matter to try to disentangle malnutrition from the other environmental factors which handicap children in developing countries. For the purpose of prevention, the more we can sort these things out, the better. Admittedly everything possible must be done to prevent nutritional injury to the brain in the critical period; but if, as I believe, some measure of rehabilitation is possible, then the scope for action is wider, and extends throughout the period of the child's physical and mental development.

The articles in The Lancet and the British Medical Journal are evidence of the increasing interest in this subject. This is a testimony to the work of Herbert Birch. His sudden death is a severe setback to the advance of knowledge in a particularly difficult field, and a sad loss to those who worked with him. He was a pioneer, and a man of outstanding intellect, one of the very few who had a thorough understanding of both the biochemical and the psychological approaches to this problem.

The Jamaica study was, I believe, Birch's last major field project. It was an international cooperative effort of American, West Indian, and British workers. The Medical Research Council has come under criticism from some quarters because of the belief that there are economic standards of living. But an effect of variations in the relative prenatal survival-rates cannot be so easily dismissed. Leck and Record found that the high rates for anencephaly observed in Birmingham in 1954-59 were by no means consistently higher in the northern States. Indeed, the results of several recent studies suggest that some point in time the rates for anencephaly and spina bifida in the northern States may actually exceed those in the north. Contrary to the reports of decreasing anencephaly rates in New York State and Boston, reports from Alabama and the Carolinas suggest that the condition may be on the increase. A contrast in the secular mortality trends for spina bifida among White infants in north-eastern States (those included in the New England and Mid-Atlantic regions) and south-eastern States (South Atlantic and East-South Central regions) is shown in the accompanying figure. The rates prior to 1962 were adjusted by using the comparability ratio for spina bifida between the sixth and seventh revisions of the International Classification of Diseases, and by somewhat crudely estimating the effect of introducing the new I.C.S. number, 751B, in 1962. The latter procedure was performed by assuming a constant ratio for I.C.S. 751/751 + 752.

Because of the nature of the condition it seems unlikely that the reports of opposite secular trends between the north-eastern and south-eastern areas of the United States for anencephaly can be explained in terms of changes in diagnostic acumen, postnatal differential survival, or economic standards of living. But an effect of variations in the relative prenatal survival-rates cannot be so easily dismissed. Leck and Record found that the high rates for anencephaly observed in Birmingham in 1954-59 were by no means consistently higher in the northern States. Indeed, the results of several recent studies suggest that some point in time the rates for anencephaly and spina bifida in the northern States may actually exceed those in the north. Contrary to the reports of decreasing anencephaly rates in New York State and Boston, reports from Alabama and the Carolinas suggest that the condition may be on the increase. A contrast in the secular mortality trends for spina bifida among White infants in north-eastern States (those included in the New England and Mid-Atlantic regions) and south-eastern States (South Atlantic and East-South Central regions) is shown in the accompanying figure. The rates


SPINA BIFIDA, ANENCEPHALY, AND POTATO BLIGHT

Sir,—Renwick has claimed a similarity between the reported geographic patterns of potato blight and infant-mortality from spina bifida among United States White infants (there appears to be a lack of any noticeable geographic variation among non-White infants). On the basis of the variations by degrees longitude, this claim seems justified. The extent of the similarity by degrees latitude, however, is much less impressive. Along the eastern side of the United States the percentage of potato loss due to blight appears markedly higher among those States adjoining the Atlantic and the Gulf coasts, while the spina-bifida death-rates for White infants are by no means consistently higher in these northern States. Indeed, the results of several recent studies suggest that at some point in time the rates for anencephaly and spina bifida in the southern States may actually exceed those in the north. Contrary to the reports of decreasing anencephaly rates in New York State and Boston, reports from Alabama and the Carolinas suggest that the condition may be on the increase. A contrast in the secular mortality trends for spina bifida among White infants in north-eastern States (those included in the New England and Mid-Atlantic regions) and south-eastern States (South Atlantic and East-South Central regions) is shown in the accompanying figure. The rates

GLIADIN FRACTIONS IN CELIAC DISEASE

Sir,—We were interested in the letter of Dr Patey and Dr Evans (Feb. 3, p. 263), and are looking forward to reading about their fractionation methods of gliadin once these are published. We doubt that our gliadin fraction was contaminated with glutenin, because gliadin is the ethanolic extract of gluten and glutenins are insoluble in ethanol as well as in neutral salt solutions,19 as were used in our fractionation procedure. Further work has shown that high-molecular-weight material was indeed present also as a fraction.

This was found not to be "sub-

fractionated with glutenin, because gliadin is the ethanolic extract of gluten and glutenins are insoluble in ethanol as well as in neutral salt solutions,22 as were used in our fractionation procedure. Further work has shown that high-molecular-weight material was indeed present also in our "x" gliadin. This was found not to be "sub-

fractionated with glutenin, because gliadin is the ethanolic extract of gluten and glutenins are insoluble in ethanol as well as in neutral salt solutions,22 as were used in our fractionation procedure. Further work has shown that high-molecular-weight material was indeed present also in our "x" gliadin. This was found not to be "sub-

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FENFLURAMINE IN MANIA

SIR,—Two articles21,22 and subsequent correspondence have served to highlight the complexity and confusion in the understanding of the biochemistry of affective disorders. One way of increasing knowledge in this area is to study the changes in mood produced by drugs known to act on the central nervous system. Fenfluramine ("Ponderax") is such a drug and is believed to act pre-

dominantly on the serotoninergic system. A side-effect of fenfluramine is depression. The results of a two-weeks pilot study of the use of fenfluramine in mania are reported briefly here. 4 patients in hospital with severe symptoms of manic-depressive psychosis in the manic phase were studied. They had all experienced a persistent and morbid elevation of mood, continued (when he was speaking) to jump from one subject to another, and remained smiling and cheerful. He could produce several jokes immediately after physostigmine over 35 minutes.

Patient 2 is a 30-year-old man who has had five previous admissions for recurrent mania. He received 4-2 mg. of physostigmine over 35 minutes. In both patients physostigmine caused within 20 minutes an obvious change in behaviour. There was a reduction in talking and in associated gesturing; they became less active, less distractable, and much less aggressive in their verbal symptoms. All patients developed an anergic syndrome and some also became depressed. Our results agree substantially, but not completely, with these observations.

We carried out four physostigmine tests in three patients. Two patients were manic at the time of testing; the third, who was tested twice, had a corticosteroid-induced psychosis with both manic and confusional features. A single-blind design was used.

Patient 1 is a 55-year-old recurrent manic-depressive who relapsed into mania while taking lithium carbonate for prophylaxis. His plasma-lithium concentration had been falling and was 0-6 meq. per litre at the time of the test. He received 2-4 mg. of physostigmine over a 20-minute period.

Patient 2 is a 30-year-old man who has had five previous admissions for recurrent mania. He received 4-2 mg. of physostigmine over 35 minutes. In both patients physostigmine caused within 20 minutes an obvious change in behaviour. There was a reduction in talking and in associated gesturing; they became less active, less distractable, and much less aggressive in their verbal symptoms. All patients developed an anergic syndrome and some also became depressed. Our results agree substantially, but not completely, with these observations.

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