reticular system. These findings could help in the differentiation of the similar histiocytic disorder of Letterer-Siwe disease. Chromosomal analysis should be extended to include bone marrow cells and the histiocytic cell line. The demonstration of an XX cell line in a male patient would obviously be strong evidence of chimerism. These studies might also help to clear up the doubt about the malignant nature of the histiocytes.

It has been suggested (Buist *et al.*, 1971) that the disease may be a recessively inherited malignancy. The evidence is from the occurrence of this rare disease in sibs and first cousins (Goodall, Guthrie, and Buist, 1965). It may be of relevance that the patient in this latest report was born of a cousin marriage.

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Dr. G. Blennow comments as follows:

Drs. Wainscoat and Hann point to three observations that they consider are against a state of chimerism. We would like to comment on their remarks.

(1) In the case of a graft rejection, the peripheral blood lymphocytes are expected to be of host origin as in our patient.

(2) One characteristic feature of haemophagocytic reticulosis is remarkable increase in phagocytic reticulo-endothelial cells in various organs. It is possible that grafted, antibody-coated Rh-negative erythrocytes were rapidly eliminated by these phagocytic cells and therefore escaped detection in the mixed field tests.

(3) The antiglobulin test was negative. As mentioned, grafted cells may well be rapidly phagocytosed *in vivo*. However, the results of the erythrophagocytosis experiments *in vitro* may indicate that a few red cells coated by antibody were actually present in the patient's peripheral blood.

We cannot therefore agree that the three observations mentioned are definitely against a state of chimerism. In our report it was not claimed that chimerism was

proven in our patient. However, we suggested that future cases of haemophagocytic reticulosis should be examined with such a possibility in mind. As pointed out by Drs. Wainscoat and Hann, karyotype analyses of the bone marrow would then be of great importance.

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Phenylalaninaemia

Sir,

The article on phenylalaninaemia by Blaskovics, Schaeffler, and Hack (1974) is timely in that it emphasizes the need for careful evaluation of all suspected cases of phenylketonuria; some patients may be in danger if treatment is too restrictive, others may not need any dietary treatment. The rather complex classification proposed by the authors receives some support from their own observations, but may need to be modified when improved techniques permit more accurate studies of enzyme activities. We prefer the simpler and more practical classification given by Scriver and Rosenberg (1973). They cover 5 types described by Blaskovics *et al.*, in three groups. (1) 'Classical' phenylketonuria. (2) Phenylketonuria ('mild' variant with relaxed phenylalanine tolerance). (3) Phenylketonuria ('transient' variant).

This grouping is more helpful in the clinical context. The authors stress the importance of estimating the daily phenylalanine tolerance of patients on treatment; in the variant forms this is usually over 500 mg/day.

We estimated the daily phenylalanine intake required by 24 of our patients on a low phenylalanine diet at some point between the ages of 11 and 13 months, and at a time when the serum phenylalanine was at an acceptable level. In 18 cases the intake was between 275 and 450 mg/day (mean 365, 2 SD 120). They are all, to the best of our knowledge, cases of classical phenylketonuria. 5 patients were able to tolerate 500 to 600 mg phenylalanine/day. 4 of these returned to normal diet between the ages of 1 year 3 months and 3 years. On normal diet one patient maintains a serum phenylalanine level of 2-3 mg/100 ml, in the other 3 the range is 7-13 mg/100 ml. These 5 children are all developing normally. All show impaired phenylalanine tolerance on a loading test, giving curves above that expected from a heterozygote, but below that of a child with classical phenylketonuria. Perhaps none needed treatment, yet at the time of diagnosis all but one had a serum phenylalanine above 20 mg/100 ml and metabolites of phenylalanine were detected in the urine. The fifth 'atypical' patient tolerated exactly 500 mg phenylalanine/day but was maintained on a diet for 7 years because she had 2 mentally retarded sibs.

Our present practice is to start treatment if the serum