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Effect of LSD on Human Pregnancy

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The frequencies of spontaneous abortions, premature births, and birth defects in 121 human pregnancies following relatively infrequent, low doses of medically administered lysergic acid diethylamide are within the normal ranges. The incidence of spontaneous abortions was above average for a small sample of 27 pregnancies where LSD was ingested under both medical and nonmedical conditions. Spontaneous abortions occurred significantly more frequently when the mother received LSD as opposed to the father only; however, the data do not permit the establishment of a clear causal relationship.

Considerable medical and social interest has focused on the potential genetic and teratogenic effects of lysergic acid diethylamide (LSD). A number of human somatic-cell (primarily lymphocytes) chromosome studies have not yielded consistent to conclusions as to whether chromosome damage results from in vivo exposure to LSD[1-4]; these variable results remain unexplained. Human meiotic chromosome analyses might better answer the question of whether children of persons exposed to LSD may be expected to have chromosomal alterations. One study of two male subjects exposed to LSD failed to demonstrate meiotic chromosome damage.[5] Meiotic studies in animals have given divergent results, with two reports on male mouse meiosis showing chromosome damage following LSD exposure,[6,7] while a third study showed no evidence for meiotic chromosome damage in male and female mice.[8] The latter report also notes the importance of studies on both males and females in view of differences in germ-cell production in the two sexes.

The few reports on congenitally defective children of parents exposed to LSD give no clear indication of a cause-and-effect relationship between LSD and congenital defects.[9-12] The results of fetal exposure to LSD in animal models have also been inconclusive.[13-16]

See also page 1488.

Methods

To further evaluate the effects of LSD on pregnancies, we have studied the outcome of 148 human pregnancies following parental ingestion of this drug. The data are part of a larger follow-up study of 300 persons (randomly drawn from a population of 750) who initially received LSD orally from one of three physicians in either experimental or psychotherapeutic settings during the period 1955 to 1961. Of this sample, 247 were located and personally interviewed in 1967 to 1968. Data were not available for 53 subjects; 16 were not located, 16 refused, 12 were deceased, and 9 were outside the United States. The mean age of the sample of 247 at the time of LSD administration was 35 years; hence, only a minority

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Table 1.—Outcome of Pregnancies Following Ingestion of LSD

Conditions of LSD Exposure	No. of Pregnancies*		Spontaneous Abortions		Premature Births†	
	LSD Only Medically	LSD Medically and Nonmedically	LSD Only Medically (%)	LSD Medically and Nonmedically (%)	LSD Only Medically (%)	LSD Medically and Nonmedically (%)
One or both parents prior to conception	121	27	15	37 (24)‡	7	12
Only father	75	8	8	12	4	14
Only mother	21	3§	29	33	20	0
Both parents	25	16	24	50 (30)	5	12
More than one year prior to conception	97	8	14	38	6	20
Within one year prior to conception	24	19	17	37 (15)	10	8
<5 ingestions (total for both parents)	91	6	13	17	6	20
≥5 ingestions (total for both parents)	30	21	20	43 (27)	8	8
Ingested during pregnancy	3	9	33	56 (0)	0	0

*Does not include pregnancies terminated by induced abortion.
†Percent of live births that were premature.
‡Numbers in parentheses indicate respondent with five abortions and one live birth deleted.
§Both parents received LSD; one or both received LSD nonmedically.

(81) of the respondents (or their spouses) became pregnant subsequent to LSD exposure of one or both parents. With the exception of any induced abortions, for which data were not collected, the 148 pregnancies include all pregnancies which occurred in the sample of 247 between the time of initial LSD administration and the interview. Data related to pregnancies and LSD use were obtained for both parents; however, the remainder of the descriptive information is only for the respondent, ie, the parent interviewed (60 men and 21 women). All are white and typically of above average socioeconomic status; 85% had attended college, and 65% hold bachelor or higher degrees. The mean age of the father and mother at the time of pregnancy was 34 and 30 years, respectively.

The number of medical LSD exposures prior to conception was typically small. For 47% of the pregnancies, it involved only a single administration for one parent. The range of combined exposures for both parents was 1 to 85, with 26% having 5 or more and 16% having 10 or more. The usual and maximum dose of LSD was recorded in each case. The usual single dose ranged from 25μg to 400μg with a median of 125μg; the maximum ranged from 75μg to 500μg with a median of 150μg. The accumulated amount of LSD ingested prior to conception ranged from 75μg to 10,000μg with a median of 200μg. Sixteen percent of the respondents received total amounts in excess of 1,000μg. For 27 of the 148 pregnancies, there was additional use of LSD under nonmedical conditions by one or both parents prior to conception. The range of medical plus nonmedical exposure for both parents in these cases was 2 to 165, with a median of 25. Information on the use of other drugs was available only for the parent who served as the respondent. For the 121 pregnancies where LSD exposure was restricted to medical conditions, the use of other psychotropic drugs prior to conception was minimal. Eight percent had used marihuana more than ten times, and 5% had ingested strong hallucinogens such as peyote, mescaline, and psilocybine. The comparable percentages for the 27 pregnancies preceded by nonmedical LSD use were 52% and 78%.

Results

Table 1 shows the outcome of pregnancies in relation to the conditions of LSD exposure. The data are presented separately for those pregnancies where LSD exposures include nonmedical use, since these cases typically involved the use of other psychotropic drugs in addition to LSD, and were more likely to include use during as well as before pregnancy. The spontaneous abortion rate for the group limited to medical LSD administration is 15%, which is within the usual range for recognized human pregnancies.[17] The rate for those exposed to LSD nonmedically (37%) is considerably higher, although one woman in this group accounted for five of the ten abortions reported. In this family, LSD was taken frequently by both parents before and during these five pregnancies, and one other abortion had occurred prior to the use of LSD by either parent (but subsequent to the use of peyote). A recent chromosome analysis (12 years after the first pregnancy) for the mother was normal; the father is deceased. The percentage of abortions for the

Table 2.—Outcome of First Pregnancy Following Ingestion of LSD

Conditions of LSD Exposure	No. of Pregnancies*		Spontaneous Abortions	
	LSD Only Medically	LSD Medically and Nonmedically	LSD Only Medically (%)	LSD Medically and Nonmedically (%)
One or both parents prior to conception	67	14	18	36
Only father	39	6	10	17
Only mother	13	2	38	50
Both parents	15	6†	20	50

*Does not include pregnancies terminated by induced abortion.
†Both parents received LSD; one or both parents received LSD nonmedically.

Table 3.—Clinical Findings in Children Born to Parents Exposed to LSD Prior to Conception

Case	No. of LSD Exposures		Sex	Finding in Child	Probable Cause
	Father	Mother			
7	1	0	M	Turned-in feet*	Unknown
111a	2	0	M	Turned-in feet†	Familial‡
111b	2	0	M	Turned-in feet†	Familial‡
111c	2	0	M	Turned-in feet†	Familial‡
128	1	0	F	"Crimped" ureter	Familial§
132a	2	0	M	Tibial rotation†	?Familial, two first cousins
132b	2	0	M	Tibial rotation†	?Familial, two first cousins
133	13	0	F	Turned-out feet*	Familial§
158	2	0	M	Pyloric stenosis, surgically corrected	Genetic(?); no family history
164	4	0	M	Bone deformity of legs and deafness	Postrubella syndrome
170	0	1	M	Premature; died with acute pulmonary edema	Unknown
203a	0	1	F	Cystic fibrosis	Genetic; no family history
203b	0	1	M	Turned-in left foot*	Unknown
235	0	1	M	Premature; hyaline membrane disease	Unknown

*Corrected with shoes.
†Corrected with cast.
‡Father and paternal grandmother affected.
§Mother and maternal grandmother affected.

group receiving LSD nonmedically is shown in Table 1 both with and without the data for this respondent.

Both the groups receiving medically and nonmedically administered LSD reported more abortions when the mother (or mother and father) received LSD than when only the father received LSD. For those restricted to medically administered LSD, the percentage of abortions is 26% and 8% for maternal vs only paternal ingestion, respectively (chi-square = 6.04, $P < 0.02$). For the combined medical and nonmedical sample, the corresponding percentages are 32% and 8%.

Of the 120 live births (67 boys and 53 girls), birth certificates were available for 81. The mean weight for these births was 3,175 gm (7.0 lbs). Babies with birth weights of less than 2,410 gm (5.5 lbs) were defined as premature; a gestation period of 37 weeks or less was used as the criterion when birth weights were unavailable. The percentage of live births that were premature (Table 1) is about the same as the norm of 7%.[18]

Pregnancy outcome showed no direct relationship to the proximity of LSD exposure and the time of conception. The incidence of abortions and number of LSD sessions prior to conception showed a small positive relationship for the medical sample and a much stronger one for the group receiving the drug nonmedically (the latter including the five abortions in a single respondent). Of the 12 pregnancies when LSD was ingested during pregnancy, six ended in abortions, again, five in one respondent.

Analysis based on the total number of pregnancies, as shown in Table 1, raises a question concerning independence of observations, since some individuals account for multiple pregnancies. The one respondent in the group receiving LSD nonmedically who had had five abortions was already mentioned. Of the remaining 23 abortions, one woman accounted for three, and two other women had two abortions each. To eliminate any bias caused by including more than one observation per subject, the analysis shown in Table 1 was repeated, using only the first pregnancy which followed exposure to LSD. Table 2 shows the abortion rate as a function of parent exposed to LSD for the 81 pregnancies in this category. The results are essentially the same as those based on the full sample. For individuals restricted to LSD given medically, the percentage of abortions is 29% and 10% for maternal versus only paternal exposure, respectively (chi-square = 2.57, $P < 0.15$). For the combined medical and nonmedical sample, the corresponding percentages are 33% and 11% (chi square = 4.68, $P < 0.05$). The results for premature births and proximity and number of LSD exposures for the sample of 81 are essentially the same as those for the full sample (Table 1), and are not shown in Table 2 because of the small number of cases in the subcategories.

For each of the 120 live births, the respondent was questioned concerning birth defects and abnormal development in the child. Table 3

provides details of the 14 reported instances of "congenital anomalies," including minor anomalies not usually considered significant. In all 14 cases, LSD use was limited to medical administration; the dose range was 75μg to 250μg with a median of 100μg; LSD ingestion was within one year prior to conception for cases 7 and 111a; and none received LSD during pregnancy.

Comment

A major concern of persons exposed to LSD is related to the possible genetic and teratogenic effect on their future children. By evaluating the outcome of pregnancies when one or both parents were exposed to LSD, we have attempted to determine if these individuals are at increased risk to have spontaneous abortions, premature births, or children with birth defects. Within the confines of the study, the only increased risk observed was a possible higher incidence of spontaneous abortions among women exposed to LSD.

A speculative explanation for the higher incidence of abortions when the mother as opposed to only the father was exposed to LSD might be related to the long period from the start to the finish of meiosis in the woman (several years) as compared to that of the man (several weeks). The more rapid production and turnover of sperm in the man may rid him of defective gametes, while damaged ova may remain until ovulation. Examination of nondrug explanations revealed no appreciable difference in parents' age or socioeconomic status between the group with maternal versus only paternal LSD exposure. There is, however, one difference between the groups that may be relevant. In approximately one half of the cases where the mother received LSD medically, it was administered as an adjunct to psychotherapy. In those cases where only the father received LSD medically, we do not know the percent of the mothers who were in psychotherapy which did not involve LSD, although it may be safely assumed that the proportion was much less than one half. Assuming that persons in psychotherapy are under greater emotional stress and that such stress increases the probability of an abortion,[19] this might be an alternative explanation for the higher abortion rates among mothers receiving LSD. When LSD was restricted to medical use, 36% of the 25 pregnancies following administration of LSD to the mother in psychotherapy ended in abortion. By comparison, 14% of the 21 pregnancies following administration of LSD to the mother in an experimental setting terminated in abortion. The psychotherapy group as a whole received a somewhat larger number of LSD administrations than did the experimental group; however, for the pregnancies that terminated in abortion, the number of exposures for the mother was never more than three for either group.

Although the number of "congenital anomalies" (14 of 120) suggests a possible increase over the normal expectation, a closer evaluation of the findings in Table 3 seems to discount this possibility. In five instances there is a positive family history of the same problem in one parent and in two others, two first cousins have a similar problem (noted as "? familial" in Table 3). The most likely interpretation is that the defects in these instances are familial (probably genetic), although a possible effect of LSD cannot be entirely excluded. Cystic fibrosis, which is present in one child, is a known genetic disorder and probably is not related to LSD exposure. Pyloric stenosis, which is present in another child, is also generally considered to have a strong genetic component. Among the four instances of persons with defects for which there is no clear etiology, two have turned-in feet, a common minor anomaly. The other two are premature and neither has a known anatomical defect, although one died with pulmonary edema and the other had hyaline membrane disease. Except for pyloric stenosis, none of these would probably be considered as a major or significant congenital defect. Although birth certificates were available for all 14 cases, none of the congenital defects listed in Table 3 was noted, with the exception of the one death.

Thus, there is no evidence of a relation between parental LSD exposure and major congenital defects in their offspring in the present study. However, the study of the products of only 120 pregnancies does not rule out the possible alteration in frequency of some of those major defects which usually occur on the order of one per 1,000 pregnancies. Norms for minor defects, such as the majority of those listed in Table 3, are not well established; however, the data do not suggest a clear correlation between the unexplained defects and LSD exposure.

The advantages of this study are the following: (1) all of the persons in the study were exposed to pure LSD of a known dose; (2) except for the small group who subsequently used LSD nonmedically, exposure to other drugs is probably not atypical; and (3) there has been a relatively long-term follow-up. Limitations include the following: (1) the doses of LSD used are generally low; and (2) exposures were not frequent. Thus, while these results may not be generalized to persons exposed to frequent, large doses of LSD as well as other drugs, the following tentative conclusions may be made with regard to relatively infrequent use of LSD in low doses: (1) there is no evidence that use of LSD by men prior to conception in the amounts described here is related to an increase in the rate of abortions, premature births, or birth

defects; (2) there is some indication that the use of LSD prior to conception by women may increase the incidence of spontaneous abortions, although the data do not permit the establishment of a clear-cut causal relationship; and (3) there is little to suggest that exposure to LSD by either parent prior to conception and in the amounts described here increased the risk of having a child with a congenital defect.

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