6. D. D. Woods, *Brit. J. Exptl. Pathol.* 21, 74 (1940).
7. E. R. Waygood, *Methods in Enzymology* (Academic Press, New York, 1955), vol. 2, pp. 836–846.
8. I. Dyrendahl, *Nord, Veterinärmed.* 6, 873 (1954).
9. The Diamox was supplied by the Lederle Laboratories Division, American Cyanamid Co.
10. This work was supported in part by a grant from the Rockefeller Foundation.

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New "Fast" Hemoglobin Associated with Thalassemia

To date, through electrophoresis, four variants of human hemoglobin with higher anodic mobility than normal adult hemoglobin have been recognized (hemoglobins H, I, J, and K) (*1*). Recently we identified another "fast" hemoglobin in the cord blood of a full-term infant. Through paper electrophoresis of hemoglobin solutions in both barbitone (*p*H 8.8; $\Gamma/2$, 0.025) and phosphate (*p*H 6.5, 0.03*M*) buffer, two spots were obtained: a large one, corresponding to a mixture of hemoglobins F and A, and a smaller one which migrated toward the anode. Comparison of the latter with hemoglobin H (*2*) proved that H is of higher anodic mobility in both alkaline and acid buffers (Fig. 1); it was possible to separate the artificial mixtures in both buffers. The new hemoglobin also differs from hemoglobin I (*3*); at *p*H 6.5, hemoglobin I showed almost no separation from hemoglobin A, while the new hemoglobin migrated clearly away from A. Hemoglobin I, of all fast hemoglobins with the exception of H, takes a more anodic position in acid buffer (*4*). Consequently, the new hemoglobin differs from both hemoglobins J and K, which on paper at *p*H 6.5 resolve less than hemoglobin I (Fig. 2).

The new hemoglobin is not alkali-resistant. At the birth of the infant it amounted to 14 percent of the total (determined by elution), the content of hemoglobin F being 60 percent, and of A, 26 percent. The infant was neither anemic nor icteric. During the next 3 months there was a progressive reduction in the amount of the fast fraction present to 4 percent, and of hemoglobin F, to 20 percent.

An investigation of the infant's family showed that the mother has thalassemia major, while the father has thalassemia minor. Three of the grandparents, all having thalassemia minor, originated from the same village in Asia Minor (Fig. 3). Consanguinity is denied by them. The results of genotyping with eight antisera were consistent with the claimed parentage. Fast hemoglobin was found in neither the parents nor in the relatives who were examined. The hematologic and genetic data indicate that the infant definitely carries one, and possibly two, doses of the thalassemia gene (*5*).

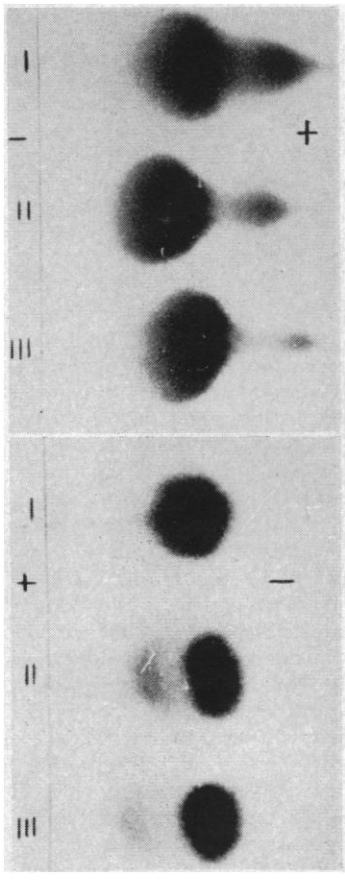

Fig. 1. Electrophoresis of (I) hemoglobin I + A, (II) new hemoglobin and A + F, (III) hemoglobin H + A. (Top) Electrophoresis in barbitone buffer (*p*H 8.8; $\Gamma/2$, 0.025; 10 hr, 0.3 ma/cm; Whatman No. 3). (Bottom) Electrophoresis in phosphate buffer (*p*H 6.5; 0.03 *M*; 5 hr, 1 ma/cm, Whatman No. 3).

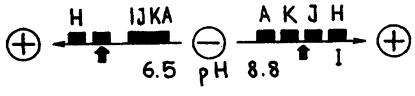

Fig. 2. Schematic representation of relative positions of "fast" hemoglobins as found through paper electrophoresis. Arrows indicate the position of the new fraction.

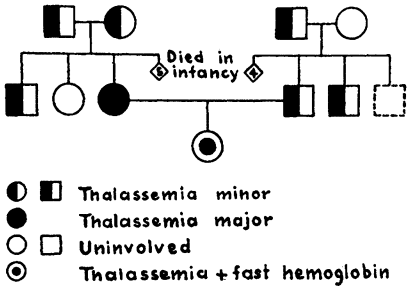

Fig. 3. Family tree showing occurrence of thalassemia and new "fast" hemoglobin.

The presence of the abnormal hemoglobins S, C, D, E, I, J, and K is genetically determined, and the abnormal component is always found in at least one parent of affected persons. Hemoglobin H differs from these in that it appears in the phenotype only in association with the thalassemia gene (*2*, *6*). The appearance of the hemoglobin under study could be compared with the genetic behavior of H; this hemoglobin differs from H, however, since neither the father, who has one dose of the thalassemia gene, nor the mother, who has a double dose, shows the abnormal component. The data on hand are suggestive that this may be an abnormal form of fetal hemoglobin, hitherto not recognized, which found expression because of its association with the thalassemia gene. An alternative explanation could be that we are in the presence of a mutation.

The thalassemia gene, although it is not responsible for the synthesis of a specific abnormal hemoglobin, is considered to be the causative factor of such alterations of the hemoglobin pattern as (i) the persistence of a high percentage of fetal hemoglobin beyond infancy; (ii) the increase of hemoglobin A_2 several times above normal (*7*, *8*); (iii) the increased production of hemoglobins S, C, E, and possibly G (*9*) when associated with the respective genes thereof; and (iv) the "phanerosis" of hemoglobin H. In the present case, a further alteration seems to have been caused by the thalassemia gene (or genes), the abnormal component being already present at birth. Further investigations on new-born infants likely to be affected by thalassemia are necessary (*10*).

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References and Notes

1. H. Lehmann, *Blood* 12, 90 (1957).
2. This hemoglobin was obtained from patients on whom a report was made previously [A. Gouttas *et al.*, *Le Sang* 26, 911 (1955)]. It has been compared with and found identical with hemoglobin H [described by D. A. Rigas, R. D. Koler, E. E. Osgood, *Science* 121, 372 (1955)]. We are indebted to Dr. Rigas for the comparison.
3. Kindly supplied by Dr. R. Cabannes, Algiers, Algeria.
4. A. R. Robinson *et al.*, *Blood* 11, 902 (1596).
5. A detailed report is in preparation.
6. A. G. Motulsky, *Nature* 178, 1055 (1956).
7. H. G. Kunkel and G. Wallenius, *Science* 122, 288 (1955).
8. Unpublished observations.
9. H. C. Schwartz *et al.*, *Blood* 12, 238 (1957).
10. In order to avoid confusion, we postpone assigning a letter to this hemoglobin until all workers in the field are in agreement.

5 September 1957