Electroencephalogram in Anticonvulsant-induced Folate Deficiency

W. I. M. DOW

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Since the recognition of folate deficiency with or without megaloblastic anaemia in patients taking long-term anticonvulsant therapy (Mannheimer *et al.*, 1952; Badenoch, 1954; Reynolds *et al.*, 1966) folic acid has been prescribed for epileptic patients, particularly those with a low serum folate, showing the effects of anticonvulsant toxicity. More recently the role of vitamin B_{12} has become of greater importance, and there is evidence of antagonism between vitamin B_{12} and folic acid with the recognition of the development or precipitation of subacute combined degeneration of the cord in patients with pernicious anaemia treated with folic acid alone (Ross *et al.*, 1948; Conley and Krevans, 1955; Baldwin and Dalessio, 1961). Folic acid is also reported to result in an increase in frequency of fits, though it may improve the mental state (Reynolds, 1967). Neubauer (1970) recommends that folic acid and vitamin B_{12} should be given to any patient started on anticonvulsant therapy in order to prevent mental retardation, with special reference to children and adolescents, and emphasis on accurate estimations of serum folate and vitamin B_{12} is stressed in the accompanying leading article (*British Medical Journal*, 1970).

Little mention has been made of the electroencephalogram in situations of anticonvulsant intoxication and folate deficiency, and the following case is reported to stress the value of serial electroencephalographic studies.

Case Report

The patient, a 44-year-old housewife, was admitted to hospital in the summer of 1969 as an emergency case in a drowsy and confused state. She had had epilepsy since the age of five, but had not had any recent fits, and was currently taking primidone 250 mg six times a day, pheneturide 200 mg four times a day, methylphenobarbitone 60 mg twice a day, and sulthiame 200 mg twice a day. Examination showed ataxia of all limbs, nystagmus on gaze to the right, and areflexia but no sensory loss. Haemoglobin and blood film were normal, with no evidence of megaloblastosis, and serum vitamin B_{12} was 444 pg/ml. The serum folate was 0·3 ng/ml. An air encephalogram showed evidence of early cerebral and cerebellar atrophy, with some asymmetry in size of the lateral ventricles, which was first noted on an air encephalogram eight years previously. The cerebrospinal fluid was normal.

The E.E.G. on admission (Fig. 1) showed traces of alpha activity at 10-11 c/s, but was dominated by continuous theta activity at 4-5 c/s and runs of delta activity down to 1·5 c/s widely. One week after admission, and after reduction of primidone dosage only (on normal ward diet), the E.E.G. (Fig. 2) showed pronounced improvement, with dominant activity in the 6-7 c/s range and disappearance of the delta rhythms. Two weeks after admission, when the patient was on folic acid 5 mg three times a day and her serum folate was 16 ng/ml, the E.E.G. (Fig. 3) had returned to "within normal limits," with the dominant activity back in the alpha range (8-9 c/s), little theta activity, and no paroxysmal features. The patient's mental state and ataxia improved in parallel with her E.E.G., and fit frequency was reduced on continued folic acid therapy.

Wessex Neurological Centre
W. I. M. DOW, M.B., CH.B., Senior Registrar in Clinical Neurophysiology

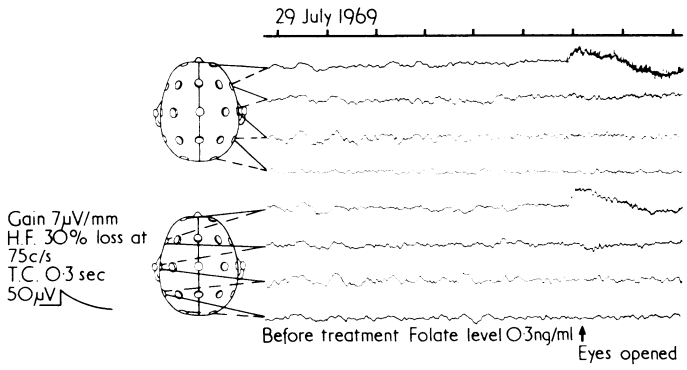

FIG. 1—E.E.G. taken at time of admission

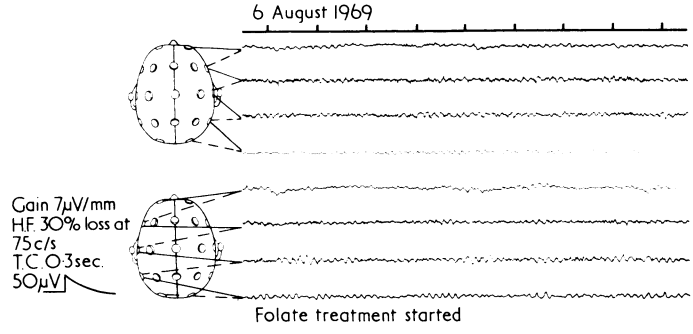

FIG. 2—E.E.G. appearances one week after admission

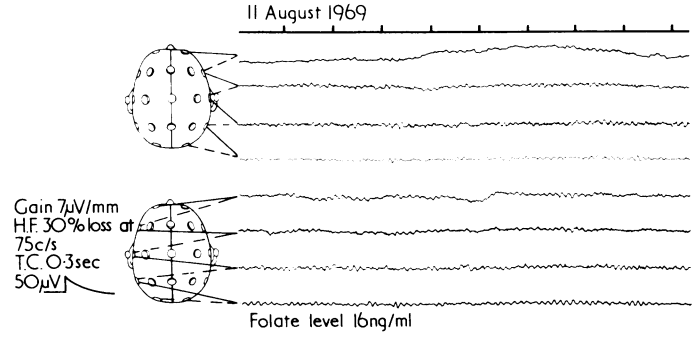

FIG. 3—E.E.G. appearances two weeks after admission

Comment

It is suggested that the E.E.G. may be of value in the assessment of severity of anticonvulsant-induced toxicity states with folate deficiency and in control of replacement therapy.

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