

Complete text

SVI LSD No.168 (§102a)

Z 355 tolerance

K 25 pyretogenic effect

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Tolerance to the pyretogenic effects of lysergic acid diethyl-
amide.

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Tolerance to the administration of lysergic acid diethylamide (LSD-25) has been reported by Isbell *et al.* (1955) in which eleven patients showed a rapid diminution of LSD effects after approximately seven days. A pyretogenic effect of LSD in rabbits has been reported by Horita and Dille (1954) in which the possibility is suggested that this pyretogenic effect in rabbits may parallel the mental effects of LSD-25 in humans.

This paper reports the development of tolerance to the pyretogenic effect of LSD in rabbits after daily administration of the drug and the duration of this tolerance after stoppage of the administration.

PROCEDURE. Rabbits were used in these experiments. The LSD-25 was supplied in solution in ampuls containing 100 micrograms per ml. A dose of 50 micrograms per kgm. was administered by marginal ear vein. The solution was undiluted for the injection.

Temperatures were measured rectally with a clinical thermometer. All temperature measurements were made by one experimenter and care was taken to keep all procedures as uniform as possible. Temperature readings were taken every half hour over a period of eight hours after administration of the LSD.

RESULTS. Production of Tolerance. The results obtained from ten rabbits administered 50 micrograms per kgm. daily for five days are shown in figure 1. The mean maximum rise was from 39.6°C. to 41.8°C. Two control rabbits that had received an equivalent volume of physiological saline showed little variation in temperature maintaining a body temperature of approximately 39.6 during the period of the experiment. On the fourth and fifth days the rise in temperature after administration of the standard dose of LSD was approximately 0.8°C. Since there was little change between the fourth and fifth day it was assumed that the tolerance had developed to its full degree on the fourth day.

Duration of Tolerance. Using the ten rabbits now tolerant to the pyretogenic effect of LSD, the following program was carried out in order to obtain the duration of tolerance. A test dose of 50 micrograms/kgm. was administered to one of each of the rabbits of the group of ten, allowing one additional day interval to elapse for each rabbit. These results are summarized in figure 2. As the days are allowed to lapse without administration of LSD the pyretogenic response to the test dose of 50 micrograms per kgm. gradually returns. At the end of the ninth day it has practically reached the mean response and is within the range of response seen in the first day curve of figure 1.

DISCUSSION AND SUMMARY. Tolerance to the pyretogenic effect of LSD is

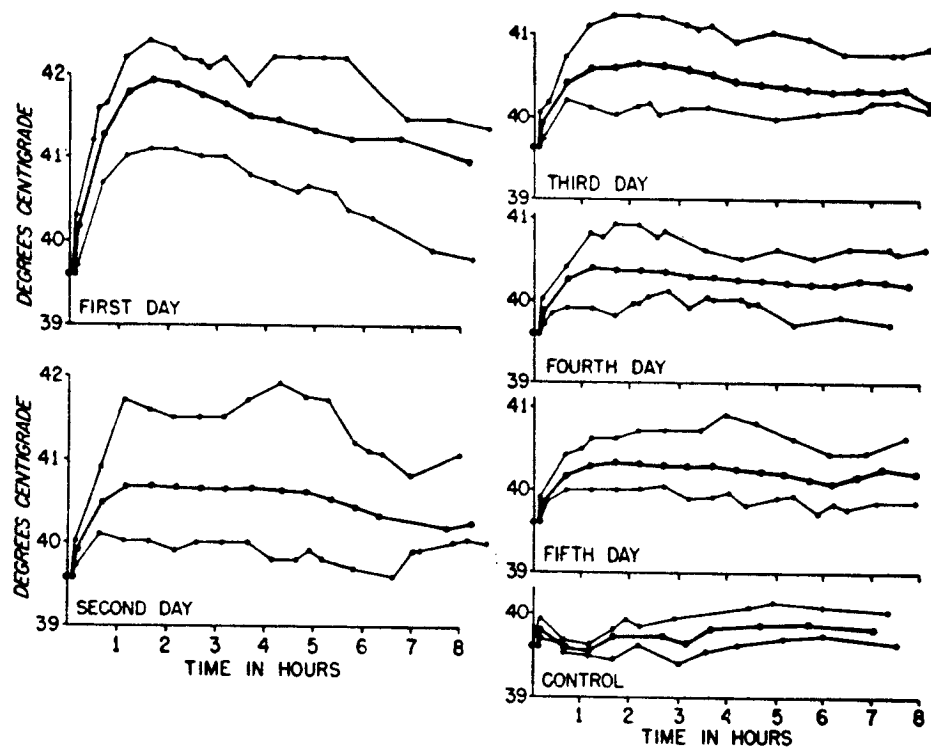


FIG. 1. The development of tolerance to the pyretogenic effects of LSD-25 when 50 micrograms are administered daily for five days. The heavy line is the arithmetic mean of the responses of ten rabbits. The upper and lower lines are the range of responses.

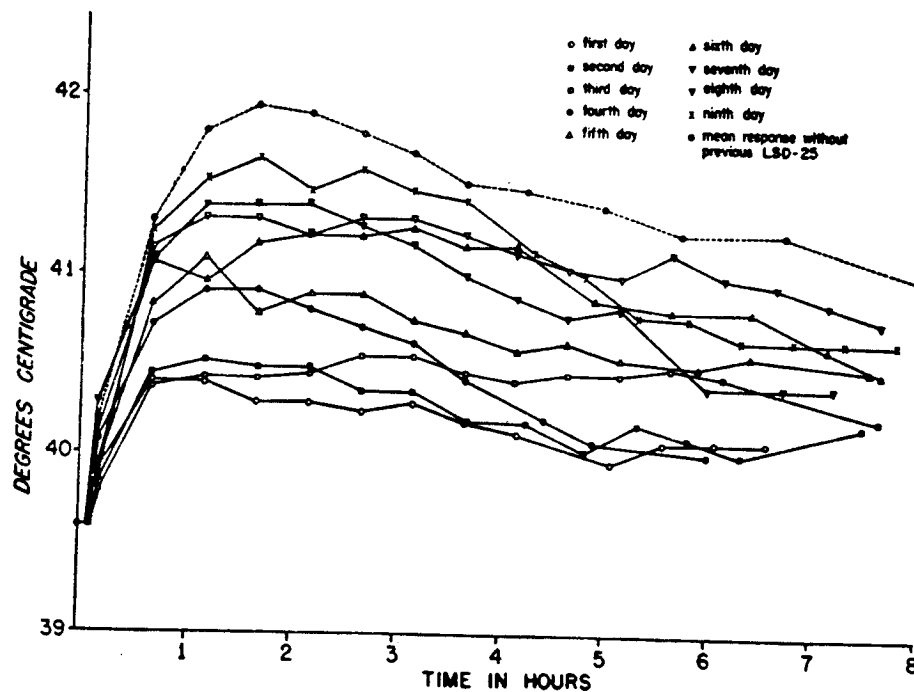


FIG. 2. The recovery from tolerance to the pyretogenic effects of LSD-25. Each curve represents the response of a rabbit to a test dose of 50 micrograms per kgm. after an interval in successive rabbits of from 1 to 9 days abstinence.

produced by daily administration of 50 micrograms per kgm. for a period of four to five days. Complete abolition of the effect is not secured in this time but the response is so much reduced from the original that tolerance may certainly be said to exist. Once established the tolerance persists for at least nine days. The parallelism between the pyretogenic effect in rabbits and the tolerance to the psychic effect of LSD reported by Isbell *et al.* (1955) in humans suggests the possibility that the pyretogenic effect of agents of this type might give useful preliminary information as to the possibility of psychic effects in humans.

REFERENCES

- HORITA, A., AND DILLE, J. M.: *Science*, **120**: 1100, 1954.
ISELL, H. F., ET AL.: *Fed. Proc.*, **14**: 354, 1955.

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(Gewöhnung an die fiebererzeugende Wirkung von LSD).

Bei Kaninchen bewirkte tägliche Verabfolgung während 4 - 5 Tagen von 50 μ /kg LSD Gewöhnung an dessen pyretogene Wirkung. Die Toleranz hielt mindestens 9 Tage an.

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(Accoutumance à l'effet pyrétogène du LSD).

Chez le lapin, l'administration quotidienne de 50 μ /kg de LSD pendant 4 à 5 jours provoque une accoutumance à l'effet pyrétogène du LSD. Une fois provoquée, cette accoutumance persiste pendant au moins 9 jours.

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