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X-LINKED DUCHENNE MUSCULAR DYSTROPHY

Motor Funktions and Prognosis

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ABSTRACT. 69 patients with x-linked Duchenne Muscular Dystrophy (DMD) were included in a retrospective investigation from 1975–1986. A mean profile of the decline of the motor functions was made by using the median age at which the patients were unable to perform specific motor functions by request. It was found that 81.2 % of the personal profiles followed the pattern shown in the mean profile of the disease and that DMD is progressing in a uniform way, but with a different progression rate in every DMD patient. Good correlation between two motor functions made it possible to predict a personal prognosis of the decline of the motor functions in the DMD patient. No correlation between late walkers (later than 18 months) and rapid progression was found.

Key words: Duchenne Muscular Dystrophy, motor functions, prognosis.

X-linked Duchenne Muscular Dystrophy (DMD) has a characteristic clinical picture with onset before the age of 7 years (usually about the age of 3—4 years) with clumsiness in walking and frequent falling (2–5, 11). In the early stages symmetrical weakness is present in the muscles of the pelvic and shoulders girdles. Involvement of the respiratory muscles and distal muscles of the limbs follows later (3–5, 11). The DMD patients become chairbound about 10 years old, and most of the affected children die in the second decade (3–5, 11). The aims of this study were to find the median age at which DMD patients became unable to perform specific motor functions and to predict a personal prognosis of the decline of the motor functions in the DMD patient. The hypothesis is that the proportion between the inability ages of two motor functions would be the same in every DMD patient in spite of different progression rate of the disease.

MATERIAL AND METHODS

In the county of Aarhus (590 000 inhabitants), nearly all patients suspected of neuromuscular disorders are referred to the department of Neurology, Aarhus Kommunehospital. In addition, a limited number of such patients are referred by neurologists or paediatricians in other counties. No selection or screening of admission is made by the hospital medical staff. The present series comprises all patients who were discharged from the neurological department with a firm diagnosis of DMD in the period 1975–1986.

69 patients were included in the investigation and the diagnosis was based on clinical criteria, markedly raised serum creatine-kinase, histology, EMG and genetic pattern. Patients were enrolled at any stage of the course of the disease, depending on their age at the first visit in the department. A simple 'all or none' motor function test was developed in the department and used at the regularly controls every 6–12 months. The patients were requested to perform specific movements in fixed body positions, as shown by the symbols in Fig. 1. We recorded the onset of independent walking in childhood, the age at which the patient was unable to perform the specific motor functions, and the age at death. Median age and a range, limited by 90% quantiles, were used, because the results did not form a Gaussian curve. The result of each group of motor function was compared with each of the other groups of motor functions, and it was presupposed that the correlation between two motor functions was linear. This ideal line would pass through the point (0, 0) and the point determined by the mean of each sample. The slope expresses the proportion between the inability ages of two motor functions. The coefficient of correlation (r) and the regression line (method of least squares) were calculated. If the regression line did not pass the point (0, 0), it was tested whether the deviation differed significantly from the ideal line (t-test, 95% confidence limit)—and it was decided not to use the results if the deviation was outside the confidence limit. Only r-values greater than 0.71 (equals coefficient of determination greater than 0.5) were accepted in order to obtain a good correlation between the motor functions.

RESULTS

The results are shown graphically in Fig. 2 and the data have been arranged in order of median age, and a mean profile of the decline of the motor functions of the disease appears.

Table I shows in per cent how well the 69 patients followed the mean profile, when two motor

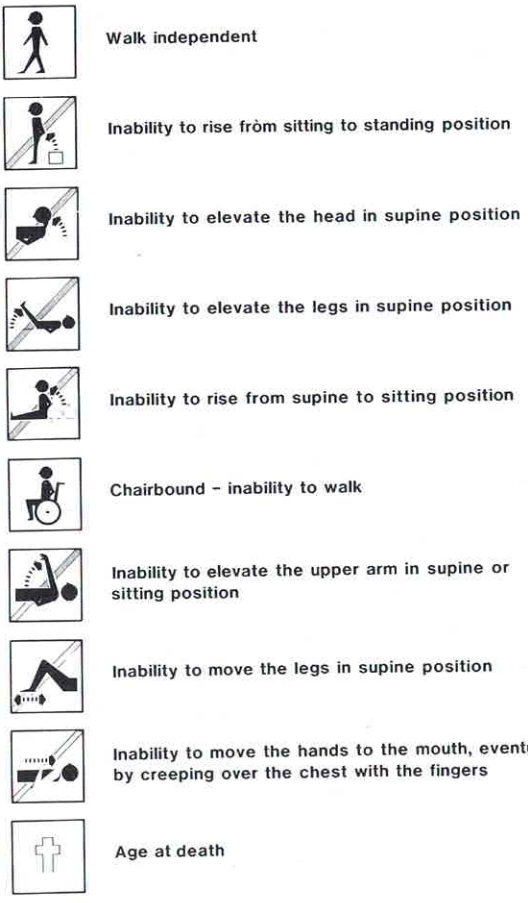


Fig. 1. Scheme used at the clinical examination. Symbols with an oblique line means: inability to perform the specific motor function. The age was noted, when a patient fulfilled the criteria.

Table I. *Table I shows in per cent how well the DMD patients follow the mean profile (Fig. 2) of the decline of the motor functions of the disease*

Example: in 34 patients 76.5% were unable to rise from supine to sitting position before they became chairbound

Motor functions	Number of patients	% following mean profile
before	29	65.5 %
before	28	50.0 %
before	25	72.0 %
before	34	76.5 %
before	35	100.0 %
before	31	87.1 %
before	34	91.2 %
before	28	100.0 %

functions were compared, and it was found, that 81.2% followed the pattern of the mean profile. One motor function, i.e. inability to elevate the head in supine position, has a very wide range compared with those of the neighbouring motor functions. If this motor function is removed from the mean profile, the proportion of patients who follow the mean profile then will be 88.2%.

Only 19 (35.2%) could walk independently before the age of 15 months and 27 (50.0%) before the age of 18 months. None of the DMD patients could walk independently before the age of 12 months.

35 comparisons of two individual motor functions were possible. No correlation was found between age of independent walk and inability age of any of the other motor functions (concerning 8 comparisons), not even if only the late walkers (later than 18 months) were considered. Good correlation was found in 60% of the remaining 27 comparisons. Fig. 3*a* and *b* shows two examples of good correlation between two motor functions—in this case, inability to rise from sitting to standing position vs. cessation of ambulation (chairbound)—and, inability to rise from supine to sitting position vs. inability to elevate the upper arm. In order to test the validity of the results, coefficient of correlation and the regression line again were calculated, now using assessing the over-all strength of multiple muscles is by means of functional testing. Although it is less by whom a prediction of the decline of the motor functions was desired.

In all cases coefficient of correlation (r) remained greater than 0.71 and the regression line did not deviate outside the 95% confidence limit of the ideal line. In a few comparisons the number of patients became too small. At last, the results of the remaining half were plotted into their respectively new graphs of prediction, and it was found that all the results were inside the 95% confidence interval.

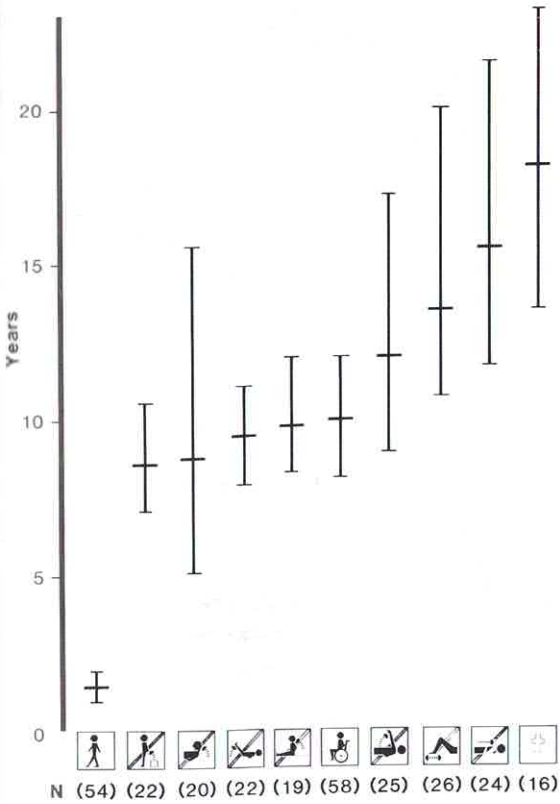


Fig. 2. Mean profile of the decline of the motor functions in DMD. Median age and range (limited by 90% quantiles). *N*=number of patients.

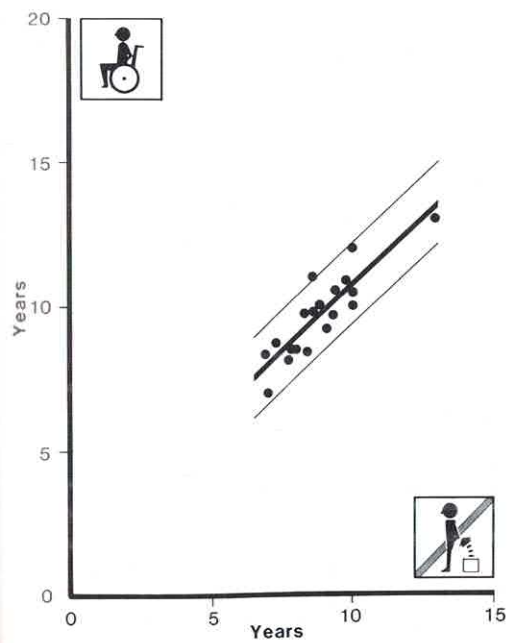
DISCUSSION

The usual methods of manual testing of the muscles is time-consuming and not well suited for routine use. Judging the DMD patient's physical capacity simple methods are needed, and a better method of assessing the over-all strength of multiple muscles is by means of functional testing. Although it is less precise than determination of strength of individual muscles, it is useful and functionally more accurate than rough clinical estimates of muscular strength.

Previously published functional classification tests and modifications are based on the ability and methods used in activities concerned with ambulation, strength of the muscles, and respiration (1, 7, 9, 10, 12), but attached with different importance.

The motor function test given is performed on request without any physical contact between the investigator and the patient, and represents an "all or non" functional test, reflecting the muscular strength in both proximal and distal parts of the limbs. The mean profile of the disease (Fig. 2) reflects the previously known progression of the disease. Muscles of the pelvic girdle are severely affected before the muscles of the shoulder girdle, and upper limbs are affected less or later than lower limbs.

The DMD patients walked independently later than healthy children (6), and this result is very



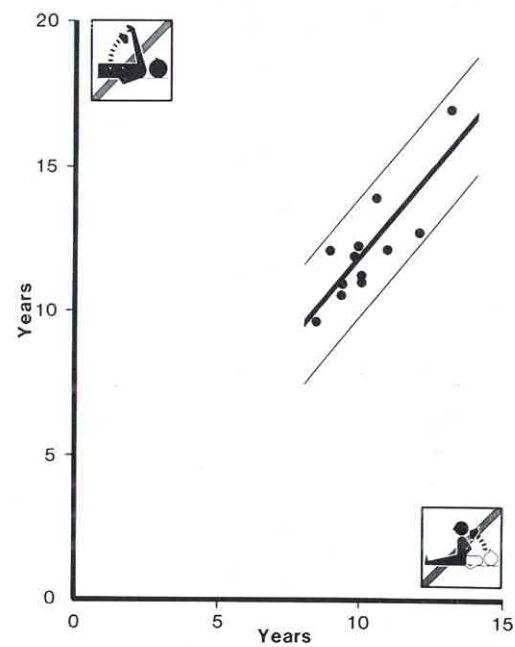


Fig. 3 a and b. Correlation between two motor functions. Thin lines represent the 95% confidence limit.

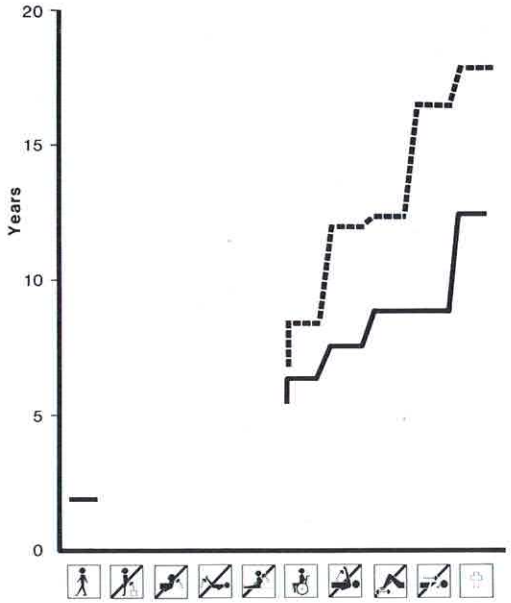


Fig. 4. Two personal profiles showing different rate of progression of the disease. Only informations available are shown.

similar to what Dubowitz (3), Crisp (2) and Miller (8) found, and was valid even if only late walkers (later than 18 months) were considered. No correlation between the age of independent walk and inablity age of any other motor function was found. This indicates a lacking correlation between late walkers and rapid progression of the disease.

The range interval seems to be expanding with age, except the motor function concerning elevating the head in supine position. This specific motor function does not fit into the pattern of the mean profile, because of the very wide range; the reason is unknown.

The results indicate that the disease, concerning the muscular involvement, is progressing in a most uniform way, but at a different rate as shown in Fig. 4 and this confirms the previously postulated hypothesis.

Prognostic assessments are necessary for realistic planning in terms of locomotor activity, and the presented motor function test has proved to be a valuable tool in this judgement, so for instance, facilities can be available at the proper time, when needed. The correlation between two motor functions is so strong that the regression line with a 95% confidence limit can be used as a graph of prediction of the decline of the motor functions in the individual DMD patient.

If a DMD patient is unable to rise from supine to sitting position at the age of 11 years (Fig. 3*b*), the probability of being unable to elevate the upper arm is 50% at the age of 13.2 years and 97.5% at the age of 15.3 years.

It is concluded that DMD progresses in a most uniform way, but at different rates in different DMD patients and that the rate of progression can be predicted in the individual patient on the basis of a few and easy performed functionally tests at an early stage of the disease.

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