Table 1 X;autosome translocations in girls with muscular dystrophy

Reference	Autosomal breakpoint	Age at reporting	Age of onset	Loss of ambulation	Still walking	IQ	Conclusions
Canki *et al.* (1979)[10]	3q13	4 yr	10 mth	–	+	R	? DMD*
Lindenbaum *et al.* (1979)[6]	1p34	8 yr	< 2 yr	+ (8 yr)	–	N	DMD†
Greenstein *et al.* (1980)[16]	11q13	16 yr	?	?	?	?	? DMD or BMD
Jacobs *et al.* (1981)[7]	5q35	9 yr	4 yr	–	+	N	DMD
Zatz *et al.* (1981)[8]	6q21	11 yr	5 yr	+ (10 yr)	–	N	DMD
Emanuel *et al.* (1983)[11]	9p22	9 yr	< 2 yr	–	+	R	? DMD
Nielsen *et al.* (1983)[15]	11q23	13 yr	< 2 yr	–	+	N	? BMD
Perez Vidal *et al.* (1983)[12]	6q16	4½ yr	< 3 yr	–	+	?	? DMD
MacLeod *et al.* (1983)[14]	2q36	?14 yr	< 2 yr	+	–	R	? DMD
Verellen-Dumoulin *et al.* (1984)[2]	21p12	20 yr	2 yr	–	+	N	BMD
Bjerglund-Nielsen (1984)[9]	9p21	23 yr‡	< 2 yr	+ (12 yr)	–	R	DMD§
Saito *et al.* (1985)[13]	4q26	3 yr	2 yr	–	+	?	? DMD

N, normal; R, retarded; DMD, Duchenne muscular dystrophy; BMD, Becker muscular dystrophy.
* Associated dysmorphic syndrome.
† Personally examined.
‡ Died.
§ Associated Turner's syndrome.

addition, all five patients of Monaco *et al.*[21] with deletions for pERT 87 were found to have deletions for XJ-1.

Although all the reported cases of X;autosome translocation with muscular dystrophy have apparently had the breakpoint in the same region of the short arm of the X chromosome (Xp21), there may be variations from case to case in the exact location of the breakpoint[22]. It may thus be of interest and importance when cloning sequences from these X-chromosome breakpoint regions, and applying them in the detection of RFLPs close to the Duchenne/Becker dystrophy genes, and looking for deletions in individual male cases, to know whether the original source came from a Duchenne or a Becker type case, and in addition to have adequate documentation of the dystrophic nature of the underlying muscle disorder.

Note added in proof: A further case, conforming to Duchenne severity, with an X;5 translocation, has recently been documented by Nevin *et al.*[23].

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WORTON REPLIES—Dubowitz raises a very valid concern about the phenotypes of girls with myopathic disease secondary to an X;autosome translocation. Certainly the X;21 translocation patient whose junction has been cloned has a mild form of muscular dystrophy more like the Becker form of the disease and should perhaps be reclassified as such.

However, there are two very important points to be made about the translocation patients in general. First, all have translocation exchange points in band Xp21 despite the fact that some have a severe (Duchenne) phenotype and others appear to have the milder (Becker) phenotype. This fits with the linkage data that map the gene for both Becker and Duchenne muscular dystrophy to this region of the X chromosome. As Dubowitz points out the two diseases may in fact be due to allelic mutations at the same locus. Thus, although it is important to have the phenotype of patients accurately described, the Duchenne and Becker variants of muscular dystrophy may simply represent different manifestations of the same disease.

The second important point, and one not discussed by Dubowitz, is that the expression of muscle disease in these girls who are heterozygous for the mutation (translocation) is a function of the non-random inactivation of the normal X chromosome carrying the wild-type allele. In many of the girls examined, the preference for normal X inactivation is not complete; up to 10% of the lymphocytes examined displayed a late replicating (inactive) translocation X and an early replicating (active) normal X. If this pattern holds in muscle, a proportion of the nuclei in a multi-nucleated myotube may be capable of producing the normal gene product. Since the 50% level of gene product expected of a non-translocation carrier female is sufficient to prevent the disease, a level of 5% or 10% may well be sufficient to modify the severity of the disease. In translocation patients a mutation at the 'Duchenne gene', therefore, may result in a Becker phenotype. This complicates the picture and suggests that neither term is really appropriate to the translocation females. Only through detailed genetic studies of the Becker/Duchenne muscular dystrophy locus will the true relationship between the two diseases be understood.

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