spina bifida; α -fetoprotein concentrations were raised in serum and amniotic fluid in all these cases. In eight women whose pregnancies were terminated the fetus had anencephaly and in all these cases the serum α -fetoprotein concentration was raised. Two cases of spina bifida were missed; both women had normal serum α -fetoprotein values, and in both cases the spina bifida was of the "closed" type. No normal pregnancies were terminated as a result of the screening. Generally we have found that patients are keen to have the test and this enthusiasm is shared by all those involved in running the programme, which makes for easier communication. Thus our experience differs from that of Susan Standing and her colleagues. We also consider the following points to be important.

(1) We regard serum α -fetoprotein screening as a means of identifying those patients at risk who require further investigation. Susan Standing and her colleagues suggest that they expect their programme to detect the fetuses with neural-tube defect and use amniotic fluid α -fetoprotein measurement merely to confirm. It is important to appreciate that the laboratory diagnosis of neural-tube defect can be made at present only by analysis of amniotic fluid. A pregnancy should not be terminated only on the basis of a raised serum α -fetoprotein concentration.

(2) Having amniotic fluid α -fetoprotein analysed in a laboratory different from the one analysing serum α -fetoprotein is a major disadvantage, leading to delays and difficulties in communication and transport of specimens and results. It is important that for any individual patient the chances of neural-tube defect are estimated by considering both the serum and the amniotic fluid results together³ by those who have worked out reference ranges for the population being screened.

(3) The use of commercial kits for the α -fetoprotein assay adds to the cost and is unnecessary now that reagents and a method protocol can be obtained within the Health Service. Information can also be obtained from the organisers of the National External Quality Assessment Scheme for α -fetoprotein. We find that addition of a crystal of sodium azide and storage of the specimen in a refrigerator at 4°C is adequate if the specimen is to be assayed within a few days. Samples which are frozen need time to thaw and each has to be adequately mixed before it is ready for analysis.

(4) We do not agree that a screening programme would detect preferentially fetuses that would perish spontaneously. The severity of a lesion is not necessarily related to the amount of α -fetoprotein exchange between fetal serum, amniotic fluid, and maternal serum compartments; and lesions classified as closed (and therefore undetectable by α -fetoprotein screening) may be severe and incompatible with life.

We agree that the distributions of α -fetoprotein concentrations for neural-tube defect and normal pregnancies overlap.⁴ This is one reason why it is more difficult to obtain cost-effective results with a screening programme in a low-incidence area. But by centralisation of laboratory services for a number of districts and the use of efficient low-cost techniques the laboratory costs of the programme can be kept to a minimum.

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³ UK Collaborative Study on Alpha-fetoprotein in Relation to Neural-tube Defects. *Lancet* 1979;ii: 651-61.

⁴ UK Collaborative Study on Alpha-fetoprotein in Relation to Neural-tube Defects. *Lancet* 1977;ii: 1323-32.

SIR,—Screening for neural-tube defects can be a disappointing business, as Dr Mary J Seller points out (7 November, p 1262), but it is doubly disheartening in an area of high incidence.

In Poole last year we screened, along conventional lines, 85% of the 2329 patients delivered. We detected seven cases of anencephaly and one of severe spina bifida at an early stage, and these pregnancies were terminated. However, we failed to detect three cases of spina bifida. One was booked at 19 weeks and was not screened. Another had a second serum α -fetoprotein level just above the normal range but this was accepted as normal by a locum registrar, and neither ultrasound nor maniocentesis was carried out. The third had a very low serum α -fetoprotein level, but an ultrasound examination much later in the pregnancy suggested that the fetus was much less mature than expected and that the blood test had been done at 11 weeks. None of these babies survived and the net result of the year's screening could fairly be said to be zero—or in fact a net loss, as one (possibly two) normal pregnancies were casualties of amniocentesis.

This is disappointing, but not necessarily an indication for discontinuing the programme. Our experience this year has been quite different. To date we have detected two anencephalics and one case of spina bifida and have missed a small closed encephalocele, which has been corrected surgically. No other neural-tube defects have been missed and the incidence so far this year is 2:1000 (4.3:1000 in 1980). This rather paradoxical variation in detection with incidence surely adds weight to the opinion that even two or three years may not be enough to assess such screening programmes.

The first conclusion we have come to about the programme in Poole is that the fewer people involved in its administration the better, and that these should be permanent staff members. Secondly prompted by our third missed spina bifida case in 1980, we have started scanning all patients with very low serum α -fetoprotein levels and are impressed by the detection rate of abnormality, an important aspect of which is mistaken maturity.

Another interesting factor in this profit-and-loss equation is whether the return from chromosome analysis of amniotic fluid obtained from patients screened is worthwhile. Dr Christine Gosden and others (24 January, p 255) concluded from their figures that it was not but our more limited experience is different. All our samples are sent for chromosome analysis. Last year we detected one case of trisomy 21 out of 87 amniocenteses performed for non-genetic reasons, and so far this year we have found one case of trisomy 13. This may be luck, but it has certainly encouraged us to continue the practice, and incidentally the neural-tube defect screening programme, pending more extensive experience of its value locally.

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Caution on preventing neural-tube defects

SIR,—In discussing dietary factors in the aetiology of neural-tube defects, Dr V C Talwalkar (3 October, p 917) states that the "Indian experience of neural-tube defects does not support the idea that poor diet may

have something to do with their causation." He goes on to argue against the possible importance of selective malnutrition in explaining the high rates among Punjabis. Interestingly, we suggested just the opposite in a paper discussing zinc deficiency and neural-tube defects.¹

Several years ago we suggested that the high rates of central nervous system malformations, particularly anencephaly, found in the Near East (Egypt and Iran) might be related to the zinc deficiency prevalent in that area.^{2,3} In a later paper, which more extensively reviewed the epidemiological and nutritional literature, we suggested that the high rates of anencephaly observed in Bombay and among Sikhs might be related to maternal zinc deficiency.¹ Our discussion focused on the potential importance of the chapatti, which contains high levels of phytate, as a dietary staple. Phytates interfere with zinc absorption, binding it and making it biochemically unavailable. Research on zinc deficiency has shown that a diet may appear adequate in nutritional content and yet be deficient in available zinc.¹

While I am not aware of any published studies on zinc deficiency in India, I hope that this discussion illustrates how a dietary factor could contribute to the aetiology of neural-tube defects in India. Recent data from Turkey support our earlier suggestion of a role for zinc deficiency in the aetiology of neural-tube defects in the Near East.⁴

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⁴ Sever LE. *Teratology* 1981;23:417.

Haemolytic disease of the newborn due to antibodies other than rhesus anti-D

SIR,—With reference to your leading article "Haemolytic disease of the newborn due to antibodies other than rhesus anti-D" (22 August, p 514), the results of a survey we have carried out in our department might contribute to the discussion. The investigation included all babies born in the Odense area during 1969-80 (about 35 000). Among these newborn babies 630 had evidence of haemolytic disease of the newborn as judged by a positive direct antiglobulin test. Rhesus anti-D was responsible in 145 cases (119 were newly immunised); 30 cases were due to irregular antibodies other than anti-D. Eventually we found 455 cases due to anti-A and anti-B. The prophylactic treatment of giving anti-D immunoglobulin to the Rh-negative mother immediately after delivery of a Rh-positive baby was started in March 1970.

The accompanying figure illustrates the distribution of new cases due to anti-D and the other irregular antibodies during the 12-year period. One to two years after the introduction of the prophylactic treatment a distinct decline in the number of new cases due to anti-D was seen. Since 1974 the frequency has been more or less unchanged (0 to 8 cases a year, mean 4.6 cases a year). However, the prevalence of irregular antibodies other than anti-D is the same during the 12-year period (0.6 cases a year, mean 2.5 cases a year). Out of the 30 cases of babies