



DEPARTMENT OF  
HEALTH, EDUCATION, AND WELFARE

~~FEDERAL SECURITY AGENCY~~

PUBLIC HEALTH SERVICE

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IN REPLYING, ADDRESS THE  
MEDICAL OFFICER IN CHARGE  
PUBLIC HEALTH SERVICE HOSPITAL

NIMH Addiction Research Center

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You may be interested in the progress of our experiments with LSD to date. Originally we had planned to determine the threshold dose for each patient individually, and this was attempted early in August, using a supply of LSD which was more than two years old.

Negative subjective reports were obtained with doses of 20 to 70 micrograms. Finally, patients were given 100 micrograms in divided doses, with marked subjective effects (as well as objective) appearing in all 5 patients. We then attempted to titrate the effects in each patient, giving doses of 80 to 90 micrograms. Very little effect was observed. These doses were administered on the day following the 100 microgram dose. These doses were raised progressively until 120 to 130 micrograms were being given to 4 of the subjects and 90 micrograms to the other, without any significant effects of any kind. It was found that the time of day did not alter the lack of effects and, also, that a fresh supply of LSD produced no change in the effects, or lack of them.

Since the lack of effects might be due to tolerance, administration of the drug was discontinued and after five days was again administered, with marked subjective and objective changes appearing with doses of 90 to 120 micrograms. Meanwhile, tests of the drug in individuals who had not been receiving it had shown strong positive results. The findings were very suggestive of rapid development of tolerance.

It was, therefore, necessary to obtain measurements after single doses at widely scattered intervals. As long as the interval was as much as 5 days, there was no noticeable

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decrease in effect, but there may be some decrease in effect if the drug is administered every third day.

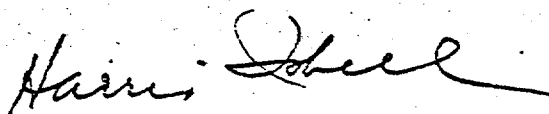
When given at proper intervals, LSD induces very definite blood pressure rise, pupillary dilatation, increase in deep tendon reflexes, and diminution in superficial skin reflexes. The pupillary effects and blood pressure effects appear to be suitable for measurements of tolerance.

LSD appears to facilitate synchronization of the electroencephalogram by photic stimulation. Photic stimulation also seems to enhance the perception of elementary hallucinations.

Apparently the supply of LSD is quite limited and we may be unable to obtain sufficient amounts of the drug to carry out the study as originally planned. However, we believe we have sufficient material to accomplish the following:

- 1) Effects of larger doses in non-tolerant patients;
- 2) Determination of whether tolerance occurs after one single dose of LSD;
- 3) Controlled studies of tolerance development in 5 patients;
- 4) Comparison of LSD with LAE.

Sincerely yours,



Harris Isbell, M.D.  
Director of Research

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