

Abnormalities of the Electrocardiogram in Hereditary Myopathies

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Cardiac as well as skeletal muscle is affected in the severe X-linked recessive form of Duchenne muscular dystrophy. Clinically this is evidenced by persistent tachycardia, arrhythmias; non-specific murmurs and sudden death from cardiac failure is common in this disorder. Histological evidence of cardiac muscle involvement includes variation in fibre size, hyalinization, fatty infiltration, and connective-tissue proliferation. Such histological changes in cardiac muscle have been observed in patients who did not necessarily have any symptoms of heart disease during life (Globus, 1923; Bevans, 1945; Nothacker and Netsky, 1950; Rubin and Buchberg, 1952; James, 1962; Storstein, 1962; Gilroy *et al*, 1963; Warlamidis and Ludwig, 1966; Perloff, de Leon, and O'Doherty, 1966; Perloff *et al*, 1967; Jedrzejowska-Kulakowska *et al*, 1968; Slucka, 1968; Baghirzade and Weiss, 1970).

Various abnormalities of the electrocardiogram (ECG) have been observed in patients with Duchenne muscular dystrophy (reviewed by Lowenstein, Arbeit, and Rubin, 1962) the most frequent and consistent abnormality being tall R waves in the right praecordial lead (Fig. 1). This ECG abnormality appears to be uncommon in other forms of dystrophy (Schott, Jacobi, and Wald, 1955; Manning and Cropp, 1958; Skyring and McKusick,

1961; Welsh, Lynn, and Haase, 1963), and when present is much less marked (Perloff *et al*, 1966). The vectorcardiogram is not as reliable as the ECG as an index of cardiac involvement in muscular dystrophy (Perloff *et al*, 1966; Demany and Zimmerman, 1969).

The present communication concerns the result of ECG studies in patients all of whom presented with limb girdle weakness yet suffered from different neuromuscular disorders including various forms of muscular dystrophy and the benign spinal muscular atrophy of Wohlfart-Kugelberg-Welander (Wohlfart, Fex, and Eliasson, 1955; Kugelberg and Welander, 1956). The algebraic sum of the R and S waves (R-S) in V_1 has been used as a measure of cardiac involvement since previous studies have indicated that this may be a useful index for distinguishing certain forms of dystrophy (Skyring and McKusick, 1961; Emery, 1969).

Materials and Methods

The various types of muscular dystrophy, all of which presented with predominantly limb girdle weakness, have been classified according to clinical and genetic criteria (Emery and Walton, 1967). The autosomal recessive form of Duchenne muscular dystrophy is defined clinically as being similar to the X-linked form but is somewhat milder and in any particular family affects either a single girl or a brother and sister.

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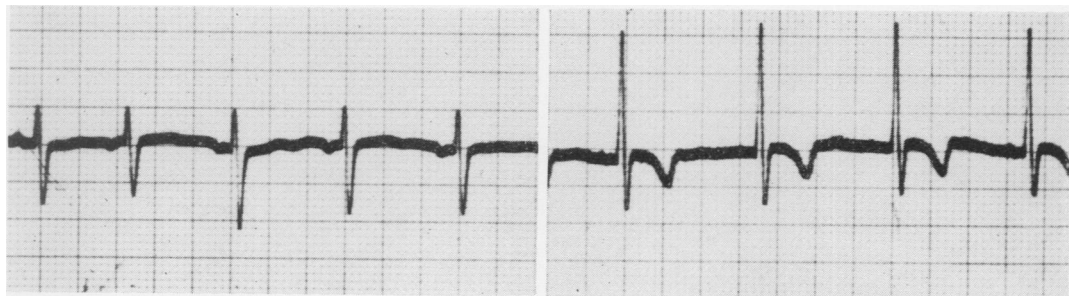


FIG. 1. Right praecordial lead (V_1) in a healthy boy (left), and in a boy with Duchenne muscular dystrophy (right) both aged 10.

Becker type muscular dystrophy refers to a relatively benign limb girdle myopathy which affects several males in different generations of the same family, the pattern of inheritance being consistent with that of an X-linked recessive trait (Emery, Smith, and Sanger, 1969). Limb girdle muscular dystrophy refers to a limb girdle myopathy with onset in early adult life which occurs sporadically in males and females or in any particular family affects only sibs. At least one person in each of the above families has had muscle biopsy, the histology in each case being consistent with that of muscular dystrophy. Patients referred to as having the Wohlfart-Kugelberg-Welander type of spinal muscular atrophy presented with mainly proximal muscle weakness in childhood or adolescence with electromyographic and muscle histological evidence of neurogenic atrophy.

Conventional 12-lead ECGs (leads I, II, III, aVR, aVL, aVF, and V_{1-6}) were carried out on all individuals. Values for R-S in V_1 in healthy children were those given by Nadas (1963). Normal values for adults were obtained from healthy individuals with no clinical evidence of cardiovascular disease (including hypertension) or muscle disease. All the control records appeared normal by conventional criteria. The R and S waves were measured to the nearest 0.5 mm and the average of several readings was recorded for each individual.

Results

The results for R-S in V_1 for boys with Duchenne muscular dystrophy are shown in Fig. 2. The proportions with abnormal values are given in Table I. The results indicate that whereas over 80% of boys with the X-linked recessive form of

Duchenne muscular dystrophy have high values for R-S in V_1 , this does not seem to be the case in the autosomal recessive form of this disease or in benign spinal muscular atrophy. In all but 3 of the ECGs from individuals with spinal muscular atrophy a fine tremor was observed in the record particularly in the limb leads (Fig. 3). This was rarely found in records from healthy individuals or patients with other neuromuscular disorders. Brandt (1950) has reported a similar ECG abnormality in patients with Werdnig-Hoffmann's disease.

Six *preclinical* cases of X-linked Becker type muscular dystrophy have also been studied. These boys belonged to 3 large families affected with this type of dystrophy. None had any muscle weakness but all had enlarged calves, a tendency to walk on their toes and elevated levels of serum creatine kinase as reported previously in preclinical cases of this disease (Emery, 1968). None of these boys had an abnormal value for R-S in V_1 (Table I).

With regard to the findings in adult males (all over age 15) there was no significant regression on age for R-S in V_1 in healthy adults (aged 15 to 45, mean = 35.2; SD = 7.8), adult males with Becker type muscular dystrophy (aged 16 to 55, mean = 31.2; SD = 12.1), or limb girdle muscular dystrophy (aged 15 to 56, mean = 35.9; SD = 12.4). There were no significant differences between the mean values for R-S in V_1 in these three groups (Table II). The number of values which exceeded the normal 95th centile (-1.45 mm) was not greater than would be expected by chance in either

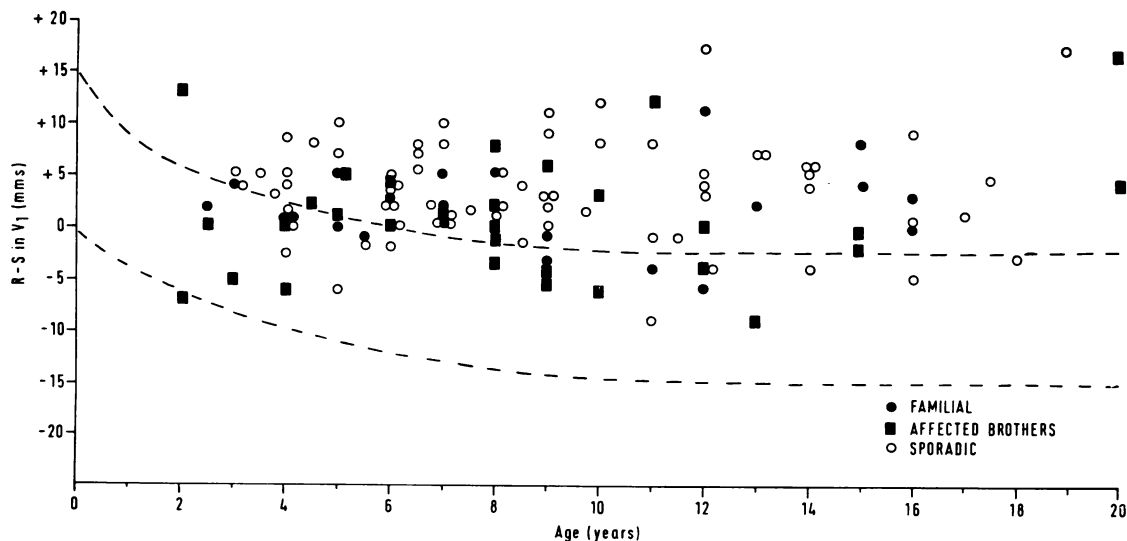


FIG. 2. Algebraic sum of R-S in V_1 for boys with Duchenne muscular dystrophy. Normal 90% confidence limits from Nadas (1963).

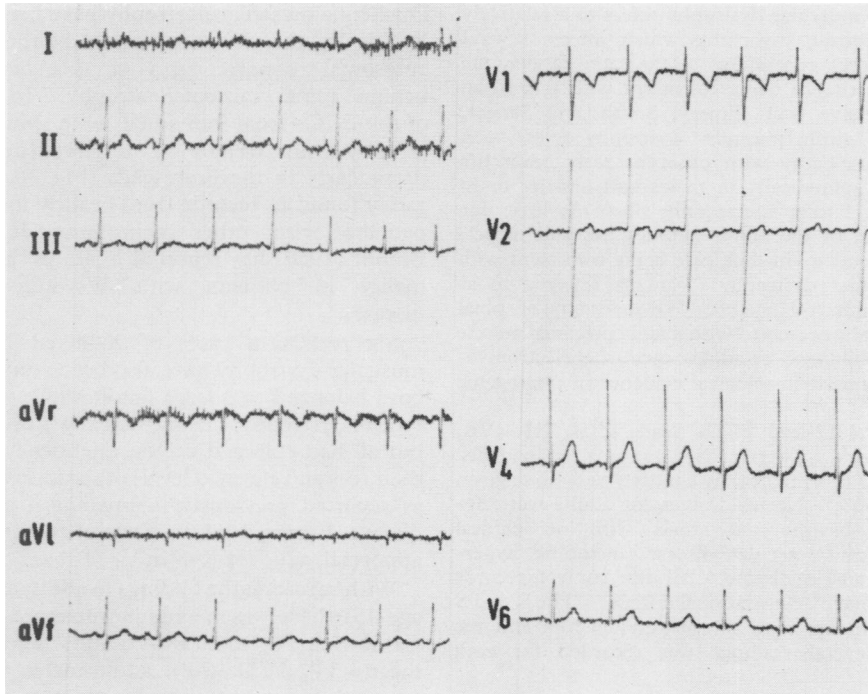


FIG. 3. ECG record of a boy (aged 9) with benign spinal muscular atrophy. Note the fine tremor particularly in the limb leads.

TABLE I

ALGEBRAIC SUM OF R-S IN V_1 IN CHILDREN

Type	Age 2+		Age 6+	
	Total	Abnormal*	Total	Abnormal*
X-linked Duchenne muscular dystrophy				
Familial	22	14 (64%)	15	12 (80%)
Two or more affected brothers	30	19 (63%)	20	14 (70%)
Sporadic	69	58 (84%)	54	48 (89%)
Total	121	91 (75%)	89	74 (83%)
Autosomal recessive Duchenne muscular dystrophy	10	0 (0%)	9	0 (0%)
Spinal muscular atrophy	20	1 (5%)	9	1 (11%)
Becker muscular dystrophy (preclinical)	6	0 (0%)	5	0 (0%)

* Values which exceed the normal 95 centile (Nadas, 1963).

males with Becker muscular dystrophy or males with limb girdle muscular dystrophy.

Discussion

Evidence of cardiac pathology in muscular dystrophy has been reviewed by several authors (see Gailani, Danowski, and Fisher, 1958; Lowenstein *et al*, 1962; Storstein, 1962; Solti, Zádory, and Bekény, 1963; Storstein, 1964; Demany and

TABLE II

ALGEBRAIC SUM OF R-S IN V_1 IN ADULTS

Condition	No.	R-S in V_1		No. of Values which exceed Normal 95th centile*
		Mean	SD	
Controls (healthy adult males)	102	-6.71	3.19	4
Becker muscular dystrophy	14	-7.39	5.35	1
Limb girdle muscular dystrophy	19	-5.92	4.06	2

* Mean plus SD multiplied by t_{90} ie, $(-6.71) + 3.19(1.65) = -1.45$ mm.

Zimmerman, 1969). Particularly in the Duchenne type of X-linked muscular dystrophy the most consistent ECG abnormality is the presence of tall R waves in the right praecordial lead (Weisenfeld and Messinger, 1952; Schott *et al*, 1955; Gailani *et al*, 1958; Manning and Cropp, 1958; Skyring and McKusick, 1961; Gilroy *et al*, 1963; Perloff *et al*, 1966 and 1967; Jedrzejowska-Kulakowska *et al*, 1968; Slucka, 1968; de los Arcos, Cascos, and de Rabago, 1969). The present study has confirmed this finding and shown that over 80% of boys with X-linked Duchenne muscular dystrophy have abnormally high values for R-S in V_1 . A previous study of 50 female carriers of X-linked Duchenne

muscular dystrophy revealed that 4 had values for R-S in V_1 which exceeded the normal 99th centile in healthy women. The values in women with limb girdle muscular dystrophy, however, did not differ significantly from the controls (Emery, 1969). The results of the present study indicate that abnormally tall R waves in V_1 are not a characteristic ECG finding in children with the autosomal recessive form of Duchenne muscular dystrophy, preclinical Becker muscular dystrophy or benign spinal muscular atrophy, or in adult males with Becker or limb girdle muscular dystrophy. In facioscapulohumeral muscular dystrophy cardiac involvement is rare (Walton and Gardner-Medwin, 1969) and the ECG is usually normal (Schott *et al*, 1955; Manning and Cropp, 1958; Welsh *et al*, 1963; Perloff *et al*, 1966).

Thus it would seem that ECG evidence of tall R waves in V_1 is characteristic only of the X-linked form of Duchenne muscular dystrophy occurring in over 80% of affected boys and in roughly 10% of female carriers (Hausmanowa-Petrusewicz *et al*, 1968; Mann *et al*, 1968; Emery, 1969). In female carriers of Duchenne muscular dystrophy there was no significant correlation between the value of R-S in V_1 and the serum level of creatine kinase (Emery, 1969). However when serum creatine kinase levels in carriers with values of R-S in V_1 which exceeded the normal 95th centile ($n=6$; mean = 243.2; SD = 153.2) were compared with those from carriers with values of R-S in V_1 below the normal 95th centile ($n=17$; mean = 114.9; SD = 70.5) the difference was significant ($t=2.79$; $0.01 < p < 0.02$).

The findings in affected boys and carriers of Duchenne muscular dystrophy have certain implications. Firstly, electrocardiography might be a useful additional tool for differentiating the X-linked form of Duchenne muscular dystrophy from other disorders which can present as limb girdle weakness in childhood. Secondly, since these ECG changes have not been found in women with limb girdle muscular dystrophy, electrocardiography might prove useful in distinguishing a manifesting carrier of X-linked Duchenne muscular dystrophy from a woman with limb girdle muscular dystrophy.

The aetiology of tall R waves in the right praecordial lead of the ECG in X-linked Duchenne muscular dystrophy is not clear. Various explanations have been suggested including thoracic deformity, pulmonary hypertension, conduction defect due to myocardial dystrophy, and ventricular septal hypertrophy. The evidence for and against these various possibilities has been extensively reviewed by Perloff *et al* (1966) who concluded that none of these suggestions was entirely satisfactory.

They proposed that the anterior shift of the QRS complex may be due to diffuse interstitial fibrosis in the posterobasal portion of the left ventricle though why this portion of the myocardium should be so selectively involved in this particular form of dystrophy is not clear and awaits further investigation.

Summary

Abnormally tall R waves in the right praecordial lead of the electrocardiogram have been observed in over 80% of boys with the X-linked recessive form of Duchenne muscular dystrophy and in roughly 10% of female carriers of this disorder. This does not appear to be a consistent feature of the electrocardiogram in other forms of dystrophy which present as limb girdle weakness or in benign spinal muscular atrophy. On the basis of these results it is suggested that this might be a useful means of differentiating the X-linked form of Duchenne muscular dystrophy from other causes of limb girdle weakness in childhood, and perhaps also for distinguishing a manifesting carrier of this disorder from a woman with limb girdle muscular dystrophy.

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