The Dombrock System: Linkage Relations with Other Blood Group Loci

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The recognition of the blood group system called Dombrock was reported in 1965 by Swanson and her colleagues. In 1967 Tippett gave an account of the genetics of the system which included an analysis of the linkage relations of the *Do* locus to other blood group loci, based on families tested in the MRC Blood Group Unit up to April 1966. The present account brings the linkage analysis up to the end of May 1972. As before, the calculations were by the method of Morton (1955) as instructed by Maynard Smith, Penrose, and Smith (1961).

The earlier series of families served to exclude close linkage between *Do* and any of the other loci but in certain comparisons the lod scores were positive for recombination fractions ranging from 0.2 upwards, as may be seen in the Appendix and the Table. These positive scores were small but left open the possibility that a linkage might ultimately be detectable. The addition of the present series of families has reduced the possibility of linkage of *Do* with *Rh* and with *Fy* (Appendix) but increased the evidence for linkage between *Do* and *MNSs* (Table).

The antilogs of the total *Do*:*MNSs* lod scores in the Table, plotted in Fig. 1, show the relative probabilities of the recombination fractions when the scoring was through males, through females, and through either parent.

That the slight evidence of linkage between *Do* and *MNSs* is given when scored through doubly heterozygous females as well as males may be a warning that chance rather than linkage may be responsible for our results. The increased recombination rate in the human female, recognized by Cook (1964/1965) and by Renwick and Schulze (1964/1965), has now been observed in several linkages. If θ' for the male were indeed about 0.33 as hinted by our data (Fig. 1) then the females would not be expected to give any indication of linkage. However, as Cook and his colleagues

FIG. 1. *Do* and *MNSs*: relative probabilities of the various recombination fractions given in the Table. Δ = scored through males ($\theta' = 0.33$); $\bullet$ = scored through females ($\theta = 0.37$); $\times$ = scored through males and females ($\theta' + \theta = 0.34$).

(1971/1972) point out, an increased female rate of recombination does not apply to all of the linkages in the mouse (Dunn and Bennett, 1967) so may not apply to all in man.

The most straightforward evidence in favour of a *Do*:*MNSs* linkage is to be found in the Table in the phase-known non-recombinant and recombinant children of doubly heterozygous males (6 non-recombinants:2 recombinants) and doubly heterozygous females (9 non-recombinants:3 recombinants). This ratio of 15:5 departs significantly from the 50:50 expected if there were no linkage ($\chi^2_1 = 5.0$, $p = 0.03$).

If the testing of further families eventually confirms linkage between *Do* and *MNSs* then will be the time to try to organize the testing of families with the rare condition *gnodermatose sclro-atrophiant* (sclerolyosis) the locus for which is known to be linked to *MNSs* (Mennecier, 1967; Deminatti *et al*, 1968).

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TABLE
A SUGGESTION OF LINKAGE BETWEEN *Do* AND *MNSs*: LOD SCORES

Doubly Heterozygous Parents	No. of Scoring Parents: Children		Phase-known Non-recombinant: recombinant		Recombination Fraction							
					0.05	0.1	0.2	0.25	0.3	0.35	0.4	0.45
<i>Males</i>												
First series	30	110	3	1	-11.253	-5.014	-0.559	+0.254	+0.540	+0.573	+0.382	+0.158
Present series	17	48	3	1	-5.242	-2.416	-0.396	-0.032	+0.130	+0.175	+0.146	+0.080
Sum					-16.495	-7.430	-0.955	+0.222	+0.670	+0.748	+0.528	+0.238
Antilogs							0.11	1.67	4.68	5.60	3.37	1.73
<i>Females</i>												
First series	23	81	6	3	-13.880	-7.458	-2.256	-1.106	-0.348	+0.008	+0.148	+0.107
Present series	16	51	3	0	-4.790	-1.732	+0.370	+0.734	+0.625	+0.625	+0.416	+0.179
Sum					-18.670	-9.190	-1.886	-0.427	+0.386	+0.633	+0.564	+0.286
Antilogs							0.01	0.37	2.43	4.30	3.66	1.93
<i>Males and females</i>												
First series	53	191	9	4	-25.133	-12.472	-2.815	-0.852	+0.192	+0.581	+0.530	+0.265
Present series	33	99	6	1	-10.032	-4.148	-0.026	+0.647	+0.864	+0.800	+0.562	+0.259
Sum					-35.165	-16.620	-2.841	-0.205	+1.056	+1.381	+1.092	+0.524
Antilogs							0.00	0.62	11.38	24.04	12.36	3.34

We look back with regret on many fine families tested in the Unit in the last few years who were not tested for the Dombrock groups; but now having woken up to the possibility of linkage, we shall find time to use anti-*Do*^a on all appropriate family samples.

Summary

A second series of families tested in the MRC Blood Group Unit for the Dombrock blood groups strengthens a hint of linkage between *Do* and *MNSs* given by the first series: if the linkage should become established the present scores suggest that the most likely recombination fraction will prove to be about 0.33. Linkage between *Do* and other blood group loci was either ruled out or made unlikely.

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Appendix

Failure to Detect Linkage between the Dombrock Locus and Loci for Some Other Blood Group Systems: Lod Scores*

Loci	Transmission through Doubly Heterozygous Males								
	No. of Scoring Fathers: Children		Phase-known Non-recombinant: Recombinant		Recombination Fraction (θ')				
					0.05	0.1	0.2	0.3	0.4
<i>ABO</i>									
First series	28	111	0	5	-24.250	-14.474	-6.079	-2.454	-0.722
Present series	16	54	0	0	-10.180	-5.790	-2.176	-0.732	-0.151
Sum					-34.430	-20.264	-8.255	-3.186	-0.873
<i>P</i>									
First series	5	19	0	0	-3.694	-2.110	-0.788	-0.255	-0.048
Present series	7	24	0	0	-0.170	+0.197	+0.320	+0.209	+0.064
Sum					-3.864	-1.913	-0.468	-0.046	+0.016
<i>Rh</i>									
First series	27	100	4	0	-13.185	-6.404	-1.418	+0.111	+0.280
Present series	22	79	0	0	-14.367	-7.983	-2.806	-0.870	-0.161
Sum					-27.552	-14.387	-4.224	-0.759	+0.119
<i>Lu</i>									
First series	3	13	1	1	-3.396	-2.042	-0.858	-0.345	-0.074
Present series	4	11	0	0	-1.522	-0.948	-0.423	-0.167	-0.039
Sum					-4.918	-2.990	-1.276	-0.512	-0.113
<i>K</i>									
First series	4	14	0	0	-2.307	-1.302	-0.488	-0.167	-0.035
Present series	3	8	0	0	-2.884	-1.775	-0.776	-0.303	-0.071
Sum					-5.191	-3.077	-1.264	-0.470	-0.106
<i>Fy</i>									
First series	12	36	0	0	-1.917	-0.401	+0.486	+0.471	+0.180
Present series	5	20	0	0	-5.512	-3.336	-1.418	-0.542	-0.125
Sum					-7.429	-3.737	-0.932	-0.071	+0.055
<i>Jk</i>									
First series	13	40	1	2	-6.859	-3.790	-1.319	-0.406	-0.101
Present series	9	24	0	1	-4.017	-2.251	-0.842	-0.314	-0.104
Sum					-10.876	-6.041	-2.161	-0.720	-0.205
<i>Yt</i>									
First series	2	8	0	0	-2.163	-1.331	-0.582	-0.227	-0.053
Present series	0				-2.163	-1.331	-0.582	-0.227	-0.053
Sum									
<i>Co</i>									
First series	0								
Present series	1	2	0	2	-2.000	-1.398	-0.796	-0.444	-0.194
Sum					-2.000	-1.398	-0.796	-0.444	-0.194
<i>Se</i>									
First series	2	6	0	0	-1.145	-0.635	-0.226	-0.072	-0.015
Present series	3	9			-1.395	-0.849	-0.364	-0.140	-0.033
Sum					-2.540	-1.484	-0.590	-0.212	-0.048
<i>Le</i>									
First series	1	3	0	0	-0.769	-0.482	-0.216	-0.086	-0.020
Present series	0				-0.769	-0.482	-0.216	-0.086	-0.020
Sum									

* In the present series, as in the first, practically all the information comes from z_1 scores. In the first series the comparatively uninformative z_2 and z_3 scores were also used on the relatively few families to which they applied: in the present series z_2 and z_3 scores were ignored, except when they could contribute to comparisons in which information was slight (*P*, *Lu*, *K*, and *Se*).

In this table the incidence of phase-known children is much higher when transmission is through females than when through males, and this requires explanation: very many of the families were primarily tested in connection with X-linkage and parents of mothers were specially sought out, thus providing 3 generation information; no special effort was made to get samples from parents of fathers.

Transmission through Doubly Heterozygous Females									Loci
No. of Scoring Mothers: Children		Phase-known Non-recombinant: Recombinant		Recombination Fraction (θ)					
				0.05	0.1	0.2	0.3	0.4	
17 14	60 47	3 3	5 1	-12.407 -6.158 -18.565	-7.167 -2.960 -10.127	-2.735 -0.544 -3.279	-0.952 +0.160 -0.792	-0.228 +0.182 -0.046	<i>ABO</i> First series Present series Sum
3 8	20 29	0 0	0 0	-2.012 -4.113 -6.125	-1.006 -2.444 -3.450	-0.230 -0.979 -1.209	+0.009 -0.377 -0.368	+0.027 -0.070 -0.043	<i>P</i> First series Present series Sum
21 23	72 63	5 4	3 7	-12.775 -13.993 -26.768	-7.079 -8.034 -15.113	-2.429 -3.117 -5.546	-0.648 -1.158 -1.806	-0.033 -0.354 -0.387	<i>Rh</i> First series Present series Sum
1 2	3 5	0 0	0 0	-0.769 +0.057 -0.712	-0.482 +0.043 -0.439	-0.216 +0.021 -0.195	-0.086 +0.008 -0.078	-0.020 +0.002 -0.018	<i>Lu</i> First series Present series Sum
1 7	7 32	0 0	0 0	-0.658 -4.959 -5.617	-0.392 -2.805 -3.197	-0.162 -0.996 -1.158	-0.061 -0.281 -0.342	-0.013 -0.039 -0.051	<i>K</i> First series Present series Sum
14 9	49 23	2 3	4 4	-9.380 -4.976 -14.356	-5.275 -2.946 -8.221	-1.892 -1.220 -3.112	-0.610 -0.496 -1.106	-0.172 -0.154 -0.326	<i>Fy</i> First series Present series Sum
8 6	21 17	0 2	1 2	-4.810 -2.557 -7.367	-2.932 -1.325 -4.257	-1.258 -0.384 -1.642	-0.549 -0.081 -0.630	-0.170 -0.007 -0.177	<i>yk</i> First series Present series Sum
1 0	8	0	0	-1.906 -1.906	-1.116 -1.116	-0.448 -0.448	-0.163 -0.163	-0.036 -0.036	<i>Yt</i> First series Present Series Sum
0 2	6	1	1	-2.164 -2.164	-1.331 -1.331	-0.582 -0.582	-0.227 -0.227	-0.053 -0.053	<i>Co</i> First Series Present series Sum
3 1	11 2	0 0	0 0	-2.083 -0.721 -2.804	-1.083 -0.444 -1.527	-0.314 -0.194 -0.508	-0.063 -0.076 -0.139	-0.003 -0.018 -0.021	<i>Se</i> First series Present series Sum
1 0	3	0	0	-0.769 -0.769	-0.482 -0.482	-0.216 -0.216	-0.086 -0.086	-0.020 -0.020	<i>Le</i> First series Present series Sum