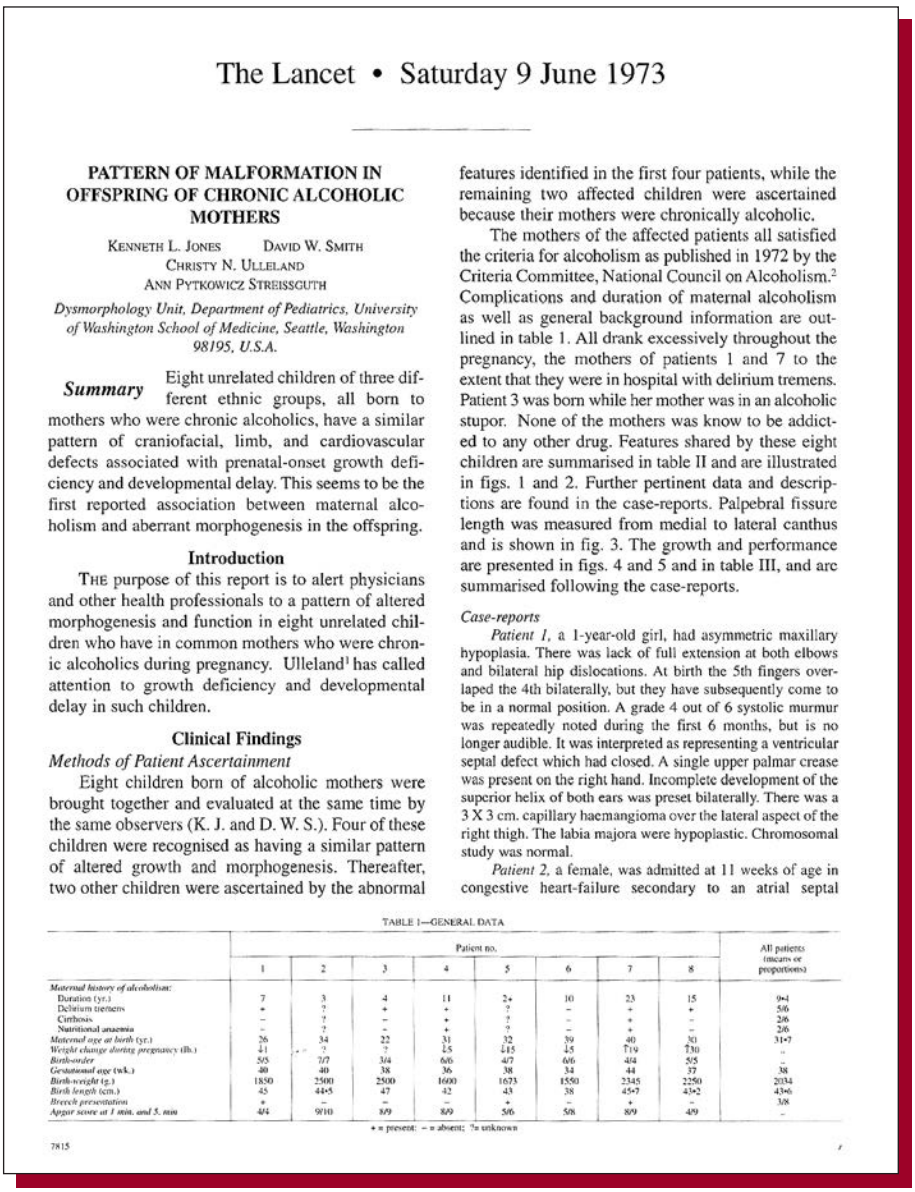

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PATTERN OF MALFORMATION IN OFFSPRING OF CHRONIC ALCOHOLIC MOTHERS

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Summary Eight unrelated children of three different ethnic groups, all born to mothers who were chronic alcoholics, have a similar pattern of craniofacial, limb, and cardiovascular defects associated with prenatal-onset growth deficiency and developmental delay. This seems to be the first reported association between maternal alcoholism and aberrant morphogenesis in the offspring.

Introduction

THE purpose of this report is to alert physicians and other health professionals to a pattern of altered morphogenesis and function in eight unrelated children who have in common mothers who were chronic alcoholics during pregnancy. Ulleland[1] has called attention to growth deficiency and developmental delay in such children.

Clinical Findings

Methods of Patient Ascertainment

Eight children born of alcoholic mothers were brought together and evaluated at the same time by the same observers (K. J. and D. W. S.). Four of these children were recognised as having a similar pattern of altered growth and morphogenesis. Thereafter, two other children were ascertained by the abnormal features identified in the first four patients, while the remaining two affected children were ascertained because their mothers were chronically alcoholic.

The mothers of the affected patients all satisfied the criteria for alcoholism as published in 1972 by the Criteria Committee, National Council on Alcoholism.[2] Complications and duration of maternal alcoholism as well as general background information are outlined in table 1. All drank excessively throughout the pregnancy, the mothers of patients 1 and 7 to the extent that they were in hospital with delirium tremens. Patient 3 was born while her mother was in an alcoholic stupor. None of the mothers was know to be addicted to any other drug. Features shared by these eight children are summarised in table II and are illustrated in figs. 1 and 2. Further pertinent data and descriptions are found in the case-reports. Palpebral fissure length was measured from medial to lateral canthus and is shown in fig. 3. The growth and performance are presented in figs. 4 and 5 and in table III, and are summarised following the case-reports.

Case-reports

Patient 1, a 1-year-old girl, had asymmetric maxillary hypoplasia. There was lack of full extension at both elbows and bilateral hip dislocations. At birth the 5th fingers overlaped the 4th bilaterally, but they have subsequently come to be in a normal position. A grade 4 out of 6 systolic murmur was repeatedly noted during the first 6 months, but is no longer audible. It was interpreted as representing a ventricular septal defect which had closed. A single upper palmar crease was present on the right hand. Incomplete development of the superior helix of both ears was preset bilaterally. There was a 3 X 3 cm. capillary haemangioma over the lateral aspect of the right thigh. The labia majora were hypoplastic. Chromosomal study was normal.

Patient 2, a female, was admitted at 11 weeks of age in congestive heart-failure secondary to an atrial septal

TABLE I—GENERAL DATA

	Patient no.								All patients (means or proportions)
	1	2	3	4	5	6	7	8	
Maternal history of alcoholism:									
Duration (yr.)	7	3	4	11	2+	10	23	15	9·1
Delirium tremens	+	?	+	+	?	–	+	+	5/6
Cirrhosis	–	?	–	+	?	–	+	–	2/6
Nutritional anaemia	–	?	–	+	?	–	+	–	2/6
Maternal age at birth (yr.)	26	34	22	31	32	39	40	30	31·7
Weight change during pregnancy (lb.)	41	?	?	25	415	45	719	730	..
Birth-order	5/5	7/7	3/4	6/6	4/7	6/6	4/4	5/5	..
Gestational age (wk.)	40	40	38	36	38	34	44	37	38
Birth-weight (g.)	1850	2500	2500	1600	1673	1550	2345	2250	2034
Birth length (cm.)	45	44·5	47	42	43	38	45·7	43·2	43·6
Breech presentation	+	–	–	–	+	–	+	–	3/8
Apgar score at 1 min. and 5. min	4/4	9/10	8/9	8/9	5/6	5/8	8/9	4/9	..

+ = present; – = absent; ? = unknown

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Jones, K.L.; Smith, D.W.; Ulleland, C.N.; and Streissguth, A.P. Pattern of malformation in offspring of chronic alcoholic mothers. Lancet *7815:1267–1271, 1973.*

PATTERN OF MALFORMATION IN OFFSPRING OF CHRONIC ALCOHOLIC MOTHERS

Commentary by Carrie L. Randall, Ph.D., and Edward P. Riley, Ph.D.

KEY WORDS: prenatal alcohol exposure; fetal alcohol effects; fetal alcohol syndrome; gestation; congentital anomaly; fetal alcohol development; teratogens

The identification of the characteristics defining fetal alcohol syndrome (FAS) is usually credited to observations made in this Jones and colleagues' 1973 article. Although a previous report in a French medical journal several years earlier recognized a similar pattern (Lemoine 1968), it was Jones and Smith who actually coined the label "fetal alcohol syndrome" in a followup paper to this seminal article by Jones and colleagues, entitled "Recognition of the fetal alcohol syndrome in early infancy" (Jones and Smith 1973).

Historically, it was considered common knowledge that alcohol consumption during pregnancy was hazardous, and women were warned accordingly; around the turn of the century, there were even a few clinical and experimental reports published that outlined negative effects of such consumption. However, the clinical inquisitiveness and astute diagnostic skills of Jones and the rest of the team of physicians at the University of Washington, led by the late Dr. David W. Smith, was the impetus for the work published in this landmark article.

The observed characteristics caused by maternal drinking and reported by Jones and colleagues in the article interested practicing clinicians around the world, stimulating many international case reports that further confirmed these findings. The observations in the article also had a monumental impact on the scientific community. They demonstrated that alcohol ingested by the mother adversely affected fetal growth and development. Thus, as with thalidomide, alcohol was being implicated as a teratogen, or an agent capable of altering normal fetal growth and development, and this was an exciting development.

Since the original identification of FAS in 1973, approximately 600 additional cases have been reported in the alcohol literature. Abel (1990) published a compendium of these cases. Basically, all the cardinal features of FAS described in the 1973 article by Jones and colleagues of low birth weight; small eye openings; joint, limb, and cardiac defects; developmental delays; and mental retardation have withstood the test of time. In addition, some anomalies not initially included in the characteristics they outlined, such as a thin upper lip (narrow vermilion border) and a broad flat area under the nose (long smooth philtrum), are now considered features of FAS.

One area of science inadvertently stimulated by this article was that of behavioral teratology. In an attempt to develop animal models of FAS, researchers found that prenatal alcohol exposure in rats was associated with behavioral anomalies in the absence of gross physical defects. This meant that the brain could be affected while other major organ systems appeared normal. As a result of this research, alcohol today is considered by

many scientists as a substance that leads to birth defects manifested in behavioral problems.

Jones and colleagues' work also has had a tremendous impact on society in general. In 1989, warning labels issued by the U.S. Surgeon General began appearing on alcoholic beverage containers, and they included the phrase ". . . women should not drink alcoholic beverages during pregnancy because of the risk of birth defects." Numerous States have statutes concerning the issue of drinking during pregnancy and/or have established a department or agency to deal with issues related to prenatal alcohol exposure. A national newsletter, the *Iceberg,* published in Seattle, WA, helps parents raising children with FAS, and a national organization, the National Association on Fetal Alcohol Syndrome, has been established to increase awareness of the adverse consequences of drinking during pregnancy to help prevent FAS.

A search of the National Institute on Alcohol Abuse and Alcoholism's Alcohol and Alcohol Problems Science Database using "fetal alcohol syndrome" or "fetal alcohol effect" as key words revealed that approximately 2,800 articles appeared between 1973 and 1993 attempting to substantiate, clarify, and understand the various ramifications of prenatal alcohol exposure in both humans and animals. Additionally, in the last decade, investigators have published articles that have attempted to identify potential mechanisms of action of alcohol on the body from the physiological to the molecular level.

Further evidence of this article's importance to the alcohol field is the fact that this 20-year old article has been cited more than 1,050 times (*Science Citation and Social Science Citation Index* 1994). To put this in perspective, the median citation count for articles published in 12 alcohol and drug journals in 1984 was two citations over a 4-year period (Howard and Howard 1992). The more than 2,300 basic and clinical research papers confirming the teratogenicity of alcohol in many different species can be attributed to Jones and colleagues' seminal article.

No doubt this initial observation has had far-reaching clinical, scientific, societal, and political implications of greater significance than the authors could have imagined. ■

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