completely obstructed by mucus, yet the deep glands were histologically normal.

Within the bronchitic group of biopsies, the degree of mucous change was not related to the use of tobacco or the presence of infection but depended on the duration of the disease. Anything more than slight change was only found in bronchitics with at least ten years' history, while the most severe changes occurred in patients with over twenty years' history.

Goblet cells are more easily studied in biopsy that in necropsy specimens. In the series referred to above, goblet cell hyperplasia was equally common in cases of bronchitis, asthma, and bronchitis with asthma. It bore no relation to the degree of mucoid change in the deep glands but was significantly more frequent where there was infection with *H. influenzae*.—I am, etc.,

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REFERENCES

1 Glynn, A. A., and Michaels, L., *Thorax*, 1960, **15**, 142.
2 Houston, J. C., De Navasquez, S., and Trounce, J. R., ibid., 1953, **8**, 207.

Megaloblastic Madness

SIR,—We would like to congratulate Dr. A. D. M. Smith (December 24, 1960, p. 1840) on his important paper. Dr. Smith refers to the results of our study of 14 male patients with tobacco amblyopia seen at the Bristol Eye Hospital which showed that an essential feature was a low vitamin-B_{12} concentration in the serum.[1] However, his statement that "unfortunately bone-marrow studies were not performed in this series" is not strictly accurate. It was, in fact, decided that biopsy of the sternal marrow should be undertaken in every case of tobacco amblyopia with histamine-fast achlorhydria and evidence of neurological involvement, irrespective of whether or not anaemia was present. Using this method of selection we found two patients had a megaloblastic bone-marrow and one patient a normoblastic marrow.

We certainly did not expect that low or very low serum vitamin-B_{12} levels would also be found in patients with free acid on gastric analysis, and in this clinical trial we did not feel justified in withholding treatment with cyanocobalamin till the results of microbiological assay were available in view of the frequency of severe and progressive deterioration of vision. Now, being wise after the event, we entirely agree with Dr. Smith that it would have been of considerable interest to know if biopsy of the marrow showed normoblastic or megaloblastic erythropoiesis in our remaining cases.

In this connexion, we would like to refer briefly to one of our cases included in our series. The presentation of tobacco amblyopia and mental changes, consisting of acute depression, irritability, lack of concentration, and failing memory, in a non-anaemic man, aged 52, is of particular interest. Although free acid was present in the gastric juice, the serum vitamin-B_{12} level was exceptionally low at 15 $\mu\mu$g./ml. We therefore suggested that in any case of unexplained peripheral neuropathy, myelopathy, or encephalopathy the concentration of vitamin B_{12} in the serum should be measured, *even if histamine-fast achlorhydria is not present*. The interesting findings of Dr. Smith add further support to this view.—We are, etc.,

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REFERENCE

1 Heaton, J. M., McCormick, A. J. A., and Freeman, A. G., *Lancet*, 1958, **2**, 286.

SIR,—May I plead that your contributors cease using the word "madness" when describing a new, or apparently new, diagnostic category? Apart from the fact that this word carries prejudices in both medical and lay circles, it can mislead: madness implies a pretty severe form of mental disorder whereas, as Dr. A. D. M. Smith points out at the beginning of his excellent paper (December 24, 1960, p. 1840), the mental symptoms in "megaloblastic madness" vary from the mildest to the most severe; and a mild neurotic reaction or mood swing is not "madness."

Nearly thirty years ago, when I reported a relevant case,[1] I was content to use the phrase "mental disease." It would be interesting to know whether there is a valid medical or social reason for the increasing use of the word "madness." If one of your readers can supply this, I shall resign myself to a series of articles, not only on "megaloblastic madness," but also on "myxoedematous madness," "diabetic madness," "syphilitic madness," "influenzal madness," and so forth.—I am, etc.,

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REFERENCE

1 Atkin, I., *Lancet*, 1932, **2**, 569.

Familial Pseudocholinesterase Deficiency

SIR,—Dr. F. D. Adrianvala (December 31, 1960, p. 1955) finds that none of the members of the family of a case of suxamethonium apnoea with low pseudocholinesterase was similarly affected. He is correct in concluding that "these results lend no support to the suggestion of any genetic behaviour on the part of pseudocholinesterase deficiency." We can furnish Dr. Adrianvala with hundreds of examples of patients with low pseudocholinesterase level where there is no evidence of inheritance, but equally also with dozens where family study has borne out a "genetic behaviour on the part of pseudocholinesterase deficiency." When the genetic deficiency was first postulated[1] it was made clear that pseudocholinesterase is low in the majority of cases because of liver disease, extreme malnutrition, etc., but that there had been instances where the clinical findings did not correlate with the laboratory results. When the families of such individuals with low pseudocholinesterase (usually discovered because of their sensitivity to suxamethonium) were investigated the picture of a familial deficiency emerged.[2-5]

Fortunately it is now possible to determine *in vitro* whether a low pseudocholinesterase level is of the inherited or the acquired type. Kalow and his collaborators found in Canada[6-8] that, in the familial type, normal enzyme is replaced by another which is not only less active but also shows a diminished sensitivity to inhibition by dibucaine (cinchocaine). The percentage inhibition is constant for any one individual and is independent of variations in enzyme level. Kalow has devised a test system in which plasmas from normal homozygotes lose 80% of their activity in the presence of dibucaine, and those of abnormal homozygotes are inhibited to only about 16%. Furthermore, whereas the range of pseudocholinesterase levels of heterozygotes overlaps at both ends with those found in abnormal and normal homozygotes, there is no such overlap in the range of pseudocholinesterase inhibition by dibucaine, which for heterozygotes lies midway between the 80% and 16% inhibition of normal and abnormal homozygotes respectively at about 60%.

In collaboration with Professor H. Harris and Dr. Mary Whittaker we have recently compared the pseudocholinesterase activity and the sensitivity towards dibucaine in