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EDITORIAL: INHERITANCE PATTERNS IN MEDITERRANEAN ANEMIA AND SICKLE CELL ANEMIA

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EDITORIAL

INHERITANCE PATTERNS IN MEDITERRANEAN ANEMIA AND SICKLE CELL ANEMIA

IT HAS been amply demonstrated in recent years that the severest form of Mediterranean anemia known as Cooley's anemia, occurs in certain children, both of whose parents show mild forms of the disease.^{1, 2, 3}

These mild forms are transmitted by either parent in a mendelian dominant fashion and such individuals with the mild target cell or leptocytic disease may be said to be heterozygous for the condition. On the other hand, cases of the severe disease appear to be homozygous for the hereditary trait. The marriage of two heterozygous individuals results (at least theoretically and in accordance with mendelian laws of inheritance) in 50 per cent severe cases, 25 per cent mild or heterozygous and 25 per cent without any evidence of the disease.

Mediterranean anemia and sickle cell anemia show many points of similarity.² Both conditions occur primarily in special racial groups; target cells and increased resistance to hypotonic salt solutions are common to both; the anemia does not respond to either the use of iron or splenectomy. Cases of sickle cell anemia have furthermore been described in individuals of Italian and Greek origin,^{1, 2} and cases of apparently typical Mediterranean anemia are occasionally found in Negroes.⁴ As we have previously stated it is possible that both disorders may represent variants of a single larger hereditary abnormality characterized by an abnormal hemoglobin metabolism and defective, unusually thin red cells.

If the heredity of Mediterranean anemia is by now well known, that of sickle cell anemia has, at least until recently, eluded investigation. In line with the inheritance pattern in the former disease, it seemed possible that severe sickle cell anemia might be due to the inheritance of the sickle cell trait from both parents.^{2, 5}

The trait itself has been shown to be inherited as a simple mendelian dominant and it seemed likely, therefore, as Neel⁶ recently stated, "that there existed in Negro populations a gene which in heterozygous condition results in sickle cell anemia, and in homozygous condition in sickle cell anemia."

Previous studies of the parents of patients with sickle cell disease had revealed no definite pattern of heredity; in fact, in most instances, only an occasional parent was found to have the sickle cell trait. On the other hand, Neel⁶ who tested 42 parents of 29 patients with sickle cell anemia, found that "every parent tested to date has sickled."

Neel placed especial reliance for the sickle cell test on a combination of the technics described by Scriver and Waugh⁷ and by Hansen-Pruss.⁸ A tourniquet was applied to the finger for three to five minutes and then a drop of static blood from the finger was placed on a slide containing a small amount of Janus green or methylene blue; the preparation was then covered with a coverslip, which was sealed with vaseline and examined at intervals up to seventy-two hours. Five preparations were routinely made. It was felt that the variable results obtained

by other observers might be explained in terms of lack of familiarity with the technics necessary to elicit sickling.

This important observation will of course require confirmation from other sources before it can receive complete acceptance. However, the results by this experienced geneticist are so clear cut and at the same time so logical that negative results by other workers will, from now on, require considerable scrutiny. That the sicklers are heterozygous and the cases of sickle cell anemia homozygous explains much that has hitherto remained obscure. Nevertheless, the reason for red cell sickling and the exact difference between the red cells of the sickle cell trait and those of sickle cell anemia remain as mysterious as ever.

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