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Prenatal Alcohol Exposure and Neurodevelopmental Disorders in Children Adopted From Eastern Europe

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Pediatrics 2010;125;e1178; originally published online April 12, 2010;
DOI: 10.1542/peds.2009-0712

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WHAT'S KNOWN ON THIS SUBJECT: Adoption brings environmental improvement over an institutional upbringing in the country of birth. Alcohol is a teratogen that causes a spectrum of malformations and neurologic, cognitive, and behavioral deficits that are fully preventable.

WHAT THIS STUDY ADDS: FASDs were extremely common in a follow-up study of children adopted from eastern Europe. Children with FASDs often (95%) had comorbid neurodevelopmental/cognitive disorders. Familiarity with diagnostic guidelines for FASDs is essential for assessment and treatment.

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KEY WORDS

fetal alcohol syndrome, autism, attention-deficit/hyperactivity disorder, developmental coordination disorder, adopted children, mental retardation, microcephalus, ocular malformations

ABBREVIATIONS

ADHD—attention-deficit/hyperactivity disorder
ARBD—alcohol-related birth defect
ARND—alcohol-related neurodevelopmental disorder
DCD—developmental coordination disorder
DSM-IV—*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*
FAS—fetal alcohol syndrome
FASD—fetal alcohol spectrum disorder
IOM—Institute of Medicine
WISC-III—Wechsler Intelligence Scale for Children, Third Revision
PFAS—partial fetal alcohol syndrome
OFC—occipitofrontal circumference

www.pediatrics.org/cgi/doi/10.1542/peds.2009-0712

doi:10.1542/peds.2009-0712

Accepted for publication Jan 21, 2010

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*

abstract

OBJECTIVES: The purposes of this investigation were to determine the frequencies of and associations between different neurodevelopmental disorders and to study the potential lasting effects of alcohol on children adopted from eastern Europe.

METHODS: In a population-based, prospective, observational, multidisciplinary, cross-sectional, cohort study of 71 children adopted from eastern Europe, children were assessed 5 years after adoption, from pediatric, neuropsychological, and ophthalmologic perspectives.

RESULTS: Fetal alcohol spectrum disorders, that is, fetal alcohol syndrome (FAS), partial FAS, and alcohol-related neurodevelopmental disorders, were identified for 52% of children; FAS was found for 30%, partial FAS for 14%, and alcohol-related neurodevelopmental disorders for 9%. Alcohol-related birth defects were found for 11% of children, all of whom also were diagnosed as having FAS. Mental retardation or significant cognitive impairment was found for 23% of children, autism for 9%, attention-deficit/hyperactivity disorder for 51%, and developmental coordination disorder for 34%.

CONCLUSIONS: Fetal alcohol spectrum disorders and neurodevelopmental disorders were common in this long-term follow-up study of children adopted from orphanages in eastern Europe. Maternal alcohol consumption during pregnancy has long-lasting adverse effects, causing structural, behavioral, and cognitive damage despite a radically improved environment. *Pediatrics* 2010;125:e1178–e1185

Since the 1960s, there has been a steady increase in the number of internationally adopted children. The influx of adoptees from Russia to the United States has increased in the past decade, to ≥25 000 since 2002.[1] To date, >40 000 internationally adopted children have entered Sweden, with most coming from Asia, South America, and Africa; there are now >2500 children from different eastern European countries.

We reported a population-based study from western Sweden that covered background factors, health at arrival into the adoptive family, and health status 5 years later.[2] At arrival, increased rates of various infections, poor nutrition, and developmental delays, as well as a high incidence of congenital malformations, were observed. Alcohol is a teratogen that causes a spectrum of neurologic, cognitive, and behavioral deficits. During the subsequent 5 years, a high rate of abnormal growth and development, suggesting prenatal alcohol effects, was noted. To characterize the physical and mental conditions in detail and to investigate the occurrence of fetal alcohol spectrum disorders (FASDs), we performed an in-depth prospective investigation. The background factors and part of the ophthalmologic evaluation results were presented elsewhere.[2–4] The present report deals with the neurodevelopmental disorders of this group of children, assessed 5 years after adoption.

METHODS

Study Group

Ninety-nine children who were born between 1990 and 1995 in Russia, Poland, Romania, Estonia, or Latvia, were adopted to Sweden in 1993–1997, and live in western Sweden were invited to participate in the study, through all 4 adoption agencies registered in the region. There were 19 parental refusals and 4 nonrespondents, 4 parents allowed only study of records, and 1 child participated only in the ophthalmologic assessment. We were able to contact 13 of the 19 parents who declined participation. In 4 cases, the reason for not participating was frequent contact with other doctors. The remaining 9 parents reported no regular medical contact. There was no difference regarding gender and age between the participants and the nonparticipants.

An assessment procedure was performed after a mean period of 5 years with the adoptive family. Seventy-one children (40 boys and 31 girls), with a mean age of 7.5 years (range: 4.8–10.5 years), were examined. According to the medical charts, low birth weight, defined as ≤2500 g, had been recorded for 41% of subjects ($n = 29$) and probable intrauterine alcohol exposure for 34% ($n = 24$). Alcohol exposure during pregnancy was considered to have been the case if it was stated specifically in the charts or had been reported originally to the adopting parents.

Assessment

The assessment consisted of pediatric, neuropsychological, and ophthalmologic evaluations covering 3 areas, namely, somatic health, growth, and structural development; neuropsychological features; and ophthalmologic features. The investigation was performed on 2 separate days for each of the 71 children.

The pediatric examination included measurements of height, weight, head circumference, reflexes, and muscle tone, tests of fine and gross motor function,[5] standardized assessment of stigmata according to the dysmorphology scoring system described by Hoyme et al,[6] facial photography, and evaluation of the child's attentional, linguistic, and social abilities. Height, weight, and occipitofrontal circumference (OFC) were converted to SD scores. Three primary facial features, namely, palpebral fissure length, upper lip, and philtrum, were assessed independently and were scored by using a ruler and the "lip-philtrum guide."[7] Behavior was evaluated by using structured questionnaires from the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV), criteria for conduct disorder, oppositional-defiant disorder, obsessive-compulsive disorder, and tic disorders.[8] The Asperger Syndrome Screening Questionnaire[9] also was administered.

The psychological examination included the Wechsler Intelligence Scale for Children, Third Revision (WISC-III), with a full IQ test and verbal comprehension and perceptual organization factor scores,[10] and Leiter-Revised tests, consisting of an IQ screen representing total IQ with fluid reasoning, visualization, associative memory, recognition memory, and spatial memory, as well as the Leiter-Revised rating scales (for parents and psychologists).[11] The testing was conducted by the same psychologist (L.S.), who also reported a standardized observational protocol for attention and activity. This protocol was also followed by the ophthalmologist and the pediatrician.

The ophthalmologic examinations included assessment of visual acuity, refraction, ocular motility, and stereo acuity, inspection of the ocular adnexa and anterior and posterior segments of the eye, and photography of the retinal fundus.[3] A history of problems with visual perception was obtained,[12] and assessment of ocular dimensions (ie, axial length and length of the palpebral fissures[13]) was performed.

Microcephaly was defined as values ≤ minus 2 SDs below the reference mean OFC, which is a stricter definition than required by the Institute of Medicine (IOM) of the National Academies

(Washington, DC) for diagnosis of microcephaly in fetal alcohol syndrome (FAS). Mental retardation was defined as IQ scores of ≤70 in 2 standardized psychometric tests (ie, the WISC-III and the Leiter-Revised test). Significant cognitive impairment was defined as performance in <3rd percentile in ≥3 domains of brain function (ie, language, logic, visual perception, memory, motor coordination, and attention). Cognitive dysfunction was defined as IQ scores of 71 to 85, and partial dysfunction was defined as performance in ≤15th percentile in ≥3 domains of brain function. Assessment of attention was based on standardized parental interviews by the pediatrician and the psychologist (Leiter-Revised parental rating scale) and structured observation of the child by a psychologist (Leiter-Revised psychologist rating scale). Attention-deficit/hyperactivity disorder (ADHD) and developmental coordination disorder (DCD) were diagnosed according to DSM-IV criteria, on the basis of information from parents and observations by the pediatrician, psychologist, and ophthalmologist. The diagnosis of autism was accepted if it was reported in records from child psychiatric or habilitation units by experienced clinicians using the DSM-IV criteria.

Fetal Alcohol Spectrum Disorders

Data were gathered for 5 diagnostic domains, namely, alcohol exposure in utero, characteristic facial phenotype, growth deficiency, abnormal brain growth and morphogenesis, and central nervous system dysfunction, and each child was assigned to a FASD diagnostic category according to the clarification of the 1996 IOM criteria.[6] Briefly, the 5 domains are as follows: (1) confirmed prenatal alcohol exposure; (2) ≥2 cardinal facial anomalies, including thin upper lip and smooth philtrum (a score of 4 or 5 with the lip-philtrum guide) and short palpebral fissures (palpebral fissure length of ≤10th percentile); (3) growth retardation, defined as prenatal and/or postnatal height or weight of ≤10th percentile; (4) evidence of deficient brain growth (OFC of ≤10th percentile) or abnormal morphogenesis; and (5) behavioral or cognitive abnormalities characteristic of those associated with prenatal alcohol exposure.

In the present study, diagnosis of FAS, with or without confirmed prenatal alcohol exposure, required criteria 2, 3, and 4. For a diagnosis of partial FAS (PFAS), with or without confirmed alcohol exposure, criterion 2 and 1 of criteria 3, 4, or 5 were required. The diagnosis of alcohol-related birth defects (ARBDs) required criteria 1 (confirmed alcohol exposure) and 2 and ≥1 structural defect involving the heart, skeleton, kidney, and eye. A diagnosis of FAS or PFAS did not exclude ARBDs. The diagnosis of alcohol-related neurodevelopmental disorders (ARNDs) required criteria 1, 4, and/or 5. There are 6 unique diagnostic outcome categories, according to the IOM criteria. With regard to alcohol exposure during pregnancy, a child was considered to have been exposed if the biological mother was reported to abuse or to have abused alcohol and was considered to have had unknown exposure if alcohol exposure was not disconfirmed. In 2 cases, alcohol exposure was denied in the preadoption records.

Statistical Analyses

Statistical analyses were performed by using StatView 5.0.1 (SAS Institute, Cary, NC). Frequencies, means, SDs, SD scores, medians, and ranges were calculated for descriptive purposes. Median scores were compared by using the Mann-Whitney *U* test.

Ethical Approval

This study was approved by the ethics committee at the Medical Faculty of Sahlgrenska Academy at Gothenburg University (Gothenburg, Sweden). Informed consent was obtained from the parents of all children participating in the study.

RESULTS

Fetal Alcohol Spectrum Disorders

FASDs (ie, FAS, PFAS, and ARNDs), according to proposed revised IOM criteria, were identified for 37 (52%) of the 71 children assessed 5 years after adoption, including 21 boys and 16 girls. Each case is summarized in Table 1. Eight of 12 children with birth defects and FAS had confirmed prenatal alcohol exposure and therefore ARBDs. A clinical synopsis of the findings for each diagnostic category of FASDs is given in Table 2. The neuropsychological, pediatric, and neurobehavioral findings for the children with FAS are shown in Table 3. In the ophthalmologic assessments of the 21 children with FAS, according to the IOM criteria, 19 children (90%) had abnormal ocular and/or visual findings, 13 of whom had subnormal visual acuity and 15 of whom had refractive errors. Nine of the children with FAS had strabismus, 1 child had unilateral ptosis, and 10 children had palpebral fissure lengths below −2 SD. Four adoptees with diagnosed FAS had bilateral optic nerve hypoplasia. Signs of visual perceptual problems were found for 6 of the children with diagnosed FAS.

Growth retardation, facial anomalies, and deficient brain growth were found for 46 (65%), 39 (55%), and 40 (56%) of the 71 children, respectively. The interrelationships with FASDs and diagnosed neurodevelopmental diagnoses are shown in Fig 1.

Neurodevelopmental Disorders

A total of 64 (90%) of the 71 children adopted from eastern Europe and assessed after 5 years were identified as having a neurodevelopmental/behav-

TABLE 1 FASDs in Cohort of 71 Children Adopted From Eastern Europe to Sweden

Patient No.	IAE	FASD	Birth Defects	OFC ≤ minus 2 SDs	Mental Retardation	Cognitive Dysfunction	Autism	ADHD	CD	DCD	OCD	ODD	TD
1	Yes	FAS	Skeletal	Yes	Yes	—	No	Yes	Yes	—	Yes	Yes	No
2	Yes	FAS	No	No	No	Yes	No	No	No	—	No	No	No
3	Yes	FAS	No	Yes	Yes	—	No	Yes	No	—	No	No	Yes
4	Yes	FAS	Skeletal	Yes	No	—	No	Yes	Yes	Yes	No	Yes	No
5	Yes	FAS	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
6	Yes	FAS	Ocular	Yes	Yes	—	No	No	No	—	No	No	No
7	Yes	FAS	Cardiac	Yes	Yes	—	No	Yes	No	—	No	Yes	No
8	Yes	FAS	No	Yes	No	No	No	Yes	No	Yes	No	Yes	No
9	No	FAS	No	No	No	No	No	No	No	No	No	No	No
10	Yes	FAS	No	Yes	No	Yes	No	No	No	No	No	Yes	No
11	No	FAS	No	No	No	No	No	Yes	No	No	No	No	No
12	Yes	FAS	Ocular	Yes	No	No	No	Yes	No	Yes	No	Yes	Yes
13	Yes	FAS	Ocular	Yes	No	Yes	No	Yes	No	Yes	No	No	No
14	No	FAS	No	No	No	No	No	No	No	No	No	No	No
15	No	FAS	No	No	No	No	No	Yes	No	Yes	No	No	No
16	No	FAS	No	Yes	Yes	—	Yes	No	No	—	No	No	Yes
17	Yes	FAS	Cardiac	No	No	Yes	No	No	No	Yes	No	No	No
18	No	FAS	Ocular	Yes	Yes	—	No	Yes	No	Yes	No	No	No
19	Yes	FAS	No	No	Yes	—	Yes	No	No	—	No	No	No
20	No	FAS	No	No	Yes	—	No	Yes	No	—	No	No	No
21	Yes	FAS	Ocular	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
n (%) (*N* = 21)	14 (67)		9 (43)	13 (62)	8 (38)	6 (29)	2 (10)	13 (62)	2 (10)	9 (43)	1 (5)	8 (38)	3 (14)
22	Yes	PFAS	No	No	No	Yes	No	Yes	No	Yes	No	No	No
23	No	PFAS	No	No	No	No	No	Yes	No	Yes	No	Yes	No
24	No	PFAS	No	No	No	No	No	No	No	Yes	No	No	No
25	No	PFAS	Skeletal	No	No	No	No	No	No	No	No	Yes	No
26	Yes	PFAS	No	No	No	Yes	No	No	No	No	No	No	No
27	No	PFAS	No	No	No	Yes	No	No	No	No	No	No	No
28	No	PFAS	No	No	No	No	No	Yes	No	No	No	No	No
29	No	PFAS	Skeletal	No	No	Yes	No	Yes	No	No	No	No	No
30	Yes	PFAS	No	Yes	No	No	No	Yes	No	No	No	Yes	No
31	No	PFAS	Oral	No	No	No	No	Yes	No	No	No	No	No
n (%) (*N* = 10)	3 (30)		3 (30)	1 (10)	0 (0)	4 (40)	0 (0)	6 (60)	0 (0)	3 (30)	0 (0)	3 (30)	0 (0)
32	Yes	ARND	No	No	No	No	No	No	No	No	No	No	No
33	Yes	ARND	No	No	No	Yes	No	No	No	Yes	No	No	No
34	Yes	ARND	No	No	No	No	No	No	No	Yes	No	Yes	No
35	Yes	ARND	No	No	No	No	No	No	No	Yes	No	Yes	Yes
36	Yes	ARND	No	No	No	No	No	Yes	No	No	No	Yes	No
37	Yes	ARND	No	No	No	No	No	Yes	No	Yes	No	Yes	Yes
n (%) (*N* = 6)	6 (100)		0 (0)	0 (0)	0 (0)	1 (17)	0 (0)	2 (33)	0 (0)	4 (67)	0 (0)	4 (67)	2 (33)

A total of 64 (90%) of the 71 children received a neurodevelopmental/behavioral, cognitive, or neurologic diagnosis. Data for each child with a FASD are presented, including information about confirmed alcohol exposure, occurrence of birth defects, OFC ≤ minus 2 SDs, and neurodevelopmental/neurobehavioral comorbidity. Mental retardation excluded cognitive dysfunction and DCD. There were 12 children with FAS or PFAS and birth defects, but only 8 of them had confirmed prenatal alcohol exposure (ie, ARBDs). CD indicates conduct disorder; IAE, intrauterine alcohol exposure; OCD, obsessive-compulsive disorder; ODD, oppositional-defiant disorder; TD, tic disorder; —, mental retardation exclude cognitive dysfunction by definition.

TABLE 2 Findings for Each FASD Diagnostic Category

IOM Diagnosis	Dysmorphology Score, Mean	Height Percentile, Mean	Weight Percentile, Mean	OFC Percentile, Mean	WISC-III Full IQ, Mean	Leiter-Revised Brief IQ Test Score, Mean
FAS (*n* = 21)	16.5	9.5	7.9	0.7	74	83
PFAS (*n* = 10)	10.8	25.4	41.3	32.3	97	89
ARBD (*n* = 8)	18.4	8.8	6.9	0.1	69	82
ARND (*n* = 6)	5.7	28.6	43.2	27.1	85	90
No diagnosis (*n* = 7)	2.4	31.6	49.4	40.2	101	98

A total of 64 (90%) of the 71 children received a neurodevelopmental/behavioral, cognitive, or neurologic diagnosis. A summary of clinical findings for FASDs versus no neurodevelopmental diagnosis for 71 children adopted from eastern Europe to Sweden, at assessment 5 years after adoption, is given. Standardized assessment of stigmata was performed according to the dysmorphology scoring system described by Hoyme et al.[6]

ioral, cognitive, or neurologic diagnosis. ADHD was found for 36 children (51%), mental retardation or significant cognitive impairment for 16 (23%), autism for 6 (9%), and DCD for 24 (34%). Structural birth defects were found for 17 (24%) of the 71 children, microcephaly for 21 children (30%), and epilepsy, cerebral paresis, and myelomeningocele for 1 child each. Comorbidity between neurodevelopmental disorders and FAS is

TABLE 3 Comparison of Findings for 21 Children Adopted From Eastern Europe and Diagnosed as Having FAS and 7 Children Without Diagnoses in Same Cohort

	P
Neuropsychological testing	
Lower WISC-III total IQ	.0011
Lower WISC-III verbal factor	.0638
WISC-III perceptual organization	.0005
Leiter total IQ (brief IQ test)	.0411
Leiter logic	.0147
Leiter visual	.1494
Associative memory	.0314
Leiter recognition	.0054
Leiter spatial	.0015
Pediatric assessment	
Higher neuromotor deficiency score	.0045
More ADHD symptoms	.0015
More emotional lability (Conner)	.0033
More autistic features (ASSQ)	.1445
More symptoms of ODD	.1212

ASSQ indicates Asperger Syndrome Screening Questionnaire; ODD, oppositional-defiant disorder. Median scores were compared by using the Mann-Whitney *U* test.

TABLE 4 Comorbidity of Neurodevelopmental Disorders at Assessment 5 Years After Adoption in Cohort of 71 Children Adopted From Eastern Europe

	n/*N* (%)				
	ADHD	DCD	Mental Retardation	Autism	FAS
ADHD	36/71 (51)	23/24 (96)	11/16 (69)	3/6 (50)	13/21 (62)
DCD	23/36 (64)	24/71 (34)	—	0/6 (0)	9/21 (43)
Mental retardation	11/36 (31)	—	16/71 (23)	5/6 (83)	8/21 (38)
Autism	3/36 (8)	0/24 (0)	5/16 (31)	6/71 (9)	2/21 (10)
FAS	13/36 (62)	9/24 (38)	8/16 (50)	2/6 (33)	21/71 (30)

Mental retardation excluded the diagnosis of DCD and proportion is therefore replaced by dashes.

shown in Table 4. According to the cognitive tests (the Leiter-Revised test and WISC-III), 38 children (54%) had cognitive deficits. The results of the cognitive tests used are shown in Tables 1 and 3.

DISCUSSION

In this study of children adopted from eastern Europe, we found FASDs, including FAS, in 37 children (52%) and FAS, according to the IOM revised diagnostic criteria, in 21 (30%). To the best of our knowledge, these are the highest rates of FAS and FASDs observed in studied populations throughout the world. Current estimates of FAS in the United States are 0.5 to 2 cases per 1000 live births, and those of FASDs are 9 to 10 cases per 1000 live births.[14,15] Prevalence studies of FAS in the general, Western, early school-aged population yielded rates of ~3 to 7 cases per 1000 children.[16,17] Higher rates were reported when different subpopulations were investigated; for instance, screening a foster care population produced a FAS prevalence of 10 to 15 cases per 1000 children,[18] and communities with high levels of alcohol abuse in South Africa yielded a prevalence of FAS or PFAS of 68 to 89 cases per 1000 children.[19] In Russia,

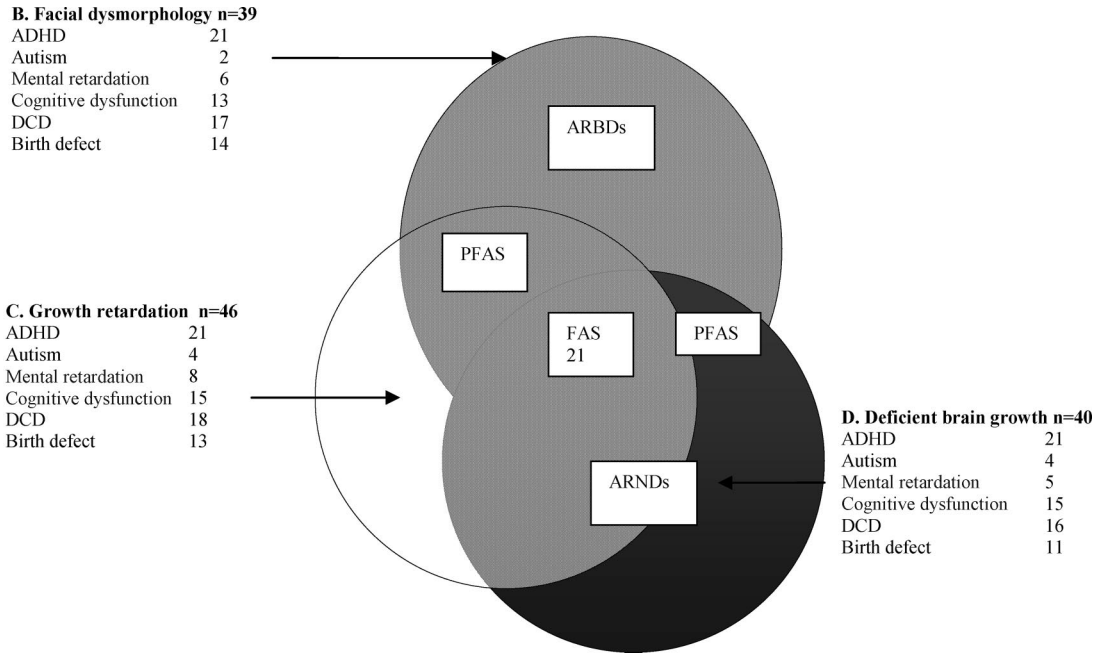

FIGURE 1
Interrelationships of findings. Data were gathered for 5 key diagnostic domains, that is, alcohol exposure, facial dysmorphologic features, growth deficiency, brain growth, and behavioral or cognitive abnormalities. The interrelationships of facial dysmorphologic features, growth deficiency, and brain growth with FASDs are illustrated. Growth retardation, facial anomalies, and deficient brain growth were noted for 46 (65%), 39 (55%), and 40 (56%) of 71 children, respectively. The diagnoses of ARNDs and ARBDs required confirmed alcohol exposure. Eleven (16%) of 71 children exhibited no growth retardation, deficient brain growth, or facial anomalies.

7.9% of the children in studied orphanages in Moscow had FAS.[20]

Our very high frequency of FASDs, with a minimum of 52% affected children, implies an extremely selected population. Even if the total population of adoptees is considered ($N = 99$), that is, 71 subjects who participated in the study, 19 subjects who refused, 4 nonrespondents, and 5 subjects who either allowed only study of their records or participated only in the ophthalmologic examination, and the latter 28 are assumed to be without disorders, this leaves us with a large number of affected children, that is, 37 (37%) of 99 children. This can be explained by a minimum of 24 (34%) of 71 mothers being reported to have abused alcohol during pregnancy, according to available preadoption records, which is in agreement with reported alcohol use by 39% of mothers of institutionalized Russian children. In fact, one main reason for leaving a child in an orphanage is maternal alcohol abuse.[1] Therefore, although it is not mentioned specifically for the other 63% of adoptees, it is likely that a larger proportion of the cohort was exposed to various amounts of alcohol in utero, which provided the conditions for the full, highly prevalent spectrum of alcohol-induced fetal disorders found.

Growth retardation, according to IOM criteria, was present in 65% of the children, deficient brain growth in 56%, and facial dysmorphia in 55%. Facial dysmorphologic features are the result of disturbed neural crest cell migration during organogenesis. Growth disturbances take place mainly during the second and third trimesters and deficient brain growth especially during the brain growth spurt.[21] One implication concerning these critical periods is that, if a pregnant woman has limited or no access to alcohol during weeks 3 and 4, for instance, her child may lack the facial dysmorphologic features but still have serious neurologic damage from later alcohol exposure. The significantly higher neuromotor deficiency scores found for the children with FAS were observed in earlier studies of FAS[22,23] and in a French study in which heavy maternal alcohol consumption (>21 drinks a week) was associated specifically with higher neuromotor deficiency scores.[24] This underscores the significant prenatal alcohol exposure in these adoptees. Table 2 shows the clinical findings across the FASD spectrum, which are almost identical to clinical findings for each diagnostic IOM FASD category based on 164 extensively reviewed cases presented by Hoyme et al,[6] all with known alcohol exposure. This is in accordance with the assumption that the adoptees in this cohort with FASDs had been exposed to alcohol prenatally, although this was not reported specifically in the background material for more than one-third of the children. A study showed that children exposed to street drugs (not alcohol) were equally often diagnosed as having ADHD, compared with the children in this study, but only the subjects with FASDs showed growth restriction combined with cognitive impairments.[25]

Abnormal ocular findings in this cohort of adopted children were found for 78% of children[3] and for 90% of the children who were later diagnosed as having FAS, which is in accordance with earlier reports.[26] In addition, many (25%) of the children (both with FASD diagnoses and otherwise) had major physical anomalies commonly associated with prenatal alcohol exposure (ARBDs), such as optic nerve hypoplasia and cardiac, skeletal, and oral malformations.[2] Visual abnormalities in 153 healthy, prospectively enrolled infants were associated with abnormal neurologic examination results but not with cigarette smoke or cocaine exposure.[27]

The assessment 5 years after adoption showed that 64 children (90%) were diagnosed as having neurologic and/or neurodevelopmental disorders, 51% of whom had ADHD and 54% of whom had cognitive deficits. Mental retardation or significant cognitive impairment was observed for 23%, DCD for 34%, autism for 9%, and microcephaly for 30%. Children diagnosed as having FASDs often (95%) had comorbid neurodevelopmental/cognitive diagnoses, such as cognitive dysfunction, ADHD, DCD, mental retardation, and autism. Only 7 children (10%) did not receive any neurodevelopmental/cognitive diagnosis. This is in accordance with reported findings, according to which ≥1 DSM-IV axis I diagnosis was found for 97% of 12-year-old children with confirmed heavy prenatal alcohol exposure and ADHD for 95%.[28] In long-term follow-up studies of children with FASDs, frequent, persistent, developmental disorders were reported.[29–31] Global cognitive deficits are the primary neurodevelopmental outcome associated with prenatal alcohol exposure,[32] and there also is a clear association with ADHD, which probably is both genetically derived and an effect of brain damage. ADHD in FASDs is more likely to have comorbid conditions,[33] as was found in this study (Tables 1 and 4). The birth defects, anomalies, and growth deviations present in this cohort of children assessed 5 years after adoption are a reminder of the potential teratogenic consequences of prenatal alcohol exposure, despite a later, favorable environment introduced by the adoption.

The IOM criteria emphasize the importance of ruling out differential diagnoses in each case. For instance, syndromes such as Williams, Cornelia de Lange, Noonan, and fetal valproate syndrome have some features in common

with FAS.[34] One child in this study, with encephalopathy and disconfirmed alcohol exposure, might have experienced adverse drug effects, because psychiatric medication was indicated as an explanation for the encephalopathy. Heredity also should be considered, because a high prevalence of neuropsychiatric morbidity in the biological parents can be expected and genetic polymorphism for the genes for the alcohol dehydrogenase enzyme family might affect outcomes.[35,36]

A comparison of the 4-Digit Diagnostic Code (Washington criteria) and the diagnostic guidelines described by Hoyme et al[6] for FASDs emphasized the importance of the specific facial phenotype for linking FAS to alcohol when exposure is unknown.[37] Applying the stricter criteria of the 4-digit system criteria for FAS to findings for the 71 children adopted from eastern Europe yielded 15 cases of FAS ($n = 10$) or PFAS ($n = 5$), compared with 21 cases of FAS and 12 cases of PFAS determined by using the IOM revised criteria. All except 1 of the 15 cases of FAS or PFAS determined according to the Washington criteria were included among the 21 cases determined according to the guidelines described by Hoyme et al.[6] The excluded case was a case of PFAS, according to both diagnostic systems. Use of the required criterion of ≥ 2 facial anomalies, as for the diagnosis of FAS and PFAS, without confirmed alcohol exposure for the ARBD diagnosis would add 5 more cases, of which 2 would fall outside FAS and PFAS. The reported 8 cases of ARBDs in this study (Table 2) were all within the FAS category. The Washington criteria may be more specific, but data from the current study indicate that their application in alcohol-exposed subpopulations misses cases of FASDs.

Only 1 of 8 children in this cohort who were diagnosed as having FAS or PFAS was previously recognized as having a FASD. This implies that familiarity with the revised IOM diagnostic guidelines for FASDs is essential for the careful assessment of children prenatally exposed to alcohol.

CONCLUSIONS

The high prevalence of FASDs in this population underscores the extent of physical and functional damage caused by prenatal alcohol exposure. There is an urgent need for public attention to be drawn to FASDs and for increased efforts to educate individuals, to change drinking behavior (eg, to involve parents in school-based preventive projects), and to counter alcohol marketing, as well as restricting the sale and use of alcohol.

ACKNOWLEDGMENTS

Grants were received from Research and Development of Region Västra Götaland, the Institute of Skaraborg Research Fund at Skaraborg Hospital, W & M Lundgrens Vetenskapsfond II, Allmänna Barnhuset, and the Gothenburg Medical Society.

We thank Dr P. O. Elfstrand and Dr J-E. Simonsson for help with the pediatric examinations, Dr M. Hök Wikstrand for help with the evaluation of facial features, and B. Melander for technical assistance.

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Pediatrics 2010;125;e1178; originally published online April 12, 2010;
DOI: 10.1542/peds.2009-0712