The affinity of cytomegalovirus for the glandular epithelium has been known for a long time (Büngeler and Wagner 1926). However, the mammary glands have never been examined in this respect. Our findings indicate the possibility that the uterus and the mammary glands are sites of virus multiplication during pregnancy, facilitating intrauterine infection of the conceptus and postnatal contamination of neonate. It is interesting to speculate about the coincidence of the breast-feeding period and the time of peak incidence of cytomegalovirus inclusions in the salivary glands of infants (table II).

TABLE II—AGE DISTRIBUTION OF NECROPSIED INFANTS EXHIBITING CYTOMEGALOVIRUS INCLUSIONS CONFINED TO THE SALIVARY GLANDS*

Age in Mos.	0	1	2	3	4	5	6	7	8	9	10	11	12	>12
No. of Cases	2	7	25	35	23	13	18	14	6	9	6	0	3	6
%	1·1	4·1	14·9	20·9	13·7	7·7	10·7	8·3	3·5	5·9	3·5	..	1·7	3·5

* Compiled from published data.

Inclusions confined to the salivary glands have never been recorded in stillborns (Diosi et al. 1965) and, excluding the cases of generalised infection, inclusions have rarely been seen in the salivary glands during the first 2 months of life (Weller and Hanshaw 1962). The peak incidence is attained at 3 months of age and after ablactation cytomegalic infection of the salivary glands becomes rare (Diosi, Nevinglovschi, Babusceac, and David 1967). Thus, acquired cytomegalovirus infection of the infant may be closely related to virus excretion in maternal milk. A distinct clinical picture of late generalised cytomegalic inclusion disease in infants, with onset at 3–4 months of age, after a symptom-free neonatal period, was tentatively outlined by Le Tan Vinh (1957).

Cytomegalovirus excretion in the urine, cervical secretion, and milk of puerperant women, approaches cytomegalic inclusion disease to certain zoonoses.

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Requests for reprints should be addressed to P. D., Department of Epidemiology, Institute of Hygiene, Timişoara, Bd. Babes 16, Rumania.

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IS LYSERGIC-ACID DIETHYLAMIDE A TERATOGEN?

HANS ZELLWEGER
M.D. Zurich
PROFESSOR OF PEDIATRICS

JOHN S. McDONALD
M.D. Iowa
RESIDENT IN OBSTETRICS

GISELA ABBO
M.T. California
RESEARCH ASSISTANT

UNIVERSITY OF IOWA

Summary A girl with a malformed right leg was born to a 19-year-old woman who had taken lysergic-acid diethylamide (L.S.D.) on the 25th day after her last menstrual period and three times between the 45th and 98th days. Her husband had also taken the drug. The child presented with the typical picture of the unilateral fibular aplastic syndrome. Since the mother took the second dose of L.S.D. in the period critical for the production of leg deformities, it is not unreasonable to suspect a causal relationship. Chromatid breaks were found in peripheral white blood-cells of the father (2 breaks), mother (5), and child (3).

Introduction

LYSERGIC-ACID diethylamide (L.S.D.) as a cause of structural alterations of chromosomes has been widely publicised lately. Chromatid and isochromatid breaks, triradial and quadriradial structures (chromatid exchanges and polyploidies), have been observed in the white blood-cells of people taking L.S.D., and in vitro, when L.S.D. was added to cell cultures (Cohen et al. 1967, Irwin and Egozcue 1967, *Journal of the American Medical Association* 1967).

We found chromatid and isochromatid breaks in ten patients who had been treated with L.S.D., and in two individuals who had taken L.S.D. for non-medical reasons. Chromatid exchanges were observed once in our series, but tetraploid cells were found with greater-than-usual frequency. A detailed report of our findings will be published elsewhere.

Chromatid breaks have been reported in two of four infants whose mothers had taken L.S.D. during pregnancy (*Journal of the American Medical Association* 1967). We made a similar observation (see table). It seems, therefore, that L.S.D. taken by the pregnant mother can affect the chromosomes of the conceptus.

Although birth defects associated with ingestion of

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CHROMOSOMAL ANALYSIS AND STRUCTURAL ALTERATIONS IN PERIPHERAL WHITE BLOOD-CELLS OF PARENTS AND CHILD

—	Age	No. of cells with chromosomes:				No. of chromatid breaks †	No. of polyploidies
		<45	45	46	47		
Father	20 yr.*	1	1	28	0	2 (A, C)†	0
Mother	19 yr.*	0	3	26	1	5 (A, A, C, C, C)	0
Proband	3 days	0	3	57	0	3 (A, B, D)	1

* Blood for chromosomal studies was obtained six months after last L.S.D. intake.
† Capital letters indicate the group to which the broken chromosomes belong

L.S.D. have not so far been described in man, an increased incidence of embryonal absorption and stillbirth has been observed in rats when L.S.D. was injected in early pregnancy (Alexander et al. 1967). Also, stunted growth in rats (Alexander et al. 1967) and cerebral malformations in mice (Auerbach and Rugowski 1967) have been noted. L.S.D. injected during later stages of pregnancy did not appear to have any untoward effect on the progeny (Alexander et al. 1967).

We describe here the case of an infant, born with a birth defect, both of whose parents had ingested L.S.D.

Case-report

A Caucasian female born Aug. 26, 1967. Family history was negative with respect to malformations and hereditary conditions. Both parents were healthy. The mother was 19 years old at the time of this, her first, pregnancy. She had some spotting in the second month of pregnancy, vulvitis (mixed *Trichomonas vaginalis* and monilial infection) in the 28th week, and pyelonephritis in the 36th week of pregnancy. Both she and her husband had taken L.S.D. on several occasions. The mother took the drug on the 25th day and three times between the 45th and 98th days after her last menstrual period. (The exact dose of L.S.D. is not known, but it was sufficient to produce the desired psychedelic effect.) The last dose was larger than the previous ones, and caused nausea and vomiting.

The baby was born seven days after the expected date of confinement. The delivery was uncomplicated. Birth-weight was 3280 g. Physical examination revealed a malformation of the right leg. There was no evidence of any other abnormality, and the rest of the physical examination yielded normal findings.

Fig. 1—Fibular aplastic syndrome of right leg.

All structures of the right leg were considerably shorter than those of the left. There was limited abduction of the right hip. The right lower leg was angulated, the angle pointing anteriorly. The right foot was shorter than the left, and showed only three toes.

X-rays of pelvis and legs revealed the following findings: dislocation of right hip, length of right femur 5·5 cm., length of left femur 8 cm., right distal femur epiphysis smaller than left, right proximal tibia epiphysis not calcified, left proximal tibia epiphysis well developed, absence of right fibula, right tibia short and angulated anteriorly. X-rays of the right foot showed one tarsal bone and three metatarsal-phalangeal rays. The left foot was radiologically normal, with three tarsal bones visible and five metatarsal-phalangeal rays.

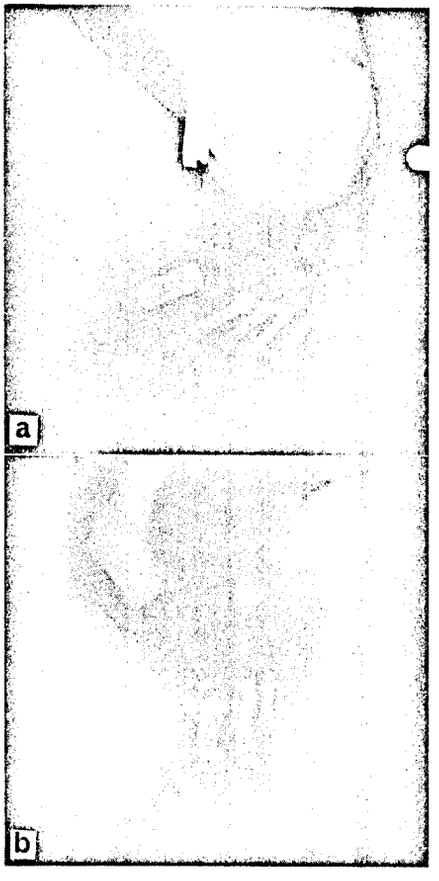

Fig. 2—X-rays of (a) the normal left foot and (b) the involved right foot.

Chromosome studies of peripheral white blood-cells were done of both parents and the proband. The results are given in the table.

Discussion

The child presented here represented the typical picture of unilateral fibular aplastic syndrome, including absence of fibula, anterior bowing of the shortened tibia, absence of lateral rays of the foot, shortening of the femur, and dislocation of the hip (Coventry and Johnson 1952, Coffey 1967). The right foot showed only one tarsal bone; but in view of the child's age, tarsal abnormalities (aplasia or fusion of tarsal bones) could not be identified with certainty.

The mother took L.S.D. four times during pregnancy, notably on the 25th and 45th days after her last menstrual period. It is important to note that the most active differentiation of the lower limb occurs in the seventh week of gestation (Bardeen and Lewis 1901). Moreover,

in investigations of the thalidomide embryopathy, leg abnormalities were noted in those infants whose mothers had taken thalidomide between the 42nd and 47th days after the last menstrual period (Lenz and Knapp 1962, Kreipe 1967). Since the mother of our proband ingested the second dose of L.S.D. exactly during the period critical for the production of leg deformities, it does not appear unreasonable to suspect a causal relationship between the L.S.D. intake of the mother and the fibular aplastic syndrome of the child.

At our present stage of knowledge, three cytogenetic and/or teratogenic complications of L.S.D. intake can be envisaged.

(1) L.S.D. produces alterations of the chromosomal structure which may last for a number of years. In one of our patients, chromatid breaks were recognised $3^1/_2$ years after the last ingestion of L.S.D. Whether such chromosomal alterations represent a risk for the progeny is not known. (The difficulty of establishing a possible causal relationship between parental chromosome break and malformations of the progeny is illustrated by the following observation: a man who had been treated with L.S.D. fathered a microcephalic child with holoprosencephaly 3 years after his last dose of L.S.D., the father's chromosomes still showed breaks at the time of the child's birth; we are reluctant to relate the malformation to the father's medication, however, especially since the family history revealed other cases of brain malformation.) Similar chromosomal alterations are found after viral infections such as measles and chickenpox (Nichols and Levan 1962, Aula 1963, Tanzer 1963), after aminopterin (Ryan et al. 1965), cyclophosphamide (Arrighi et al. 1962), nitrogen mustard (Conen and Lansky 1961), pyrimethamine (Bottura and Ferrari 1960), exposure to X rays (Buckton et al. 1962), in Fanconi's anæmia and Bloom's disease (German et al. 1965, Bloom et al. 1966), and, finally, in normal controls (Cohen et al. 1967, Irwin and Egozcue 1967, and personal, unpublished, observations). A direct connection of such chromosomal aberrations with malformed offspring has not yet been established.

(2) L.S.D. taken by expectant mothers can produce chromosomal breaks in the cells of the conceptus, but it is not known whether these chromosomal breaks can produce malformations: they have been found in newborns without any recognisable malformation (*Journal of the American Medical Association* 1967).

(3) L.S.D. taken during pregnancy may lead to abortions, as shown in rats (Alexander et al. 1967). The case reported here presented presumptive evidence that L.S.D., if taken by the mother during the organogenetic period, may lead to malformations.

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Preliminary Communications

SURFACE IgM SPECIFICITY ON CELLS DERIVED FROM A BURKITT'S LYMPHOMA

Summary Burkitt's lymphoma biopsy specimens from a 16-year-old African were found to differ from more than forty previously tested biopsy specimens from patients with this disease. Direct immunofluorescence detected a surface accumulation of IgM on living lymphoma cells, with a κ-light-chain specificity. Anti-IgM or anti-κ-light-chain sera killed the cells in the presence of complement even in high dilutions. Surface IgM specificity was maintained in three derived cell lines, grown in suspension for more than 4 months in vitro.

MATERIALS AND METHODS

FOUR biopsy specimens were obtained from a 16-year-old African Luo male (Daudi) with histologically confirmed Burkitt tumours of the occiput, orbits, abdomen, and tibia (Kenya Cancer Council no. 750), at weekly or fortnightly intervals, within a total time-span of 28 days. The fourth biopsy specimen was taken after partial regression of the tumour had been induced by cytarabine-hydrochloride treatment.

Reagents

(*a*) *Fluorescein-conjugated sera.*—These were goat anti-human IgG serum, a gift from Dr. J. B. Robbins [1]; goat anti-human IgM and IgA sera from Hyland Laboratories; rabbit anti-light-chain serum, a gift from Dr. G. Goldstein (University of Virginia); and goat anti-λ and anti-κ light-chain sera (Hyland Laboratories).

(*b*) *Non-conjugated sera.*—These were rabbit anti IgG, IgM, IgA, λ, and κ sera, gifts from the Institute of Medical Microbiology, Lund; and rabbit anti-light-chain serum from Dr. G. Goldstein.

Cells and Culture Conditions

After mincing and shaking in tissue-culture medium, the first three biopsy specimens released 80–82% viable cells; about 50% of the cells of the fourth specimen were viable. Unlike other biopsy specimens in our previous experience, cells from the first three specimens showed an immediate population increase within a week when cultivated in Eagle's basal medium with 20% fœtal calf serum. Population increase in the last specimen was not apparent before about 4 weeks.

Membrane Fluorescence Tests

Living cells, $0{\cdot}5–1{\cdot}0 \times 10^6$, were incubated with 30-µl. amounts of the reagents at 37°C for 20 minutes, and then washed 3 times with 5% fœtal calf serum in balanced salt solution. The percentage of cells showing surface fluorescence was determined according to the criteria we have described.[1–3]

Cytotoxic Test

2×10^5 cells were exposed to 50 µl. of anti-globulin serum, and 50 µl. guineapig complement diluted 1/2. After 45 minutes incubation at 37°C the percentage of cells stained with trypan-blue was determined.

RESULTS

Reactivity in the Fluorescence Test

Exposure of viable cells from the first three biopsy samples (received May 2, 9, and 23, 1967, respectively) to various conjugated reagents resulted in nearly 100% membrane staining with the anti-IgM reagent and the

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