs came from the Seattle area where they had been referred for clinical evaluation and follow-up.

The twins all received a clinical examination (usually at several ages) by a dysmorphologist or pediatrician experienced in diagnosing FAS. The French twins were all diagnosed by Dr. Dehaene, the U.S. twins by the late Dr. D.W. Smith or one of his fellows, namely Drs. J.M. Aase, S.K. Clarren, or J.W. Hanson. Standardized age-appropriate intelligence or mental development tests (see Table I footnote) were administered by clinical psychologists or psychometrists in each country who had no specific diagnostic information beyond what they themselves observed. Data on family environment and past medical history were derived from personal interview, home visits, medical records review, and reports from social agencies and schools. Additionally, the mothers of the French twins received a clinical exam for signs of alcoholism, according to the method of LeGo [1968] and/or a nutritional, alcohol history and beverage consumption questionnaire. Cardiovascular examinations of the French twins were conducted by Dr. C. Dupuis [Dupuis et al., 1978].

Each twin was classified as having the clinical characteristics of fetal alcohol syndrome (FAS), fetal alcohol effects (FAE), or no FAS/FAE according to the criteria of Clarren and Smith [1978]. Zygosity was determined by physical examination of the pair of twins (sex, hair color, eye color, size, and so forth), by determination of the number and characteristics of the placentas when available, by blood grouping, and by family interview regarding the extent to which the twins were confused with each other.

RESULTS

The sample includes 16 pairs of twins, 5 presumed MZ and 11 DZ. They ranged in age from 2 to 30 years at the time of their final examination. Table I presents demographic and outcome data on the 8 French pairs and the 8 U.S. pairs, respectively. The twins are presented in decreasing order of severity according to the effects of alcohol teratogenesis; Twin A is always the first born. The results are presented in terms of the within-pair concordance for diagnosis and the within-pair variability for IQ.

As Table I indicates, all 5 of the presumed MZ twin pairs were concordant for diagnosis. In 2 pairs both twins had FAS, in one pair, both had FAE, and in 2 pairs, both had no diagnosis. By contrast, only 7 of the 11 DZ twin pairs were concordant for diagnosis. Among the DZ twins, there were 2 pairs in which one twin had FAS and the other twin FAE, and there were 2 pairs in which one twin had no diagnosis and the other had FAE. Among the DZ twins concordant for diagnosis, there was one pair of FAS twins where only one twin had cleft lip and palate. This was the only major malformation observed among these 32 patients; the heart defects and other anomalies were generally minor and transitory.

When the within-pair IQ discrepancy was calculated, MZ twins had an average discrepancy of only 5 IQ points, while DZ twins had an average discrepancy of 11 IQ points. DZ twins concordant for diagnosis had an average within-pair IQ discrepancy of 9 points compared with a 13 point discrepancy for DZ twins discordant for diagnosis.

The cohort contains 2 sets of adult twins, one MZ pair and one DZ pair. Both diagnosed as adults, they present a typical contrast. The MZ twins (F4: both female and both FAS) were concordant in size, IQ, adaptive living, and lifestyle at age 30; both had IQ scores in the borderline range, both were in stable marriages with husbands who helped manage the household, and each had 4 children. In contrast, the DZ pair (US6: both males, one with FAE and one with no diagnosis) were extremely discordant in size, IQ, adaptive living, and lifestyle at age 23, although both had IQ scores in the normal range. The twin without a diagnosis managed the financial affairs for his twin brother. The twin with FAE lived a transient lifestyle, unable to maintain steady employment, unable to manage his finances, and without stable friendships. Although these twins ultimately had different environments, these appear to have resulted from their own early individual characteristics, particularly the extreme hyperactivity of the FAE twin during childhood and the ensuing management problems he presented as an adolescent. While the MZ twins manifested a congruent response to alcohol teratogenesis, the DZ twins, discordant for diagnosis, showed a differential expression of alcohol teratogenesis.

DISCUSSION

This study of 16 pairs of twins of alcohol-abusing mothers shows that MZ twins had a higher rate of diagnostic concordance than DZ twins and more comparability of IQ.

Altogether, 10 twin pairs exposed to alcohol in utero have been reported previously: 3 MZ and 7 DZ (a proportion similar to the 5 MZ and 11 DZ twins in the present study). Four of these are only listed [Lesure, 1988] and one [Dehaene et al., 1977] is included in the present sample. The only MZ twins reported in detail [Palmer et al., 1974] were described as almost identical at birth and on follow-up through 22 months. Mental development scores at 14 and 22 months had an intra-twin discrepancy of only 6 points. The twins were both in the mildly retarded range of mental development at 14 months, and in the borderline range at 22 months. Neither twin walked at 22 months, and both remained significantly retarded in motor development. This early report is congruent with the MZ twins in the present study.

Four pairs of DZ twins have been described in detail [Christoffel and Salafsky, 1975; Miller et al., 1981; Crain et al., 1983; Chasnoff, 1985; Riese, 1989]. In these, one twin was always said to be more severely affected

TABLE I. Demographic, Perinatal, Diagnostic and IQ Data†

Patient ID	Race	Maternal age (yrs)	Parity	Gestational age (wks)	Alcohol	Cigarettes (no.)/other drugs	Zygosity	Concordance for diagnosis	Diagnosis	Sex	Birth weight (grams)	Birth length (cm)	Birth head circumference (cm)	Exam age (for IQ)	IQ
F1	W	34	12,13	38	Chronic alcoholic drinking throughout + cirrhosis drunk/delivery	0/0	DZ	+	FAS	F	1,860	44	32.0	9–0	71
									FAS	F	2,430	44	32.5	9–0	70
F2	W	30	4,5	36	Excessive drinker w/o liver pathology LeGo +	0/0	DZ	+	FAS	F	1,950	44	31.5	7–4	54
									FAS	F	2,520	46	33.5	7–4	75
F3	W	28 **	5,6	39	Chronic alcoholic w/cirrhosis, drinking throughout	?/0	DZ	−	FAS	F	2,600	46	34	9–6	75
									FAE	M	2,200	44	31.5	9–6	87
F4	W	28 **	3,4	?	Chronic alcoholic	?/?	MZ	+	FAS	F	?	?	?	30–	73
									FAS	F	?	?	?	30–	72
F5	W	31	4,5	37	Excessive drinker w/o liver pathology LeGo +	0/0	DZ	+	FAE	F	2,220	45	31.5	2–3	95
									FAE	M	1,830	45	31.5	2–3	90
F6	W	27	5,6	29	Excessive drinker w/o liver pathology LeGo +	0/0	MZ	+	FAE	F	1,300	40	27.0	2–1	95
									FAE	F	1,100	39.5	25.5	—	—
F7	W	32	4,5	37	Excessive drinker	10/0	MZ	+	None	M	2,750	48	?	4–8	98
									None	M	1,950	44.5	?	4–8	91
F8	W	20	1,2	36	Moderate drinker LeGo −	0/0	MZ	+	None	F	2,800	?	?	7–3	111
									None	F	2,100	45	31.5	7–3	116
US1	AI	41	5,6	34–35	Chronic alcoholic w/liver pathology	3/0	DZ	+	FAS	M	2,786	?	?	6–7	66
									FAS	M	2,576	?	?	6–7	81
US2	AI	35	6,7	34	Chronic alcoholic drinking throughout	?/?	MZ	+	FAS	M	2,200	?	?	17 mo	No lang.
									FAS	M	2,600	47.0	?	17 mo	No lang.
US3	AI	26	3,4	35	Chronic alcoholic drinking throughout	10/marijuana	DZ	−	FAS	M	1,300	40.6	29.0	7–2	83
									FAE	M	1,760	43.0	30.0	7–2	90
US4	W	36	4,5	33–34	Chronic alcoholic ≥6/10 beers/day	40–60/+librium	DZ	+	FAS	M	2,080	41.5	32.0	2–4	56
									FAS	F	1,700	40.0	30.5	2–4	59
US5	W	32	2,3	36	Chronic alcoholic 8–9 years	+/librium	DZ	−	FAE	M	2,240	44.4	33.0	4–5	96
									None	F	2,557	49.5	32.4	4–5	87
US6	W	34	6,7	39	Chronic alcoholic drinking throughout except last few weeks	50/+ "heart meds"	DZ	−	None	M	2,303	45.7	30.5	23–8	120
									FAE	M	2,415	45.7	31.7	23–8	98
US7	AI	? **	1,2	36	Excessive drinker, died: liver cirrhosis, 5 yrs after birth	?/?	DZ	+	None	F	1,860	40.0	31.5	15–6	84
									None	M	1,530	42.0	?	15–6	79
US8	AI	? **	?,?	?	Alcoholic	0/?	DZ	+	None	F	1,736	43.2	?	16–8	58
									None	M	2,632	47.0	?	17–8	73

† F = French; US = United States; AI = American Indian; ? = unknown; ** = mother deceased. IQ scores derived from age appropriate IQ tests, namely, the Wechsler Adult Intelligence Scale—Revised; the Wechsler Intelligence Scale for Children—Revised; the Stanford Binet Form L–M (for US twins) and the Terman-Merrill Form L (French translation, for French twins). US twins under 2.5 years received MDI scores (Mental Development Index) from the Bayley Scales of Infant Development. French twins under 2.5 years received DQs (Development Quotients) from the Brunet-Lezine Scale.

than the other and numerous phenotypic differences were described. Only one pair [Chasnoff, 1985] was specifically described as being discordant for diagnosis (FAS vs. FAE respectively due to the absence of intrauterine growth deficiency in the twin classified as FAE). Mental development favored the FAE twin, with a 13-point discrepancy at 18 months and a 17-point discrepancy at 4½ years, although both fell within the normal range of IQ at this latter exam. Another pair of DZ twins [Christoffel and Salafsky, 1975] was described as so discrepant that the mild signs of one would not have been detected at delivery without the blatant signs of the other. At 5 years, the twin most severely affected at birth was also the most mentally retarded and hyperactive although both had psychomotor retardation [Miller et al., 1981]. Another DZ twin pair [Crain et al., 1983] was also reported in which the twin who was the most growth deficient and had the smallest head circumference was also the most retarded, although both twins were mentally retarded at age 16. The type and magnitude of the within-pair discrepancy in these DZ twins is congruent with the data in the present study.

A similar twin literature exists for a few other teratogens. Approximately 8 pairs of DZ twins exposed to thalidomide have been reported, of which 4 pairs appear to have been discordant for phocomelia [Pfeiffer and Kosenow, 1962; Mellin and Katzenstein, 1962; Schmidt and Salzano, 1980]. There are two reports of discordant expression in DZ twins exposed to anticonvulsants: DZ twin girls discordant for the fetal hydantoin syndrome [Phelan et al., 1982]; and another set with a within-pair IQ discrepancy of 12 points although both twins had subnormal IQ compared to an unaffected sibling [Loughnan et al., 1973]. DZ twin women prenatally exposed to diethylstilbesterol have also been described with major phenotypic differences in upper genital tract abnormalities who were also functionally discordant for fertility [Claman and Berger, 1990]. These case reports on twins exposed to other teratogens are in keeping with the twin literature on alcohol teratogenesis. All of these authors interpreted their findings as evidence for genetic differences in sensitivity to teratogenic influences.

This descriptive study of 16 pairs of twins born to alcohol-abusing mothers is in keeping with the small previous literature on twins exposed prenatally to alcohol as well as to other teratogens. In fact, this series appears to be among the largest number of twins exposed to any single teratogen who have been so thoroughly studied, physically and psychologically.

Lenz [1966] has suggested that differential malformations in twins exposed to teratogens could reflect differential development of the embryo at the time of exposure. Sulik et al. [1981] have documented the critical importance of timing of 2 acute alcohol doses in producing the FAS face in the mouse embryo. Shepard [1993] has confirmed the generally accepted practice in whole embryo culture of selecting rat embryos to within one to 2 somites of each other in order to obtain consistent teratogenic results. While timing may play an important role, other prenatal physiologic and genetic factors may be involved as well.

Offspring IQ scores have both genetic and environmental components. The environmental components can be either prenatal or postnatal in origin. A recent meta-analysis shows that DZ twins become less similar in IQ scores as they grow older [McCartney et al., 1990]. In the present dataset, this is true for US6, the adult DZ twin pair discordant for diagnosis. Although their IQ scores were very similar as young children, they were 22 points apart as adults. At age 23 years, the twin with FAE had an IQ score 1½ standard deviations below his twin without a diagnosis. The unrelenting early hyperactivity in the FAE twin seemed to create a set of environmental circumstances that were very different from his brother's. While it would be easy to attribute his poor outcome to these postnatal environmental factors, a more likely hypothesis is that both the hyperactivity and the lowered IQ were manifestations of his prenatal alcohol effects.

Genetic modulation of teratogenic expression has been described in experimental studies with inbred mouse strains. Strains with slower maternal ethanol metabolism had more fetal malformations despite a constant dose [Chernoff, 1980]. Strains bred for increased ethanol sensitivity (Long Sleep mice) had more offspring effects at lower levels of exposure than the less sensitive Short Sleep mice [Gilliam et al., 1988]. More recent work with rats and mice has shown genetic modulation of the effect of alcohol on brain weight, even without differences in blood alcohol level [Goodlett et al., 1989]. These authors conclude that genetic factors can strongly influence developmental exposure to alcohol. While some influences are mediated through maternal factors (such as maternal responses to alcohol and alcohol metabolism) others are mediated through the fetal genotype affecting the susceptibility of fetal tissue (e.g., the central nervous system) to alcohol [Goodlett et al., 1989].

The present study is important in showing that not all alcohol exposed offspring are affected and not all functionally disabled offspring of alcoholic mothers carry the physical characteristics of FAS. This is consistent with the basic principles of teratology [Wilson, 1977] and of behavioral teratology [Riley and Vorhees, 1986]. In terms of alcohol teratogenesis, MZ twins appear to be more concordant for diagnosis and more similar in IQ than DZ twins. These data are interpreted as reflecting the modulating influence of genes in the expression of the teratogenic effects of alcohol.

ACKNOWLEDGMENTS

We gratefully acknowledge the assistance of the French clinical team including D. Tonneau, M.F. Van den Dorpe, A. Levin, and A.M. Charles, and the U.S. clinical team, including S.P. Randels, R.N., R.A. LaDue, Ph.D., and the dysmorphologists who established the diagnosis in the U.S. twins: Drs. J.M. Aase, S.K. Clarren, J.W. Hanson, and D.W. Smith. The technical assistance of C.C. Ernst, K. Carson, and P. Swanborn is greatly appreciated, as is the cooperation of Dr. P. May and K. Hymbaugh. This research was funded in part by the U.S. Public Health Service; Indian Health Service, contracts 243880166 and 243890019; the National Institute of Alcohol Abuse and Alcoholism, grant

AA01455-01-16, the Foundations Fund for Research in Psychiatry, and the association prévenir in Roubaix, France. The opinions expressed in this paper are those of the authors, and do not necessarily reflect the views of the Indian Health Service or the USPHS.

REFERENCES

Chasnoff IJ (1985): Fetal alcohol syndrome in twin pregnancy. Acta Genet Med Gemellol (Roma) 34:229–232.

Chernoff GF (1980): The fetal alcohol syndrome in mice: maternal variables. Teratology 22:71–75.

Christoffel KK, Salafsky I (1975): Fetal alcohol syndrome in dizygotic twins. J Pediatr 87:963–967.

Claman P, Berger MJ (1990): Phenotypic differences in upper genital tract abnormalities and reproductive history in dizygotic twins exposed to diethylstilbestrol in utero: a case report. J Reprod Med 35:431–433.

Clarren SK, Smith DW (1978): The fetal alcohol syndrome. N Engl J Med 298:1063–1067.

Crain LS, Fitzmaurice NE, Mondry C (1983): Nail dysplasia and fetal alcohol syndrome: Case report of a heteropaternal sibship. Am J Dis Child 137:1069–1072.

Dehaene P, Crépin G, Delahousse G, Querleu D, Walbaum R, Titran M, Samaille-Villette C (1981): Aspects épidémiologiques du syndrome d'alcoolisme fœtal: 45 observations en 3 ans. Nouv Presse Med 10:2639–2643.

Dehaene P, Samaille-Villette C, Boulanger-Fasquelle P, Subtil D, Delahousse G, Crépin G (1991): Diagnostic et prévalence du syndrome d'alcoolisme fœtal en maternité. Presse Med 20:1002.

Dehaene P, Samaille-Villette C, Samaille P-P, Crépin G, Walbaum R, Deroubaix P, Blanc-Garin A-P (1977): Le syndrome d'alcoolisme fœtal dans le nord de la France. Rev l'Alcoolisme 23:145–158.

Dupuis C, Dehaene P, Deroubaix-Tella A, Blanc-Garin CP, Rey C, Carpentier-Courault C (1978): Les cardiopathies des enfants nés de mère alcoolique. Arch Mal Coeur Vaiss 71:565–572.

Gilliam DM, Kotch LE, Dudek BC, Riley EP (1988): Ethanol teratogenesis in mice selected for differences in alcohol sensitivity. Alcohol 5:513–519.

Goodlett CR, Gilliam DM, Nichols JM, West JR (1989): Genetic influences on brain growth restriction induced by developmental exposure to alcohol. Neurotoxicology 10:321–334.

Jones KL, Smith DW, Ulleland CN, Streissguth AP (1973): Pattern of malformation in offspring of chronic alcoholic mothers. Lancet 1:1267–1271.

LeGo PM (1968): Le dépistage précoce de l'éthylisme. Presse Med 76:579–580.

Lemoine P, Harousseau H, Borteyru J-P, Menuet J-C (1968): Les enfants de parents alcooliques: anomalies observees, a propos de 127 cas. Ouest Med 21:476–482.

Lemoine P, Lemoine Ph (1992): Avenir des enfants de mères alcoöliques (étude de 105 cas retrouvrés à lâge adulte) et quelques constatations d'intérêt prophylactique. Ann Pediatr (Paris) 39:226–235.

Lenz W (1966): Malformations caused by drugs in pregnancy. Am J Dis Child 112:99–106.

Lesure JF (1988): L'embryofétopathie alcoolique à ile de la Réunion: un drame social. Rev Pediatr 24:265–271.

Loughnan PM, Gold H, Vance JC (1973): Phenytoin teratogenicity in man. Lancet 70–72.

May PA, Hymbaugh KJ, Aase JM, Samet JM (1983): Epidemiology of fetal alcohol syndrome among American Indians of the Southwest. Soc Biol 30:374–387.

McCartney K, Harris MJ, Bernieri F (1990): Growing up and growing apart: a developmental meta-analysis of twin studies. Psychol Bull 107:226–237.

Mellin GW, Katzenstein M (1962): The saga of thalidomide: Neuropathy to embryopathy, with case reports of congenital anomalies. N Eng J Med 267:1184–1193, 1238–1244.

Miller M, Israel J, Cuttone J (1981): Fetal alcohol syndrome. J Pediatr Ophthalmol Strabismus 18:6–15.

Palmer RH, Ouelette EM, Warner L, Leichtman SR (1974): Congenital malformations in offspring of a chronic alcoholic mother. Pediatrics 53:490–494.

Pfeiffer RA, Kosenow W (1962): Letter to the editor: Thalidomide and congenital anomalies. Lancet 45–46.

Phelan MC, Pellock JM, Nance WE (1982): Discordant expression of fetal hydantoin syndrome in heteropaternal dizygotic twins. N Engl J Med 307(2):99–101.

Riese ML (1989): Maternal alcohol and pentazocine abuse: neonatal behavior and morphology in an opposite-sex twin pair. Acta Genet Med Gemellol (Roma) 38:49–56.

Riley EP, Vorhees CV (eds) (1986): "Handbook of Behavioral Teratology." New York: Plenum Press.

Schmidt M, Salzano FM (1980): Dissimilar effects of thalidomide in dizygotic twins. Acta Genet Med Gemellol 29:295–297.

Shepard TH (1993): Personal communication.

Streissguth AP, Aase JM, Clarren SK, Randels SP, LaDue RA, Smith DF (1991): Fetal alcohol syndrome in adolescents and adults. JAMA 265:1961–1967.

Streissguth AP, Clarren SK, Jones KL (1985): Natural history of the fetal alcohol syndrome: a ten-year follow-up of eleven patients. Lancet 2:85–91.

Streissguth AP, Herman CS, Smith DW (1978a): Intelligence, behavior, and dysmorphogenesis in the fetal alcohol syndrome: a report on 20 patients. J Pediatr 92:363–367.

Streissguth AP, Herman CS, Smith DW (1978b): Stability of intelligence in the fetal alcohol syndrome: a preliminary report. Alcohol Clin Exp Res 2:165–170.

Sulik KK, Johnson MC, Webb MA (1981): Fetal alcohol syndrome: embryogenesis in a mouse model. Science 214:936–938.

Wilson JG (1977): Current Status of Teratology: General principles and mechanisms derived from animal studies. In Wilson JG, Fraser FC (eds): "Handbook of Teratology, Vol. 1, General Principles and Etiology." London: Plenum Press, pp 47–74.