STUDIES IN HUMAN INHERITANCE XXXIV. FURTHER DATA ON THE LINKAGE OF THE GENES FOR SICKLE CELLS AND THE M-N BLOOD TYPES

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The demonstration of linkage between human genes has long been an ideal of laboratories of human genetics. Many studies have been made along this line, mostly with negative results. A few instances of probable linkage have been reported (Penrose, 1935; Haldane, 1936; Burks, 1937; Rife, 1941, Hoogvliet, 1942; Snyder and Palmer, 1943; Kallis and Schweitzer, 1943; Penrose, 1946; Kloepfer, 1946), but these have largely involved either sex-linked characters or variable traits, the exact hereditary nature of which is not known. For a comprehensive summary of the linkage studies carried out to date, see Kloepfer, 1946.

Recently we presented evidence for the first instance of autosomal linkage involving proved unit factors (Snyder, Russell and Graham, 1947). Both coupling and repulsion phases were demonstrated. This discovery was of sufficient importance to warrant the intensive search for more data. We have therefore concentrated our attention on the obtaining of families showing the sickle cell trait, in which the sickle cell parent was type MN. We have found a number of such families, and some of them are of suitable nature to provide linkage data. The additional families uphold the hypothesis that the genes for sickle cells and for the M-N types are linked, and that the gene for sickle cells is transmitted independently of the genes for the A-B groups and the Rh types.

The complete data, including those of Snyder, Russell and Graham, are presented below. For the association between sickle cells and the M-N types (Table I), the total score (summation of λ) is seen to be 12.72, with a variance

TABLE I

LINKAGE DATA ON THE GENES FOR SICKLE CELLS AND THE M-N BLOOD TYPES

Finney Type	Family Number	a	b	c	d	γ	K
3	30	2	0	0	0	1.00	1.000
4	7	3	0	0	1	6.00	6.000
4	8	1	0	0	2	3.00	3.000
4	11	1	2	1	0	0.00	6.000
4	17	0	1	0	1	—1.00	1.000
18	37	1	1	1	0	—0.11	0.549
18	38	1	0	4	1	—0.78	1.987
18	39	3	0	0	1	3.83	0.941
18	40	0	1	2	0	0.78	0.549
						12.72	21.026

(summation of K) of 21.026. Since the total score exceeds 2.33 times the square root of the variance (12.72 exceeds 10.69), the evidence against the hypothesis of random assortment is significant at the one percent level.

The crossover percentage (c) may be estimated from the formula $c = \frac{1}{2}\left(1 - \sqrt{\frac{\Sigma\lambda}{\Sigma K}}\right)$, which gives a value of 0.111.

For the record, the corresponding tables for the A-B blood groups and the Rh types are also presented (Tables II and III), indicating the independent transmission of these genes and the gene for sickle cells. In neither case does the total score even approach the square root of the variance.

Finney's modifications of Fisher's methods were used throughout the analyses (Finney, 1940).

TABLE II

LINKAGE DATA ON THE GENES FOR SICKLE CELLS AND THE A-B BLOOD GROUPS

Finney Type	Family Number	a	b	c	d	γ	K
5	1	1	1	1	2	—2.000	10.000
5	15	1	1	0	0	—1.000	1.000
5	20	2	1	1	2	—1.000	15.000
5	30	1	1	0	0	—1.000	1.000
5	34	2	0	2	0	—2.000	6.000
5	35	1	1	2	1	—2.000	10.000
6	16	1	1	0	0	—0.333	0.238
7	36	0	0	2	2	—0.222	1.333
7	37	1	0	1	1	—0.111	0.778
7	38	2	0	3	1	—0.500	2.778
7	39	1	0	2	1	—8.444	1.333
						—18.610	49.460

TABLE III

LINKAGE DATA ON THE GENES FOR SICKLE CELLS AND THE RH BLOOD TYPES

Finney Type	Family Number	a	b	c	d	γ	K
5	5	1	0	1	2	0.000	6.000
5	6	0	1	1	0	1.000	3.000
5	10	1	1	0	0	—1.000	1.000
5	12	3	0	1	0	0.000	6.000
5	30	1	1	0	0	—1.000	1.000
6	8	1	0	0	2	1.666	0.549
6	16	1	0	1	0	—0.111	0.238
7	38	3	1	2	0	—0.555	2.778
7	39	1	2	0	1	—1.333	1.333
7	40	2	0	0	1	0.778	0.778
8	36	1	1	1	1	—1.037	0.836
						—1.502	23.512

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