

Linkage between the loci for benign (Becker-type) X-borne muscular dystrophy and deutan colour blindness

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Summary. A family is described in which benign Becker type X-linked muscular dystrophy and deutan colour blindness are segregating. The lod scores from this family have been added to those obtained in a family previously reported (Emery *et al.*, 1968/1969) and give an estimate of 0.23 for the recombination fraction with 95% confidence limits of 0.13 to 0.43. These results confirm the linkage relationships between deutan colour blindness and Becker muscular dystrophy but since the loci for Duchenne muscular dystrophy and colour blindness are not within measurable distance of each other these results indicate that the Becker and Duchenne types of X-linked muscular dystrophy are not allelic.

Besides the severe Duchenne type of muscular dystrophy, there is a more benign form of X-linked muscular dystrophy first described by Becker (Becker and Kiener, 1955; Becker, 1957, 1962). In this latter disorder proximal muscle wasting and weakness first becomes evident in late childhood, the teens or early adult life and affected individuals usually survive at least into middle age.

Previous studies have shown that the loci for Duchenne muscular dystrophy and the Xg blood groups (Clark *et al.*, 1963; Blyth *et al.*, 1965; Filippi and Macciotta, 1967) and colour blindness (Emery, 1966) are not within measurable distance of each other. Further, the loci for Becker muscular dystrophy and the Xg blood groups are not closely linked (Emery, Smith, and Sanger, 1968/1969). However studies of one large family with this disorder in which deutan colour blindness was segregating, showed that the maximum likelihood estimate of the recombination fraction for these two loci was 0.28 (Emery *et al.*, 1968/1969). These results suggest that the loci for the Becker and Duchenne types of muscular dystrophy may not be allelic. However the confidence limits for the recombination fraction were wide (0.15 to 0.50). There was therefore a need to study further families with Becker muscular dystrophy for possible linkage with colour blindness.

In a survey of patients with Becker muscular dystrophy another family in which deutan colour blindness was segregating has been discovered, and the original family has been extended. The results of linkage studies in these two families are reported in the present communication.

Subjects

Details of the first family in which deutan colour blindness was segregating have been reported previously (Emery *et al.*, 1968/1969). The diagnosis of muscular dystrophy in the second family was confirmed by a muscle biopsy on the proband, the histology of which was consistent with the diagnosis of muscular dystrophy. Serum levels of creatine kinase were determined on all apparently unaffected males in this family since it is known that preclinical cases of Becker type muscular dystrophy can be detected in this way (Rotthauwe and Kowalewski, 1966; Emery, 1968). In none of the families studied were early contractures a prominent feature of the disease unlike the family described by Thomas, Calne, and Elliott (1972) in which deutan colour blindness was also segregating.

Methods

Serum levels of creatine kinase were determined on fresh specimens of blood by the method described by Rosalki (1967).

Colour vision was tested using the Ishihara plates and the AO-HRR (American Optical Hardy-Rand-Rittler) pseudoisochromatic plates.

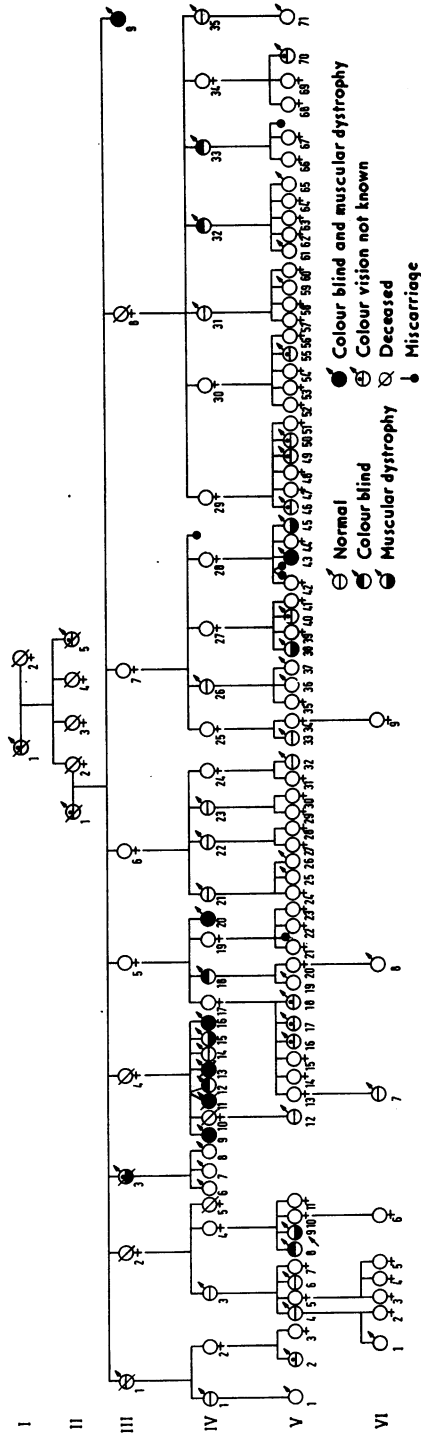


FIG. 1. Pedigree of family H.G. 588 (E).

The families

Family H.G. 588 (E). This family has been described in detail in a previous study (Emery *et al*, 1968/1969). The family has been restudied and extended. However no further cases (clinical or preclinical) have been identified and the pedigree information to date (Fig. 1) is essentially the same as previously described.

Family H.G. 153 (M). The pedigree of this family is shown in Fig. 2. Colour blindness appears to have occurred only in the offspring of III.11, although there are other males with muscular dystrophy in the family. Her father, II.3, suffered from muscular dystrophy, making her an obligatory carrier of this gene, but unfortunately nothing is known about his colour vision.

V.21, V.31, and VI.2 were identified as preclinical cases of muscular dystrophy on the basis of serum creatine kinase estimations. V.17 and V.18 were suspected of being preclinical cases several years ago and have since developed obvious signs of the disease.

Linkage analysis

The lod scores for family E were recalculated, taking into account the additional individuals in the family and without classifying III.8 as a definite carrier. These changes reduced the previous lod scores somewhat. For family M, the origin of the deutan allele is unknown and so four possibilities—

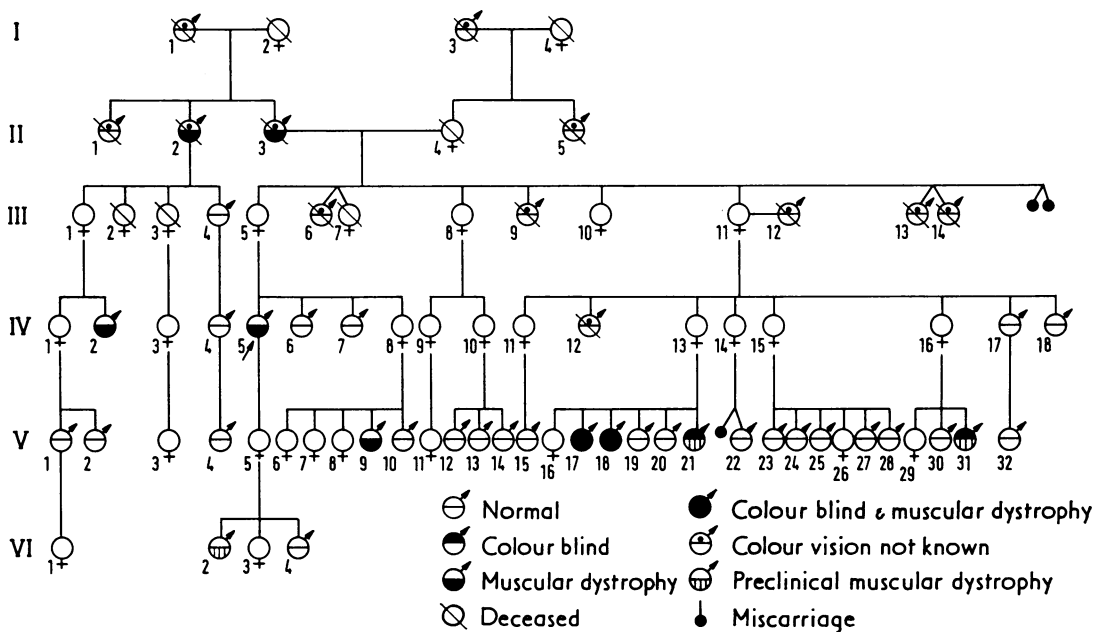


FIG. 2. Pedigree of family H.G. 153 (M).

TABLE I

BECKER-TYPE MUSCULAR DYSTROPHY AND DEUTAN COLOUR BLINDNESS; LOD SCORES AND ANTILOGS (RELATIVE LIKELIHOOD)

	Recombination Fraction (θ)								
	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45
<i>Family E</i>									
Lod score	-2.94	-1.00	-0.08	0.41	0.64	0.69	0.62	0.45	0.23
Antilog	0.001	0.016	0.83	2.57	4.37	4.90	4.17	2.82	1.70
<i>Family M</i>									
Lod score	0.39	0.83	0.90	0.80	0.61	0.37	0.14	-0.01	-0.06
Antilog	2.46	6.76	7.94	6.31	4.07	2.34	1.38	0.98	0.87
<i>Sum of scores</i>									
Lod scores	-2.55	-0.17	0.82	1.21	1.25	1.06	0.76	0.44	0.17
Antilog	0.003	0.676	6.61	16.22	17.78	11.48	5.75	2.75	1.48

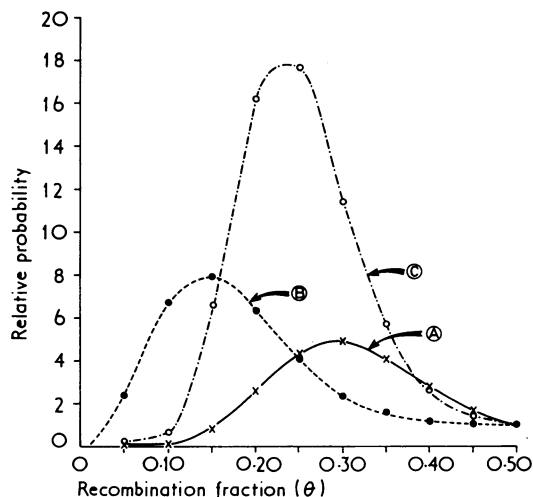


Fig. 3. Relative probabilities of linkage for various values of the recombination fraction for Becker muscular dystrophy and deutan-type colour blindness. A: family E; B: family M; C: families E and M combined.

(1) from II.3, (2) from II.4, (3) from III.12, and (4) mutation in III.11—were considered. It turned out that (1) was by far the most important in determining the lod scores which are given in Table I. The combined results indicate that the maximum likelihood estimate of the recombination fraction is 0.23 (Fig. 3) with 95% confidence limits of 0.13 to 0.43. The probability of the loci for Becker muscular dystrophy and deutan colour blindness being within measurable distance of each other is roughly 7:1.

Discussion

The results of the present study confirm that the loci for Becker type muscular dystrophy and deutan colour blindness are within measurable distance of each other. Since this is not true for Duchenne muscular dystrophy and colour blindness it seems that Becker and Duchenne muscular dystrophy, though both X-linked are not allelic.

In the previous study of Becker muscular dystrophy and deutan colour blindness (Emery *et al.*, 1968/1969) the estimate of the recombination fraction was 0.28 with 95% confidence limits of 0.15 to 0.50, and the odds on linkage was about 4:1. With the additional material presented here, the estimate becomes rather lower (0.23) with narrower confidence limits (0.13 to 0.43) and the odds on linkage now slightly greater (7:1).

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