could be due to the development of anti-reagin antibodies, since the same reaction was observed after initial injection of rabbit serum. That the refractory state is due to non-specific fixation of the injected serum proteins on monkey-skin receptor cells seems unlikely in view of the latent period required (10–14 days) and the fact that complete inhibition was observed after reinjection of as little as 5 ml. of serum. These two latter considerations suggest some immunological mechanism involving the production of host antibodies, but the immunoglobulin nature and specificity of these antibodies and their role in the mechanism of inhibition of P.C.A. with human reagins require elucidation.

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Harry Webster Thorp Laboratories,
Division of Immunochemistry
and Allergy,
McGill University Clinic,
Royal Victoria Hospital,
Montreal, Quebec, Canada.

M. RADERMECKER
L. GOODFRIEND.

LYSERGIC-ACID-DIETHYLAMIDE AND CANNABIS AS POSSIBLE TERATOGENS IN MAN

SIR,—The purpose of the present communication is to report a child with malformation of the arm whose parents had taken lysergic-acid diethylamide (L.S.D.) and had smoked cannabis (marijuana). The mother took L.S.D. before and during early pregnancy; the amount taken is unknown. She did not take L.S.D. after she realised she was pregnant. However, she smoked cannabis before and throughout the pregnancy. In addition, she took dicyclomine hydrochloride, doxylamine succinate, and pyridoxine hydrochloride during the first trimester for nausea. The baby's father was also taking L.S.D. and smoking cannabis at the time the baby was conceived. The patient was the only child born to these parents, the mother having had 2 previous pregnancies—by whom we do not know—which terminated in induced abortions. Family history revealed no other instance of congenital malformation and no suggestion of consanguinity.

The patient was born in January, 1968, weighing 6 lb. 14 oz. The delivery was entirely normal. At birth the patient was observed to have right terminal transverse acheiria (absence of hand). The stump had several vestiges, perhaps representing digits. The remainder of the right upper extremity was normal, as was the rest of the physical and developmental examination at $4^1/_2$ months of age.

Chromosomal studies of lymphocytes from the patient's mother were done in July, 1968, approximately 14 months after the last known intake of L.S.D. Thirty-four metaphase spreads were examined. None showed evidence of chromosome breakage. Chromosome studies could not be done in the patient's father, because of his death by suicide, or in the patient, because the mother refused permission.

The malformation in our patient cannot be ascribed with any certainty to parental L.S.D. exposure, since only one other malformed baby (with fibular aplasia) whose parents were exposed to L.S.D. has to our knowledge been reported.[1] The data are now conflicting as to whether leucocyte chromosome breakage occurs in any or all humans exposed to L.S.D.[2–5] Data from experiments with *Drosophila* have indicated no detectable chromosome breakage or genetic damage from L.S.D. at low and moderate dosages.[6] In experiments with a much higher level of L.S.D. a significant increase in X-linked recessive mutations occurred in *Drosophila*.[7] And in mice L.S.D. has been shown to cause chromosome aberrations in various tissues, including germinal cells in meiosis.[8]

Cannabis resin shows species differences as a teratogen, inducing a high incidence of fœtal resorption and stunting but no apparent fœtal malformations in pregnant mice.[9] When administered to pregnant rats it causes a high incidence of both fœtal resorption and fœtal malformation.[10] It may be of special interest in connection with the present case that a significant proportion (17%) of rat fœtuses whose mothers were exposed to cannabis had phocomelia or amelia.[10]

We should like to suggest (1) reporting of children with and without malformations where the parents have had L.S.D. or cannabis exposure, and (2) caution before considering L.S.D. or cannabis teratogenic in man, since the present data are so scanty.

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Crippled Children's Division,
Division of Medical Genetics
and Departments of Pediatrics
and Orthopedics,
University of Oregon Medical School,
Portland, Oregon 97201.

FREDERICK HECHT
RODNEY K. BEALS
MARTIN H. LEES.

Departments of Pœdiatrics and Obstetrics,
Charing Cross Hospital,
London W.C.1.

HUGH JOLLY
PATRICIA ROBERTS.

MANAGEMENT OF CERVICAL CARCINOMA-IN-SITU

SIR,—Mr. Way's reply (Sept. 14, p. 637) to your leader (Sept. 7, p. 548), particularly in its remarks on colposcopy as noted by Mr. Coppleson and Dr. Reid (Oct. 19, p. 873), was predictable. His modified radical hysterectomy rate of 75% in his series [11] of 551 cases (10 lost sight of) of preinvasive and microinvasive carcinoma of the cervix in the years 1948–65 resulted in only 1 case of true invasive cancer developing—but also in 5 damaged ureters and 3 postoperative deaths. In this hospital, in the years 1950–67, treatment by cone-biopsy *or lesser procedure* of 67% of 574 cases (follow-up 100%, mean 6·5±3·0 years) of preinvasive and microinvasive carcinoma of the cervix also resulted in only 1 case of invasive cancer developing—but no damaged ureters or postoperative deaths. The expected incidence of invasive cancer developing in a similar group of normal women followed for the same time, from the known age-specific incidence of invasive cervical cancer in New Zealand,[12] is also only 1 case—which reinforces the conclusion of Mr. Coppleson and Dr. Reid that we are dealing with 2 different disease processes. Why then does Mr. Way fear carcinoma-in-situ so much in his "imitating Herod . . . striking down all in his path to be sure of not missing what he wants to reach [13]"? Why, indeed, is it that Fidler et al.[14] have now screened almost *a million* cases since 1949, diagnosed nearly 3500 preinvasive and microinvasive cancers, and still cannot claim either a significant lowering of invasive cervical cancer mortality in British Columbia, or even a mortality that is any better than in the other, less-well-screened, Canadian provinces [15]? The natural history of carcinoma-in-situ is not by any means as clearcut as Mr. Way or Professor McLaren (Sept. 21, p. 683) would have us believe.

University of Auckland,
Postgraduate School of
Obstetrics and Gynæcology,
National Women's Hospital,
Auckland 3, New Zealand.

G. H. GREEN.

1. Zellweger, H., McDonald, J. S., Abbo, G. *Lancet*, 1967, ii, 1066.
2. Cohen, M. M., Marinello, M. J., Back, N. *Science, N.Y.* 1967, **155**, 1417.
3. Irwin, S., Egozcue, J. *ibid.* 1967, **157**, 313.
4. Loughman, W. D., Sargent, T. W., Israelstam, D. M. *ibid.* 1967, **158**, 508.
5. Petrakis, N. cited by Loughman et al. (footnote 4).
6. Grace, D., Carlson, E. A., Goodman, P. *Science, N.Y.* 1968, **161**, 694.
7. Browning, L. S. *ibid.* p. 1022.
8. Cohen, M. M., Mukherjee, A. B. *Nature, Lond.*, 1968, **219**, 1072.
9. Persaud, T. V. N., Ellington, A. C. *Lancet*, 1967, ii, 1306.
10. Persaud, T. V. N., Ellington, A. C. *ibid.* 1968, ii, 406.
11. Way, S., Hennigan, M., Wright, V. C. *J. Obstet. Gynæc. Br. Commonw.* 1968, **75**, 593.
12. Green, G. H. *Int. J. Obstet. Gynec.* (in the press).
13. Oberling, C. The Riddle of Cancer (translated by W. H. Woglom). Yale, 1944.
14. Fidler, H. K., Boyes, D. A., Worth, A. J. *J. Obstet. Gynæc. Br. Commonw.* 1968, **75**, 392.
15. Ahluwalia, H. S., Doll, R. *Br. J. prev. soc. Med.* 1968, **22**, 161.