The Absence of Close Linkage of Methemoglobinemia and Blood Group Loci

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HEREDITARY METHEMOGLOBINEMIA due to a limited capacity of the red cell to reduce methemoglobin (Gibson, 1948) has been shown to be due to complete absence of a DPNH diaphorase in the cells (Scott and Griffith, 1959). It is possible by enzymatic means to distinguish with fair certainty heterozygous from normal individuals (Scott, 1960). An attempt was therefore made to test for possible genetic linkage between the enzymatic type of methemoglobinemia and several blood group loci.

METHODS

The population studied consisted of 49 families with evidence of the recessive gene for methemoglobinemia. With one exception (a Navajo family) all were Athabaskan Indians or Eskimos, with some Caucasian admixture. DPNH diaphorase was determined as previously described (Scott, 1960). Transferrin and haptoglobin types were determined by starch gel electrophoresis as described by Smithies (1959). Probability of linkage was calculated by the method of Morton (1955).

RESULTS AND DISCUSSION

In 33 families, at least one parent was heterozygous both for methemoglobinemia and for one or more blood group loci. All samples tested were Lu(a—b+), Mi(a—), Vw—, Be(a—), Wr(a—), and Di(a—), and all had type C transferrin. The results on the 33 families are summarized in Table 1. Except for the Kell locus, where insufficient data are available, linkage between methemoglobinemia and any of the loci must be quite loose if it occurs. It is possible that a linkage of Rh and methemoglobinemia with a recombination fraction of about 0.3 might be demonstrated if a larger number of families could be studied.

The difficulty in classifying a small fraction of the samples as heterozygous for methemoglobinemia or as normal has been previously discussed (Scott, 1960). In this study, no family was included unless evidence of the recessive

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TABLE 1. PROBABILITY OF LINKAGE OF ENZYMATIC METHEMOGLOBINEMIA AND BLOOD GROUP LOCI

Locus	No. of Families	No. of Children	Log Probability of Linkage for Recombination Fraction of: 0.05	0.1	0.2	0.3	0.4
ABO	9	32	—5.3	—3.1	—1.2	—0.4	—0.1
MNS	26	95	—16.5	—8.6	—2.6	—0.5	0
Rh	12	47	—3.2	—0.8	0.6	0.7	0.2
Duffy	5	19	—1.3	—0.4	0.1	0.2	0.1
Kidd	13	48	—6.4	—3.1	—1.0	—0.2	0
P	4	11	—1.0	—0.4	0.1	0.1	0
Kell	1	4	0.8	0.7	0.5	0.3	0.1
Haptoglobin	4	9	—0.7	—0.2	0	0	0

All samples tested with anti-A, B, A+B, A_1; M, N, S, s; C, C^w, c, D, E, e, f (ce); Fy^a, Fy^b; Jk^a, Jk^b; P_1; K, k, Kp^a, Kp^b.

gene was found in at least two family members. Only one case was found of a child, apparently heterozygous for methemoglobinemia, with normal parents. This family and the child with the possible recombination of MN and S genes (Lewis *et al.*, 1963) were excluded from the study.

SUMMARY

Evidence was sought for genetic linkage of hereditary methemoglobinemia of the enzymatic type and the blood group loci ABO, MNS, Rh, Duffy, Kidd and P and the haptoglobins. From the study of 33 families, it is concluded that linkage with any of these loci is unlikely and must be quite loose if it occurs.

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