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EDITORIALS

Nonpsychic Effects of Lysergic Acid Diethylamide

THE ACUTE AND THE CHRONIC psychotomimetic potentials of the hallucinogen lysergic acid diethylamide (LSD) have been documented (1). That additional effects of LSD should come under scrutiny at this time is particularly pertinent considering the supposed widespread use of this drug among the population. Recent investigations have demonstrated that small doses of LSD (as low as 0.001 μg/ml) yielded a two- to threefold increase of chromosomal damage in comparison with untreated control cells. A similar in vivo effect was predicted by the finding of increased chromosomal abnormalities in one patient receiving LSD therapy for a psychiatric disorder (2). This observation was borne out in a study of eight "users" of LSD, six of whom manifested considerable chromosomal damage of their lymphocytes (3). In a recently completed investigation we have confirmed the preliminary in vitro results with additional data and have also examined the chromosomes of cultured lymphocytes from 17 individuals who repeatedly ingested LSD, 4 children who were exposed to the drug in utero, and 12 "drug-free" controls (4). Fourteen of the 17 young adults in this study demonstrated rates of chromosome breakage that were two to six times as great as those observed in the controls, with a threefold mean increase. In this series of subjects, as in the cells treated in vitro, we observed structural chromosomal rearrangements (dicentrics and exchange figures) that were absent in the controls. Of the four children exposed in utero two, born to mothers taking the usual dose (300 to 600 μg) of LSD, showed three- and fivefold increases in chromosome damage, while the remaining two, born to a mother taking only 50- to 100-μg doses, did not demonstrate a significant increase. It may be important that one of the children with a high frequency of chromosome damage was 2½ years old at the time of study and had not been exposed to the drug since birth.

Although evidence in man is not yet available, two studies with experimental animals have clearly demonstrated the teratogenic potential of LSD. When injected into rats early in pregnancy (day 4), the resultant litters were decreased in size, with a high proportion of stillborn fetuses and overall stunting of development in some of the animals. In addition, some of the liveborn rats failed to develop properly. Injections late in pregnancy had no apparent teratogenic effect (5). Similar techniques used in mice (6) produced severe malformations of the central nervous system as well as other morphologic anomalies. These effects were most dramatic if the drug was administered early in pregnancy (day 7) but were observed to a limited extent if given later.

In addition to the potential danger of teratogenesis already demonstrated by the animal studies and the likelihood of similar effects in man due to transplacental transport as evidenced by the children exposed to LSD in utero, other possible risks must be considered. Chromosome aberrations, similar to those induced by LSD, have been noted to occur spontaneously in three autosomal recessive diseases—Bloom's syndrome, Fanconi's anemia, and ataxia-telangiectasia (7–9). Patients with these syndromes also show a high propensity to

develop leukemia and other neoplasms. In this context cells of neoplastic origin quite frequently illustrate a variety of chromosomal aberrations, many of which are not unlike those seen after LSD exposure. Additionally, many agents known to produce similar chromosome aberrations (for example, radiation in man and other species, viruses in experimental animals) are known carcinogens. One of the obvious potential dangers, therefore, of exposure to agents such as LSD is the possible future increase in the incidence of leukemia and other neoplasm in the exposed individuals.

In view of the long periods after ingestion of the drug with retention of overt chromosomal damage, a pertinent analogy may be drawn to the case of therapeutic irradiation for ankylosing spondylitis (10). These studies, in which chromosome damage of long duration has been observed, demonstrate the long intermitotic life-span (over 2 years) of the circulating lymphocyte and again emphasize the association of such chromosome damage with the later appearance of an increased prevalence of leukemia.

Perhaps the greatest danger of such agents lies in potential chromosome damage to the gametes. Since LSD appears in the circulation, it presumably has free access to germ cells. Another agent, streptonigrin, known to cause chromosomal damage in human leukocytes (11, 12) and teratogenic effects in rats (13) has recently been shown to inflict damage on the meiotic chromosomes of the ova of the mouse (14). The existence of chromosome damage in these cells can only be ascertained through direct observation of germinal cells from gonadal biopsies. Chromosome rearrangements produced by breaks and subsequent incorrect healing result in structural anomalies including balanced reciprocal translocations. Ample evidence already exists that segregation of such translocations results in chromosomal imbalance leading to fetal wastage and a significant percentage of offspring with congenital anomalies and mental retardation. Since the carrier of such balanced translocations is clinically normal, as are many of his offspring, the consequences of the chromosomal imbalance may not appear for several generations. The total damage caused by LSD to the human population, both genetically and psychologically, therefore, may not be assessible for some time to come.

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REFERENCES

1. FROSCH, W. A., ROBBINS, E. S., STERN, M.: Untoward reactions to lysergic acid diethylamide (LSD) resulting in hospitalization. *New Eng. J. Med.* 273: 1235, 1965.
2. COHEN, M. M., MARINELLO, M. J., BACK, N.: Chromosomal damage in human leukocytes induced by lysergic acid diethylamide. *Science* 155: 1417, 1967.
3. IRWIN, S., EGOZCUE, J.: Chromosome abnormalities in leukocytes from LSD-25 users. *Science* 157: 313, 1967.
4. COHEN, M. M., HIRSCHHORN, K., FROSCH, W. A.: *In vivo* and *in vitro* chromosome damage induced by LSD-25. *New Eng. J. Med.* In press.
5. ALEXANDER, G. J., MILES, B. E., GOLD, G. M., ALEXANDER, R. B.: LSD: injection early in pregnancy produces abnormalities in offspring of rats. *Science* 157: 459, 1967.
6. AUERBACH, R., RUGOWSKI, J. A.: Lysergic acid diethylamide: effect on embryos. *Ibid.*, p. 1325.
7. SWIFT, M. R., HIRSCHHORN, K.: Fanconi's anemia: inherited susceptibility to chromosome breakage in various tissues. *Ann. Intern. Med.* 65: 496, 1966.
8. GERMAN, J., ARCHIBALD, R., BLOOM, D.: Chromosomal breakage in a rare and probably genetically determined syndrome of man. *Science* 148: 506, 1965.

9. HECHT, F., KOLER, R. D., RIGAS, D. A., DAHNKE, G. S., CASE, M. P., TISDALE, V., MILLER, R. W.: Leukemia and lymphocytes in ataxia-telangiectasia. *Lancet* 2: 1193, 1966.
10. BUCKTON, K. E., JACOBS, P. A., COURT BROWN, W. M., DOLL, R.: Study of chromosome damage persisting after X-ray therapy for ankylosing spondylitis. *Lancet* 2: 676, 1962.
11. COHEN, M. M., SHAW, M. W., CRAIG, A. P.: The effects of streptonigrin on cultured human leukocytes. *Proc. Nat. Acad. Sci. USA* 50: 16, 1963.
12. COHEN, M. M.: The specific effects of streptonigrin activity on human chromosomes in culture. *Cytogenetics (Basel)* 2: 271, 1963.
13. WARKANY, J., TAKACS, E.: Congenital malformations in rats from streptonigrin. *Arch. Path. (Chicago)* 79: 65, 1965.
14. JAGIELLO, G.: Streptonigrin: effect on first meiotic metaphase of the mouse egg. *Science* 157: 453, 1967.

Abortion and the Doctor

UNDER WHAT CIRCUMSTANCES and for what reasons should a doctor deliberately interrupt a pregnancy and thus arrest the beginning of a new human life? This has always been a serious question for the medical profession and for society. Society through its laws has strictly prescribed the indications for abortion, and churches of the Western world have taken definite stands on the issue. Yet the question is now being raised with increasing frequency and with a sense of urgent need to find more satisfactory answers.

This urgency is evident from the flood of books and articles in the lay press as well as in religious, legal, and medical journals (1–8). Two states, Colorado and North Carolina, have recently liberalized their abortion laws, and similar legislation has come before the legislatures of some 30 more states—some of which is still pending. The Roman Catholic church has reaffirmed its stand, and a number of Protestant churches have been considering their positions on the subject. An international conference on abortion has just been held this September in Washington (under the joint auspices of the Harvard Divinity School and the Joseph P. Kennedy, Jr. Foundation). Many medical organizations have been actively interested in the subject: Abortion was a major topic of discussion in the Colloquium on "The Changing Mores of Biomedical Research" held at the Annual Session of the American College of Physicians in San Francisco this past April (and published as a supplement to the September issue of the ANNALS); the American Medical Association adopted a new statement of policy on therapeutic abortion in June of this year (9).

The reasons for this upsurge of public concern over the problem of abortion are many, but a few are paramount. More and more people are alarmed over the tremendous number of criminal abortions that not only are performed outside the law but are attended with high morbidity and mortality rates (the number of criminal abortions in this country is estimated to be in the vicinity of 1 million each year). New medical knowledge is accumulating rapidly concerning genetic and intrauterine factors that may lead to the birth of a deformed or retarded child. Overpopulation and the threat of spreading starvation, especially in the developing countries, has emphasized the role of abortion as a backstop to failure in programs of contraception; we live in a world where already there are too many people.

Against this background many people are asking whether the absolute legal prohibition of abortion, except for saving the life of the mother, is enforceable or even desirable in today's society. Is not there a