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Maternal Phenylketonuria

SIR,-With reference to your leading article on this subject (24 October, p. 192), we have had in our care in recent years two pregnant phenylketonuric women.

The first patient made little of formal education (I.Q. 65), married, produced a phenylketonuric male child (phenylalanineloading suggested that the father was indeed heterozygotic) and after a gap of years again became pregnant. Abortion was declined. She had never previously received diet, her urine was positive for phenylketones, and her serum phenylalanine was 17 mg/100 ml. She was admitted to hospital and our usual dietary combination of Albumaid and a restricted daily phenylalanine intake from natural foods and phenylalanine-free preparations was begun. Nausea prevented her from full co-operation, however, and within a week she aborted. The conceptus was not examined.

The second patient's phenylketonuria was recognized in later childhood and she was never treated with diet. Her I.Q. is 55. She concealed the pregnancy until, it was thought, the 20th week. Therapeutic abortion was declined. She still had a positive urine test for phenylketones. The initial blood specimen went missing but her serum phenylalanine level 3 months after delivery was 24 mg/100 ml. The same dietary principles were employed but Aminogran was substituted for Albumaid. She took both with some difficulty and expressed no preference but had neither nausea nor vomiting. The serum phenylalanine was maintained between 3 and 12 mg/100 ml (average 7) and she delivered herself spontaneously at what was judged to be term. The male infant weighed 2,380 g, appeared well, showed no congenital anomalies, and in particular no phenylketonuria and no abnormalities of skull or skeleton on radiological survey, or of eye or heart. He is now 17 weeks old, is responsive, vocal, and has no obvious evidence of brain damage, although it is still too early to be sure that he has escaped it.

Within a few years from now the oldest of the successfully treated female children

in Edinburgh of normal intelligence approach puberty. If we have finally decided by that time that diet can be discontinued at some point in childhood without incurring brain damage, such women face a reimposition of diet in pregnancy when tolerance of strange tastes may be impaired. Diet is certainly more palatable than it was and further improvements can be anticipated. Nevertheless documentation of experience with such patients as the two described, whether the outcome is successful or unsuccessful, may provide guidelines for the future.

In the light of these events we are at last making a start on an experimental basis on testing all women attending an antenatal clinic. Since blood and urine are taken routinely, we shall use both the Guthrie and the Phenistix test. We are not so well informed about the effects of hyperphenylalaninaemia without phenylketonuria that we can feel confident about its benignity, and we are sufficiently informed about negative urine tests in phenylketonuria that we are unwilling to use them to exclude this disease in pregnancy.-We are, etc.,

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SIR,-I was interested to read your editorial (24 October, p. 192) on the occurrence of maternal phenylketonuria, but surprised that the writer showed so little foresight as to claim that: "The logical outcome of all these observations is that screening for phenylketonuria should become part of every antenatal examination." This kind of blanket statement on a screening procedure should never be made without carefully considering all the issues involved, a point which is cogently argued in a recent publication on screening.1

In the case of maternal phenylketonuria, I previously² drew attention to the fact that antenatal screening of a population originally screened as newborn would be expected to result in the detection, on average, of only one case of maternal phenylketonuria among total pregnancies (births) in the United Kingdom over a fiveyear period. If a previously unscreened population is to be considered, the number of pregnancies at risk will depend almost entirely upon the numbers of women with phenylketonuria and relatively normal intellect. The frequency of such persons² is probably between 1 x 10-5 and 2.5 x 10-6. Since the economic justification for screening neonates for phenylketonuria has been called in question,34 screening for a condition between 10 and 100 times less frequent would be exceedingly difficult to support on economic grounds. It may be noted that the above frequency of cases of maternal phenylketonuria (unscreened population) is of the same order of magnitude as the frequency of "missed" cases of phenylketonuria in newborn using the single Guthrie test⁵, a British study⁶ has concluded that this frequency did not warrant the use of a second test in order to ascertain those cases missed by the first.

It is worth pointing out that the number of maternal phenylketonuria cases which might be detected in such a screening programme would be even less if one had previously screened from the population the known high-risk individuals, such as female sibs of known phenylketonuria patients, and mothers of one or more children with severe non-specific mental retardation-also suggested in your leading article, and with far greater justification. An additional point of great importance² is the action to be taken upon discovering a pregnant woman apparently homozygous for phenylketonuria, but your leading article did not discuss this issue.