Chromosome Damage Not Found in Leukocytes of Children Treated with LSD-25

The report by Samuel Irwin and Jose Egozcue on "Chromosomal abnormalities in leukocytes from LSD-25 users" (*1*) has been of great concern to child psychiatrists. It describes an increase in chromosomal breakage in six out of eight volunteers who had taken LSD-25 (before the experiment was run) compared to one out of nine volunteers who had never taken the drug. Those in the first group had taken from four to 200 doses per individual, with a mean dose range of 200 to 60 μg of LSD-25, and with the last dose 1 day to 6 months before examinations of the chromosomes. None of the drug users had been examined for chromosome damage before they had taken LSD-25.

Between 1961 and 1966 we used LSD-25 in pharmacotherapy of young schizophrenic children in the Children's Unit of Creedmoor State Hospital. These children received LSD-25 each day for weeks or months in two divided doses of 100 to 150 μg with favorable results (*2*).

In a separate experiment, which did not take into consideration diagnosis or therapeutic regime, we studied the chromosomes of children in our unit who were deemed most likely to demonstrate chromosomal abnormalities because of congenital anomalies or familial history. Twenty-seven children (7 had received LSD-25; 20 had not) were investigated by the leukocyte culture method of Moorhead (*3*). At least ten metaphases were counted for each patient. Karyotyping was made by the Denver reporting system (*4*). Of the 20 children not treated with LSD-25, one child yielded, out of many studies on each, an occasional XO and an occasional 21-trisomy. This is within the normal range of technical error and normal incidence of aneuploidy.

The seven children who were treated with LSD-25 were schizophrenic, ranged in age from 7 to 11 years, and had received LSD-25 in daily doses of 100 to 150 μg from 5½ to 35 months. The LSD was discontinued from 20 to 48 months before the chromosome study on the cultured leukocytes was made. Five of these children had entirely normal karyotypes. One boy's karyotyping showed occasional XX and one XO typing. One girl had several normal karyotypings, but showed an occasional 21-trisomy. These may be within the normal limits of error or may indicate a mosaic condition. However, the reported effects of LSD-25 are confined to chromosome breakage only.

After reading the report of Irwin and Egozcue, we studied the material again for chromosome breakages. Fifty metaphase plates from five of the children who had received LSD-25 (including the two with the above described abnormalities) were mixed with 50 plates from five other subjects who did not receive LSD-25, and these were reexamined without our knowing the source of the sample. Chromosome breakages of less than 2 percent of those examined were found in the children who had received LSD-25 and also in those who had not. Irwin and Egozcue found a percentage of breakage in their LSD-25 users of 12 to 38, and a range of 7 to 13.5 in their controls.

Although this is by no means a conclusive study of the chromosomes in the children in our hospital who received LSD-25, the negative findings are significant because these children received up to 150 μg daily of pure chemical over a known period of time, even as long as 2 and 3 years, in contrast with studies by Irwin and Egozcue, whose subjects received unknown materials of unknown strength.

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Our original study (*1*) on chromosomal damage among LSD-25 users represented an effort to determine whether the findings in vitro reported by Cohen *et al.* (*2*) were relevant to the use of the drug in vivo. Available to us for study was a population of illicit users of LSD and other drugs. In this population chromosomal damage was found by us and, subsequently, by others (*3*). Insofar as LSD-25 use was the common denominator for subject selection, with coincident use of other drugs in most cases, we were careful to specify chromosomal damage "among LSD-25 users" rather than to specifically implicate LSD as such—although the latter seemed probable on the basis of the findings in vitro.

Lack of chromosomal damage in subjects administered pure LSD-25 as reported by Bender and Siva Sankar, has also been brought to our personal attention by others. In our series, also, was a negative finding in a single subject that received two doses therapeutically. Thus, except for the single positive case reported by Cohen *et al.* (*2*), there is no direct evidence to date demonstrating chromosomal damage after pure LSD-25 administration. It might conceivably have been produced by impurities present in the illicit material used. However, in our judgment, there also is insufficient data to rule out LSD as the incitant. In the study by Bender and Siva Sankar relatively low doses of LSD (100 to 150 μg) were given, and only ten metaphases per patient were studied. When investigating chromosomal breakage, we consider it necessary to examine at least 100 metaphases per subject (200 were examined in our series). Also, their subjects were studied 20 to 48 months after exposure to LSD. Since the life cycle of the circulating lymphocyte is believed to be 2 years (*4*), their negative findings (if valid) might merely reflect the normal replacement process of aging cells. There is still no data published or available to us concerning the persistence of the chromosomal damage once established. The relation between LSD-25 and chromosomal damage, thus, is by no means clear.

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