In our view Mr. Still's criticism on this point is entirely lacking in evidence to support it.

2. *The Psychoses*

Here Mr. Still is confusing the in-patient admission rate with the psychosis rate.

Total mental hospital admissions from Newton for each of the three years 1957 to 1959 were significantly lower than the expected figures based on those for England and Wales; indeed, when taken together the difference is significant at the 0·1 per cent. level.

Nearly two-thirds of the cases admitted from Newton were psychotic, and about one-third were neurotic. This proportion of neurotic admissions is twice the national figure.

During the three-year period, 42 patients were admitted for treatment to ten special psychiatric units. As we reported (Table 77, p. 151), most of these were neurosis cases, although there were three psychotics. While the inclusion of these 42 patients can be used, as we have shown (p. 146), to raise the *in-patient admission rate*, the inclusion of the three psychotic patients makes practically no difference to the *psychosis rate*.

It follows then that, as we claim (p. 146), the rate for psychoses admitted for treatment from Newton "must be even more markedly below the national figures than the overall figures (for admissions) would suggest." And this is incontrovertible.

However, as the mental hospital serving Newton is 40 miles away, we considered whether distance might be acting as a deterrent to the willingness of patients to be admitted there. If this were so, it seemed to us that more pressure would have been put on the psychiatric services which were available locally. In other words fewer in-patients might result in more out-patients. An analysis of the records of the psychiatric out-patient department at the local general hospital showed that this was not so, but that somewhat fewer patients were being referred there than would have been expected from the national usage of these services at that time.

If it is true, as we suggest would seem likely (p. 147), that the majority of patients suffering from serious mental illness—and particularly from psychosis—are brought for treatment to the specialist psychiatric services which are now available, then our findings clearly show that the incidence of such cases in Newton was low. And this finding remains valid when all reasonable corrections, for example for sex and age, have been applied.

3. *Psychiatric case-load in general practice*

Mr. Still refers, finally, to our study of the psychiatric case-load of the general practices in Newton. In a sample of about 2,800 adult patients, 16 cases of psychosis were reported by the G.P.s. This gave a rate of 5·7 per 1,000, which was higher than that found by Logan and Cushion in the general population. From our discussions with the doctors there was no evidence whatever of any hesitation on their part about referring their psychotic patients for specialist advice and treatment. Indeed, during the year 11 of the 16 patients were so referred.

We therefore concluded (p. 147) that this figure, based as it is on a small number in a *sample* population, was a *less* reliable guide to the amount of psychotic disorder present in Newton than the figures obtained through the specialist services covering three years and based on the *total* population of the town, which in 1959 was nearly 40,000.

Our confidence in the conclusions presented in our book therefore remains undisturbed.

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## VITAMIN $B_{12}$ AND FOLATE DEFICIENCIES

DEAR SIR,

May I comment on some of the issues raised by the very interesting studies of Dr. Shulman (*Journal*, March, 1967, p. 252) of vitamin $B_{12}$ and folate deficiency in an elderly psychiatric population.

1. Dr. Shulman's is the third recent report of a very high incidence of folate deficiency in geriatric patients. He has referred to the findings of Read, Gough, Pardoe and Nicholas (1965), whose study revealed an incidence of folate deficiency identical to his own figure of 80 per cent. More recently Hurdle and Picton Williams (1966) reported an incidence of 67 per cent. in those admissions to a geriatric unit with mental disorders. Even allowing for the possibilities of (1) an unduly high normal range for serum folate quoted in the studies of Shulman and those of Read *et al.*, and (2) a fall of serum folate with age, there does indeed seem to be a remarkably high incidence of folate deficiency in geriatric patients with mental symptoms. Although there are difficulties in establishing a diagnosis of nutritional folate deficiency (as discussed by Hurdle and Picton Williams) it has been concluded that this is the cause of the folate deficiency

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in all three reports. The most common mental state in the patients in these studies seems to have been dementia, and symptoms such as apathy, withdrawal, lack of motivation and depression are all quoted as indirect evidence in favour of the dietary theory. While this may prove to be either predominantly or partly correct, recent studies of folate metabolism in epileptic patients, and in particular the results of treating epileptic patients with folic acid, lead one to suggest that an alternative or additional hypothesis is worthy of consideration. This is that many of the mental symptoms in the geriatric patients are the *result* of folate deficiency. This of course includes the possibility of a vicious circle effect in which mental illness leads to secondary dietary deficiency of folic acid and aggravation of the mental state.

It is now apparent that folate deficiency due to drug treatment with phenobarbitone, phenytoin or primidone can be detected in the majority of non-anaemic epileptic patients and that this may be responsible for mental symptoms in some cases (Reynolds, Milner, Matthews and Chanarin, 1966a; Reynolds, Chanarin, Milner and Matthews, 1966b). The effects of folic acid, 5 mg. t.d.s. (together with vitamin $B_{12}$ in a few cases), on the mental state and fit frequency of 26 chronic drug treated epileptic patients with folate deficiency have been observed for from one to three years (Reynolds, 1966, 1967). In summary, an improvement in the mental state to a variable degree was noted in 22 patients. In 11 of these the improvement was marked. The type of change observed was an increase in "drive" ("motivation", "mental or psychic energy") and initiative, speed of cerebration (as seen in thought, speech and action), concentration and alertness, self-confidence and independence, sociability. In a few patients there was an elevation of mood and a tendency to less severe mood swings or aggressive behaviour. The effects of these changes, some of which took up to three months to be apparent, were particularly seen in an improved speed, quality and capacity at work and in increased social activity. The most striking and consistent alteration was the improved "drive". In 13 of the 26 patients (50 per cent.), fit frequency or severity increased, and this necessitated cessation of therapy in 9 cases. The vitamin was stopped at intervals varying from fourteen days to twenty-two months after commencement of therapy, and in 6 of the 9 cases it was after five months. In 12 patients there was no change in fit frequency, and in one fit frequency improved. It was concluded that folic acid partially reverses both the retarding effects on the mental state of the three major anticonvulsant drugs and the therapeutic (anti-epileptic) effects of the drugs.

The points to which I particularly wish to draw attention in relation to the geriatric studies are: (1) that the symptoms which are quoted in the geriatric studies as evidence in favour of dietary folate deficiency are the very ones which respond most satisfactorily to folic acid in epileptic patients and (2) that prolonged drug-induced folate deficiency ultimately leads to dementia.

The findings in the epileptic patients, and their possible implications in both geriatric and non-geriatric psychiatry, take on added significance from the observation that the C.S.F. folate level in man is three times higher than that in the serum (Herbert and Zalusky, 1961), and that low levels can be found in epileptic patients on anticonvulsant drugs (Wells and Casey, 1967; Reynolds and Chanarin, 1967). I am not aware of any substance which is concentrated in the C.S.F. to this degree, and it may be presumed to reflect nervous system requirements for the vitamin.

Among the possible causes of low serum folate levels in the geriatric patients must be considered drug therapy. Only the three major anticonvulsants are definitely incriminated at the present time, but research into the effects of other psychoactive drugs in folate metabolism has not yet begun, and all forms of barbiturate therapy at least must be considered suspect.

It is already apparent that a high incidence of folate deficiency can be found in non-geriatric psychiatric patients (Hunter, Jones, Jones and Matthews, 1967) including depression (Reynolds, Coppen, Shaw, Herzberg and Chanarin, 1967), and the problems of its aetiology and significance are probably the same as in geriatric patients. Whatever may subsequently be proved to be the origin of the folate deficiency, it is a reasonable working hypothesis that it is aggravating the underlying mental disorder.

2. Dr. Shulman casts some doubt on a causal relationship between vitamin $B_{12}$ deficiency and affective disorders on the grounds that (1) either spontaneous or drug-induced remission of the mental state may occur before treatment with vitamin $B_{12}$, and (2) relapse may occur despite treatment with vitamin $B_{12}$. There are possible explanations for all these phenomena without undermining the general thesis of a direct causal relationship. Commonly, mental illness is the result of an interaction of many factors, and the environment may be just as important as the vitamin deficiency in some cases. Alleviation of these factors might be expected to result in improvement without any change in vitamin $B_{12}$ status. Spontaneous remission of the vitamin $B_{12}$ deficiency itself has been discussed by Strachan and

Henderson (1965), but there is a lack of positive proof of its occurrence in psychiatric patients (at the present time). Response of the mental illness to drug therapy before treatment of the deficiency state is not a strong argument, as it is probable that the effects of antidepressants, etc. are non-specific and may not be correcting the basic biochemical abnormality. Relapse while on vitamin $B_{12}$ therapy is a more powerful argument, but again there are possible explanations. Environmental factors may be relevant, but it is more probable that either (1) insufficient vitamin $B_{12}$ is being administered (it does seem that larger quantities of vitamin $B_{12}$ are required to induce a remission in the mental state than are needed for the haematological disorder), or (2) the patients are also suffering from folate deficiency. From the limited experience so far gained in epileptic patients, mental illness responds more satisfactorily to a combination of folic acid and vitamin $B_{12}$ than to folic acid alone.

Until we have a clearer understanding of the metabolic interrelationships of folic acid and vitamin $B_{12}$ both within and outside the nervous system and their relative roles in the production of psychiatric illness, the possibility that some patients need to be treated with both vitamins should be kept in mind.

3. Finally, the problem of satisfactory screening procedure for vitamin $B_{12}$ deficiency. This has recently been discussed in the correspondence columns of the *Lancet* following the publication of their experience with the antigastric-antibody test by Henderson, Strachan, Beck, Dawson and Daniel (1966). Dr. Shulman concludes from his findings that careful examination of a peripheral blood film is adequate. One hopes that too much weight will not be attached to this conclusion, as half of his patients with vitamin $B_{12}$ deficiency were already anaemic. One suspects that if his patients with pernicious anaemia at least had had vitamin $B_{12}$ levels assayed years earlier, they might not have reached such a state of advanced dementia as to render them unresponsive to treatment. Certainly epileptic patients can suffer from folate deficiency for many years without any detectable trace of this being found in the peripheral blood film (Reynolds *et al.*, 1966a).

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## WHAT THEY REALLY SAID

Dear Sir,

Perhaps the least creditable aspect of the careers of those two men of genius Freud and Jung was their bitter schism; and one of its most invidious accompaniments was the subsequent vendetta between their disciples. Outliving Freud by over thirty years, Jung seemed inevitably to have the last public word on most points of contention; but even so, neither he nor Freud ever claimed to have subjected the other to a personal analysis, nor to have received one at the other's hands.