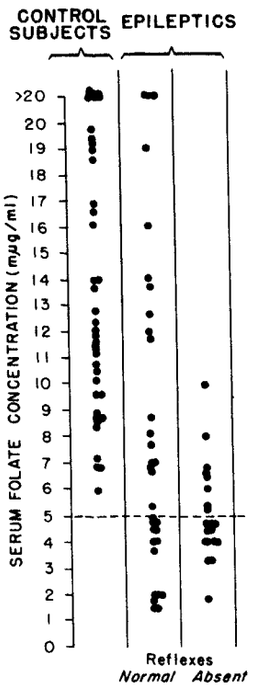
abnormal in the 12 patients with neuropathy included in the therapeutic trial. After therapy there was no significant improvement in these mean values (see table).

Discussion

No convincing causal relation has been demonstrated between folate deficiency and the development of neurological abnormalities in patients receiving anticonvulsant drugs. Such abnormalities have been described in 4 patients on anticonvulsants developing megaloblastic anæmia, but in 3 of these serum-folate concentrations were not assayed,[1-3] the serum-vitamin-B_{12} concentration was subnormal in 1,[1] and 2 of the patients with neurological improvement were treated with both folic acid and vitamin B_{12}.[1-3] The serum-folate concentration was subnormal in the patient described by Hansen et al.[4]; however, the extensive degenerative changes found in the cerebellum could have been unrelated to folate deficiency, since cerebellar degeneration has been produced experimentally in animals by acute high dosage of diphenylhydantoin.[12 13]



Serum-folate concentrations in control subjects and in epileptic patients.

Reynolds [7] has reported improvement in psychiatric abnormalities in 26 epileptic patients with low serum-folate concentration after folic-acid therapy. The subjective nature of evaluation in these patients makes the observations of Reynolds and his colleagues [5 7] difficult to assess. Organic dementia, megaloblastic anæmia, and low serum-folate levels in 2 elderly patients with poor dietary histories have been reported [6]; the dementia improved after admission to hospital and treatment with folic acid, but other variables were not controlled. Similarly, the erratic seizure pattern of many epileptic patients

MEAN NERVE-CONDUCTION VALUES IN PERONEAL AND POSTERIOR-TIBIAL NERVES (METRES PER SECOND) IN 12 PATIENTS WITH NEUROPATHY TREATED ALTERNATELY WITH FOLIC ACID AND PLACEBO FOR CONSECUTIVE 3-MONTH PERIODS

Period	Peroneal nerve*	Posterior-tibial nerve†
Pretreatment	40·2	37·4
Placebo (3 mos.)	44·1	40·7
Folic acid (3 mos.)	42·2	39·3
Pretreatment	40·3	39·6
Folic acid (3 mos.)	42·9	40·6
Placebo (3 mos.)	42·4	39·6

* Normal 51·0 (±3·26).[14]
† Normal 48·7 (±3·5).[15]

complicates the assessment of folic-acid therapy in the control of seizure frequency, which has been reported to decrease [16] and to increase [7] after such therapy. In our attempt to assess both mental changes and seizure frequency, it has proved extremely difficult to obtain objective criteria.

In this study, in which reproducible criteria of neurological disease were used, no significant correlation was found between subnormal serum-folate concentration and the development of neuropathy in epileptic patients receiving anticonvulsant drugs. Furthermore, therapy with folic acid did not result in measurable improvement of the neuropathy. Although it is possible that our observations on the relation of folate deficiency to neuropathy may not be germane to its relation to other neurological and psychiatric abnormalities in patients with epilepsy, we must emphasise that no objective evidence for the latter relationship has yet been reported.

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CANNABIS IN EARLY PREGNANCY

SIR,—Stunting and fœtal abnormalities have been observed in rats treated with lysergide (lysergic-acid diethylamide, L.S.D.) during early pregnancy,[1] and Prof. Zellweger and his colleagues (Nov. 18, p. 1066) report the first case of human teratogenicity with possible causal relationship to L.S.D.

In Jamaica, the use of the resin of *Cannabis sativa* (ganja) is widely suspected, although illegal. It produces, like L.S.D., abnormal mental phenomena in both the cognitive and perceptual spheres.[2] We tested the effects of the resin on the mouse embryo, in our programme of screening drugs of West Indian origin for embryopathic activity. The fœtuses of pregnant mice treated on day 6 of gestation with a single intraperitoneal dose (16 mg. per kg.) of the resin showed a high incidence of overall stunting. No apparent malformations were observed. The size of the litter was not significantly reduced. There were complete fœtal resorptions in animals given 16 mg. per kg. of the resin intraperitoneally daily for days 1 to 6 of gestation.

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IS LYSERGIDE A TERATOGEN?

SIR,—We should like to thank Dr. Court Brown for his comments (Nov. 25, p. 1154) on our article (Nov. 18, p. 1066), and to answer his questions.

Chromosomal analyses were done on 72-hour cultures, generally accepted as routine in our laboratory. In order to detect breaks, every plate had to be examined. Non-staining chromatid gaps were not scored. Isochromatid breaks, acentric chromosome fragments, and chromatid interchanges were absent in the plates examined. (Skin fibroblasts of the father, however, examined after our report was written, revealed such chromatid interchanges as triradial and quadriradial structures; these results did not appear in our article.) The chromatid breaks observed in the peripheral white blood-cells of the proband and her parents, and the groups to which the aberrant chromosomes belonged, were listed in our table. Approximately 8% of the cells of the persons discussed here showed chromatid breaks, while only 3·5% of the cells of "normal" controls, processed with the same techniques, showed similar alterations.

Further studies on the effect of lysergide (lysergic-acid diethylamide, L.S.D.) on the chromosomes are proceeding. As stated in the discussion in our article, the significance and effects of chromosome breaks are unknown. The purpose of ou article was to present presumptive evidence that L.S.D., if taken by a woman during the organogenetic period of her pregnancy, may have a teratogenic effect on the fœtus.

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