

Scandinavian Consensus Programme
on
Duchenne muscular dystrophy

November 2003

Scandinavian Consensus Programme for Duchenne Muscular Dystrophy

CONTENTS

	Authors.....	4
1.	Preface.....	7
2.	Clinical manifestations	8
3.	Diagnostic work up.....	11
4.	Type of inheritance, prenatal and carrier diagnosis	13
5.	Nutrition.....	16
6.	Oral care	19
7.	Neuropsychological and educational aspects.....	23
8.	Psychosocial aspects.....	24
9.	Physiotherapy and occupational therapy.....	28
10.	Medical management of muscular dystrophy.....	35
11.	Orthopaedic treatment in Duchenne muscular dystrophy.....	38
12.	Treatment of respiratory insufficiency.....	42
13.	Diagnosis and treatment of cardiac disease.....	47
14.	Rehabilitation of adult persons with Duchenne muscular dystrophy.....	51
15.	Patient organisations.....	56

Appendix

I	Nutrition: fig: 1 Weight curve for DMD-Boys, fig. 2 Hight curve.....	58
II	Oral care, fig. 1-8 + captions to figures	60
III	Corticosteroid treatment in DMD – schematic survey	64
IV	Orthoses: Text and illustrations.....	66
V	Management and co-ordination.....	68

Authors of the DMD Consensus Programme

Editors

Johannes Jakobsen, MD, Professor
Århus Sygehus, Neurologisk afdeling
Nørrebrogade 44, 8000 Århus C
e-mail: hollerup@aaa.dk

Thomas Sejersen, MD, Associate Professor
Institut för Kvinnors och Barns Hälsa
Karolinska sjukhuset, Astrid Lindgrens barnsjukhus
SE-171 76 Stockholm
e-mail: thomas.sejersen@cmm.ki.se

Norway

Chapter 9:

Trude Løvlie, Occupational Therapist
Regionsykehuset, Habiliteringsenheten for barn
Gimleveien 70, 9019 Tromsø
e-mail: trude.lovlie@unn.no

Chapter 9:

Inger Lund Petersen, Physiotherapist
Prosjekt LIBRA
priv.: Gabriel Lundsgt. 11, 4550 Farsund
e-mail: libra@prosjektlibra.org

Chapter 7:

Christian Aashamar, Headmaster
Frambu Barnehage og Skole
Sandbakkeveien 18, N1404 Siggerud
e-mail: caa@frambu.no

Sweden

Chapter 6:

Bitte Ahlberg, Dentist
Mun-H-Center, Odontologen Göteborg
Medicinaregatan 12A, SE-413 90 Göteborg
e-mail: bitte.ahlberg@vgregion.se

Chapter 5:

Lena Gummesson, Dietitian
Karolinska sjukhuset, Astrid Lindgrens barnsjukhus
Nutritionsenheten
SE-171-76 Stockholm
e-mail: lena.gummesson@ks.se

Chapter 9:

Anna-Karin Kroksmark, Physiotherapist
Regionala barn- och ungdomshabiliteringen
Box 21062, SE-418 04 Göteborg
e-mail: anna-karin.kroksmark@vgregion.se

Chapter 11:

Helena Saraste, MD (Orthopaedist)
Huddinge sjukhus, Ortopedkliniken
Rygg- och barnsektionen K64
SE-141 86 Huddinge
e-mail: helena.saraste@telia.com

Chapter 10:

Thomas Sejersen, MD
Institut för Kvinnors och Barns Hälsa
Karolinska sjukhuset, Astrid Lindgrens barnsjukhus
SE-171 76 Stockholm
e-mail: thomas.sejersen@cmm.ki.se

United Kingdom

Appendix: Management and co-ordination

Sylvia Hyde, Physiotherapist
3 & 4 The Old Cottages
Deadmans Ash Lane
Sarrat – Rickmansworth
Herts WD3 6AN

Denmark

Chapters 2 & 3:

Flemming Juul Hansen, MD
Rigshospitalet, Juliane Marie Centret
Neuropædiatrisk ambulatorium, Afsnit 5003
Blegdamsvej 9, 2100 København Ø
e-mail: fjh@rh.dk

Chapter 8:

John Marquardt, Psychologist
Institut for Muskelsvind
Bernstorffsvej 20, 2900 Hellerup
e-mail: Marquardt@mail.tele.dk

Chapter 13:

Henning Mølgaard, MD, Cardiologist
Skejby Sygehus, Hjertemedicinsk afdeling
Brendstrupgårdsvej, 8200 Århus N
e-mail: h.molgaard@dadlnet.dk

Chapter 12:

Ole Nørregaard, MD
Århus Sygehus, Respirationscenter Vest
Nørrebrogade 44, 8000 Århus C
e-mail: ono@dadlnet.dk

Chapter 14:

Jes Rahbek, MD
Institut for Muskelsvind
Kongsvang Allé 23, 8000 Århus C
e-mail: jera@muskelsvindfonden.dk

Chapter 4

Marianne Schwartz, lic.scient
Rigshospitalet, Klinisk Genetisk afdeling, afsnit 4062
Blegdamsvej 9, 2100 København Ø
e-mail: schwartz@rh.dk

Chapter 9:

Ulla Werlauff, Physiotherapist
Institut for Muskelsvind
Kongsvang Allé 23, 8000 Århus C
e-mail: ulwe@muskelsvindfonden.dk

1. Preface

The aim of the Consensus Programme for Duchenne Muscular Dystrophy (DMD) is to form a joint Scandinavian basis for diagnosis and recommendations for the management of the disease. The implementation of the same Consensus programme all over Scandinavia is feasible due to the equality of social and medical traditions in Norway, Sweden and Denmark.

A Consensus Programme is essential because:

1. DMD is a serious disease
2. The rare occurrence of DMD makes it difficult for all health professionals to acquire the necessary knowledge about the disease
3. DMD-families should be offered the most informed treatment and counselling no matter where they live
4. A joint basis for diagnostics and registration of data will make joint Scandinavian studies in DMD possible and thus increase the value of future treatment studies.

We hope that the Consensus Programme will improve the treatment of Scandinavian DMD patients and strengthen the Scandinavian co-operation about the development of new offers for treatment.

Thomas Sejersen

Johannes Jakobsen

2. Clinical manifestations

History

The course of Duchenne muscular dystrophy (DMD) was defined in studies performed in the latter half of the 19th century (Meryon 1852 (1), Duchenne 1868 (2), Gowers 1886 (3)). DMD is an X-linked disorder with a gradual progression.

0-3 years: DMD symptoms will appear when the boys start walking. You can, although rarely, see DMD signs in the neonatal period or in the first year of life. In families with a previous DMD boy you have an early suspicion of a new case. Creatine kinase is strikingly elevated from birth, often with values between 5.000 and 150.000 IU/l.

Abnormal gait with frequent falls, difficulties in rising from the floor and tiptoe walking, or delayed walking to 15 – 18 months of age are the usual presenting symptoms.

DMD is characterised by proximal muscle atrophy. Tiny pectoralis muscles can be eye catching. Weakness in the shoulder girdle is an early sign, whereas weakness in the arms/hands is a late sign. Pseudohypertrophy of muscles, especially the calves, but also the deltoid and quadriceps muscles is an early and characteristic sign. Tendon reflexes will disappear early in the arms and knees, whereas Achilles' reflexes will be preserved till late stages.

3-6 years: The gait is waddling due to weakness in the gluteus muscles. The boys are unable to keep their bodies straight when lifting one leg. They transfer their bodyweight so that the line of gravity will go through the other leg. When they take a step forward the weight will be transferred to this leg. Therefore the gait is waddling, and climbing a staircase will be an early problem. The same weakness in hip extensors (gluteus muscles) will lead to a forward pelvic tilt with a compensatory lumbar lordosis. This lumbar lordosis will disappear when sitting. Tiptoe walking will emerge before Achilles tendon contraction caused by a combination of weak tibialis ant. and an attempt to keep the balance in an upright position.

After the age of 3 all healthy children can rise from the floor without changing to a prone position. Normally this takes less than a second. DMD boys need more than 2 seconds. As the weakness progresses they must turn 45, then 90, and then 180 degrees before getting up from a supine position on the floor. With a mild weakness just a hand on the knee is needed, but eventually it takes a full Gowers manoeuvre: Turning from supine to prone, then to a knees and elbows position, a stretching of knees and arms, moving the arms close to the legs, and climbing up the legs with the hands until an upright position is obtained.

Much variation is seen in the speed of progression. Generally strength is increasing up to 4 – 6 years of age. Immobilisation, whatever the reason, diminishes strength. Stretching muscles and orthoses can prevent Achilles tendon contraction as long as the boys can walk.

7 – 13 years: Loss of ambulation occurs between ages 7 and 13. With long-leg callipers, keeping the knees stretched, the walking can be prolonged up to several years.

Around 13 years of age a marked deterioration of arm function supervenes. Lifting the arms will be difficult (4). The non-dominant hand will eventually be of little use (5). The degree of muscle brevity can vary a lot at the same age (6,7), where wrist flexion contraction and ulnar deviation occur between the 8th and 14th year.

When walking has stopped the boys tend to rapidly develop contractions and scoliosis. Along with the steady weakening of muscles an increased need for help arises – for transfer, dressing, eating, and hygiene. Most boys will be able to operate an electric wheelchair, but they may need help to put their hand on the steering unit.

Respiration will deteriorate after permanent sitting, with about 200 ml reduction in VC per year. If untreated the majority (90%) will die from respiratory insufficiency before 20 years of age. Cardiac muscles are always involved, and ECG anomaly can be seen from the age of 4. 10% will die from cardiac insufficiency (8).

Treatment, ventilation, cardiac drugs, and scoliosis surgery will prolong lifetime up to 20 years.

Cognition

Mental retardation (IQ < 75) is found in 30% (9,10). The distribution of IQ is a normal Bell curve with a shift to the left. This retardation is non-progressive and not correlated to the severity, duration or time of debut of the disease. Irrespective of intellectual capacity a special developmental profile is often seen, with reduction of verbal skills, memory dysfunction, and reading problems (9,10,11,12,13). The boys can complete a school course (see chap. 11), can administer a helper scheme, but will only rarely be selectively employed. The cause of these problems is unknown, even if it is known that dystrophin is present in normal brains (14).

Surgery / anaesthesia

In DMD there is an increased risk of anaesthesia complications (15). Even if malignant hyperthermia is a rare presentation in DMD special measures concerning anaesthesia must always be taken when preparing surgery.

Recommendations:

- Medical follow-up at least once a year by a specialist with profound knowledge of DMD.

References:

1. Meryon E. On granular and fatty degeneration om the voluntary muscles. *Med Chir Trans* 1852; 35: 73.
2. Duchenne GB. Recherches sur la paralysie musculaire pseudohypertrophique ou paralysie myosclerosique. *Arch Gen Med* 1868; 11: 5, 178, 305, 421, 552.
3. Gowers WR. A manual of diseases of the nervous system. Vol.1. London: Churchill, 1886: 386-402
4. Lord JP, Portwood MM, Lieberman JS, Fowler WM, Berck P. Upper extremity functional rating for patients with Duchenne muscular dystrophy. *Arch Phys Med Rehabil* 1987; 68: 151-154
5. Hiller LB, Wade CK. Upper extremity functional assessment scales in children with Duchenne muscular dystrophy: A comparison. *Arch Phys Med Rehabil* 1992; 73: 527-534
6. Brook MH, Fenichel GM, Griggs RC, Mendell JR, Moxley R, Miller JP, Province MA. Duchenne muscular dystrophy: 2. Determination of the "power" of therapeutic trials based on the natural history. *Muscle & Nerve* 1989; 6: 91-103
7. Wagner MB, Vignos PJ Jr, Carlozzi C. Duchenne muscular dystrophy: a study of wrist and hand function. *Muscle & Nerve* 1989; 12: 236-244
8. Perloff JK. Cardiac rhythm and conduction in Duchenne's muscular dystrophy: a prospective study of 20 patients. *J Am Coll Cardiol* 1984; 3: 1263-1268
9. Dubowitz V. Intellectual impairment in muscular dystrophy. *Arch Dis Child* 1965; 40: 296
10. Bresolin N, Castelli E, Comi GP, Felisari G, Bardoni A, Perani D, Grassi D, Turconi A, Mazzucchelli F, Gallotti D et al. Cognitive impairment in Duchenne muscular dystrophy. *Neuromuscul Disord* 1994; 4: 359-369
11. Billard C, Gillet P, Barte M, Hommet C, Bertrand P. Reading ability in processing in Duchenne muscular dystrophy and spinal muscular dystrophy. *Dev Med Child Neurol* 1998; 40: 12-20
12. Billard C, Gillet P, Signoret L, Uicaut E, Bertrand P, Fardeau M, Barthez-Carpentier MA, Santini JJ. Cognitive functions in Duchenne muscular dystrophy: a reappraisal and comparison with spinal muscular atrophy. *Neuromuscul Disord* 1992; 2: 371-378
13. Hinton VJ, De Vivo DC, Nereo NE, Goldstein E, Stern Y. Poor verbal working memory across intellectual level in boys with Duchenne dystrophy. *Neurology* 2000; 54: 2127-2132
14. Mehler MF, Haas KZ, Kessler JA, Stanton PK. Enhanced sensitivity of hippocampal pyramidal neurons from mdx mice to hypoxia-induced loss of synaptic transmission. *Proc Natl Acad Sci USA* 1992; 89: 2461-2465
15. Allen, G.C., Malignant hyperthermia and associated disorders. *Curr Opin Rheumatol*, 1993. 5(6): p. 719-24.

3. Diagnostic work up

European Neuromuscular Centre diagnostic criteria for DMD

Elements

1. Symptoms are present before the age of 5.
2. Clinical signs comprise progressive symmetrical muscular weakness; proximal limb muscles more than distal muscles; initially only lower limb muscles. Calf hypertrophy is often present.
3. Exclusions: fasciculations, loss of sensory modalities.
4. Loss of unassisted ambulation before the age of 13.
5. There is at least a 10-fold increase of serum creatine kinase (SCK) activity (in relation to age and mobility).
6. Muscle biopsy: abnormal variation in diameter of the muscle fibres (atrophic and hypertrophic fibres), (foci of) necrotic and regenerative fibres, hyaline fibres, increase of endomyseal connective and fat tissue.
7. Muscle biopsy: almost no dystrophin demonstrable, except for occasional muscle fibre (less than 5% of fibres).
8. DNA: Duchenne-type mutation within the dystrophin gene, identical haplotype involving closely linked markers, as in previous cases in the family.
9. Positive family history, compatible with X-linked recessive inheritance.

Assesment

The diagnosis is definite when:

- A The first case in a family
 - a. age <5years: (2), 3,5,6,7,(8) all present
 - b. age 5-12 years: 1,2,3,4,5 (at least once),6,7,(8) all present
 - c. age >12 years: (1),2,3,4,5 (at least once)8, (or 6 and 7) all present
- B Another case in the family (according to element 9) complies with the criteria under A
 - a. age <5 years: 5 and 9 present
 - b. age 5-12 years: 1,2,3,5 (at least once) all present
 - c. age >12 years: (1),2,3,4,5 (at least once) all present

The diagnosis is possible when:

- a. age <5 years: (2),3,5,6, all present
- b. age 5-12 years: 1,2,3,(4),5 (at least once)6, all present

Laboratory investigations:

If history and clinical examination indicates suspicion of DMD you should first do a blood sample in search of leakage of muscle enzymes into the blood. The most important enzyme, creatine kinase, is always much increased in DMD, but increased values are also found in other causes of muscle damage.

Isolated high creatine kinase in a boy means DMD in 80%, Becker's muscle dystrophy in about 15%, and something else in 5%. If it is a boy between 3 and 6 years with proximal muscle weakness, the risk of DMD is higher than 80%. High transaminase values may be a sign of muscle dystrophy.

Analysis of EDTA-blood for deletions, duplications, small mutations, and microdeletions will prove DMD in about 90% of cases. Some point mutations will not be found at present. The DNA test can differentiate DMD from BMD. (2,5)

Muscle biopsy will show severely decreased dystrophin – less than 5% of normal, and signs of dystrophy: degeneration, regeneration of muscle fibres, increased connective tissue and fat. DMD biopsies will show changes in other proteins – secondary changes – such as sarcoglykans and dystroglykans. Lack of dystrophin and structural changes in the protein will be found by Western blotting, a biochemical analysis of protein extract from the muscle (3). Lack of dystrophin in a muscle biopsy is diagnostic for DMD and means that the gene is mutated.

A muscle biopsy is recommended because the dystrophin level will tell more about the phenotype than the genetic predictions (6).

Recommendation

- . DMD should be diagnosed according to the European consensus criteria.

References

1. Diagnostic criteria for neuromuscular disorders, 2nd ed., European Neuromuscular Centre, Ed. Alan E.H. Emery, 1997
2. Monaco AP, Bertelson CJ, Liechti-Gallati S, Moser H, Kunkel LM. An explanation for the
3. phenotypic differences between patients bearing partial deletions of the DMD locus. Genomics
4. 2: 90-95
5. Hoffman EP, Fischbeck KH, Brown RH, et al. Dystrophin characterization in muscle biopsies from Duchenne and Becker muscular dystrophy patients. N Engl J Med 1988; 318: 1363-1368
6. Mendell JR, Buzin CH, Feng J, Yan J, Serrano C, Sangani DS, Wall C, Prior TW, Sommer SS.
7. Diagnosis of Duchenne dystrophy by enhanced detection of small mutations. Neurology 2001; 57: 645-650
8. Muntoni F. Is muscle biopsy in Duchenne dystrophy really necessary? Neurology 2001; 57: 574-575.

4. Type of inheritance, prenatal and carrier diagnosis.

Incidence

The incidence of DMD is 1:3000 males and is the same in all populations. The high incidence of DMD is thought to be due to the size of the DMD-gene. The prevalence in the Scandinavian countries is not known, but is believed to be 30 per 1.000.000 inhabitants.

DMD is caused by mutation in the gene, *DMD*, located on the short arm on the X-chromosome (Xp21). The gene contains 79 exons spanning 2,3 million base pairs of genomic DNA. It is the largest known human gene, encoding the protein, dystrophin. Dystrophin is a membrane-associated protein present in muscle cells and some neurons. Large rearrangements in the gene are found in about two-thirds of DMD patients, with approximately 60% carrying deletions and 5-10% carrying duplications. Most of the remaining 30-35% of patients are expected to have small nucleotide substitutions, insertions, or deletions.

Dystrophin is lacking already at birth although the first symptoms appears at the age of 1-2 years.

Genetics

Duchenne muscular dystrophy is an X-linked recessive disease. In theory, 1/3 of sporadic cases is believed to be caused by a *de novo* mutation in the proband.

If a woman is a carrier of the disease the risk for having a child with DMD is 25%, 50% of her boys will inherit the disease and 50% of her daughters will be carriers.

Genetic tests

Molecular genetic tests are available for the detection of deletion and duplication within the DMD-gene. Approximately 60 % of the patients will have a deletion and 5-10% a duplication, which can be detected by a DNA tests. The analysis is performed by a multiplex PCR reaction (MLPA) covering all 79 exons of the gene. The knowledge of the exact size of the deletion/duplication is prognostic. Deletions destroying the reading frame of mRNA (frameshift mutations) will lead to lack of dystrophin expression and tend to cause DMD. Deletion in which the reading frame is intact will lead to abnormal quality or quantity of dystrophin and cause Beckers muscular dystrophy.

Prenatal diagnosis

If the mutation in the proband is known prenatal diagnosis is possible by a direct test for the mutation on DNA isolated by a chorionic villus biopsy (CVS). The procedure is performed in the 10th week of pregnancy. The result is available within 2-3 days.

If the mutation in the proband is unknown prenatal diagnosis is only possible using linkage analysis within the family. In such an analysis the mutated gene can be tracked indirectly.

Linkage analysis takes time and requires samples from many family members. It is strongly recommended that the family has been counselled and that the appropriate analyses have been performed before a new pregnancy is started.

If the mutation cannot be detected in DNA isolated from a blood sample from the mother, the patient does not necessarily have a *de novo* mutation. The risk of a germ line mosaicism is not negligible, and the risk for future pregnancies is high. Prenatal diagnosis is always recommended.

New DNA-techniques are available in specialized laboratories, and the disease causing mutations will probably be found in all patients in the future.

Carrier diagnosis

If the mutation in the proband is known a direct DNA test can identify the carriers in the family. Genetic counselling and carrier testing should be offered to all relevant female relatives. The test only requires a blood sample. If the mutation is not known, or the patient is dead, the family can be investigated by linkage analysis, as mentioned above.

Repeated CK analyses are only suggestive, since 30% of carriers will show abnormal. The CK values depend on the age of the individual.

Preimplantation diagnosis

It is possible to test fertilized oocytes after in vitro fertilization (IVF). A single blastoma is removed at the 8-10 cell stages of the embryo for analysis.

There are two possibilities when considering pre-implantation diagnosis:

1. The sex of the embryo is determined and only female embryos are selected. All male embryos, of which 50% will be healthy, are destroyed.
2. If the mutation is known the embryos can be analysed directly for the mutation. Linkage analysis is not possible, since it will require more than one single cell.

Recommendations

- DNA-test should be performed in all DMD/BMD patients.
- Prenatal diagnosis and genetic counselling should be offered to the family.
- Genetic counselling and carrier testing should be offered to all relevant female relatives.

References

1. Liechti-Gallati S, Koenig M, Kunkel LM, Frey D, Boltshauser E, Schneider V, Braga S, Moser H (1989) Molecular deletion patterns in Duchenne and Becker type muscular dystrophy. *Hum Genet* 81:343-8
2. Beggs AH, Koenig M, Boyce FM, Kunkel LM (1990). Detection of 98% of DMD/BMD gene deletions by polymerase chain reaction. *Hum Genet* 86:45-8
3. Schwartz LS, Tarleton J, Popovich B, Seltzer WK, Hoffman EP (1992). Fluorescent multiplex linkage analysis and carrier detection for Duchenne/Becker muscular dystrophy. *Am J Hum Genet* 51:721-9
4. Grimm T, Meng G, Liechti-Gallati S, Bettecken T, Muller CR, Muller B (1994) On the origin of deletions and point mutations in Duchenne muscular dystrophy: most deletions arise in oogenesis and most point mutations result from events in spermatogenesis. *J Med Genet* 31:183-6
5. van Essen AJ, Kneppers AL, van der Hout AH, Scheffer H, Ginjaar IB, ten Kate LP, van Ommen GJ, Buys CH, Bakker E (1997) The clinical and molecular genetic approach to Duchenne and Becker muscular dystrophy: an updated protocol. *J Med Genet* 34:805-12
6. Abbs S (1996) Prenatal diagnosis of Duchenne and Becker muscular dystrophy. *Prenat Diagn* 16:1187-98
7. Lee SH, Kwak IP, Cha KE, Park SE, Kim NK, Cha KY (1998). Preimplantation diagnosis of non-deletion Duchenne muscular dystrophy (DMD) by linkage polymerase chain reaction analysis. *Mol Hum Reprod* 4:345-9
8. Sumita DR, Vainzof M, Campiotto S, Cerqueira AM, Canovas M, Otto PA, Passos-Bueno MR, Zatz M (1998) Absence of correlation between skewed X inactivation in blood and serum creatine-kinase levels in Duchenne/Becker female carriers. *Am J Med Genet* 80:356-61.

5. Nutrition

Background

The fact that 50% of the pre-puberty boys with Duchenne Muscular Dystrophy (DMD) are overweight and 50% of the older boys with DMD are underweight states that nutrition is of great importance.

With indirect calorimetric it is established that overweight younger boys with DMD has a decreased resting metabolic rate (RMR) compared to healthy controls. In average the RMR was decreased by 13%. Low resting metabolic rate together with low physic activity caused by decreased muscle mass can lead to overweight. In the group of boys with normal weight the resting metabolic rate was not different from the control group. Overweight often starts at the same time as introduction of wheelchair. (1, 2).

Increased weight is also one of the most common side effects in steroid treatment. A dietary change will then be needed and the weight should be followed up carefully. In DMD overweight leads to decreased mobility, increased respiratory problems and low self-confidence. It is preferable to prevent overweight in young DMD boys. The effort it takes to prevent overweight is much less than it takes to treat an established overweight. In treatment of overweight in DMD it is important to reduce the energy intake but keep the intake of nutrition at the recommended level. A high intake of protein could be needed to balance the higher need of protein to what it takes to maintain nitrogen balance in DMD (1,26 g protein / kg bodyweight / day). The increased protein metabolism is caused by hypercatabolism (3). There is no evidence that an energy-reduced diet in overweight boys with DMD would effect the muscle mass negatively (4-5).

Stagnation in weight gain occurs from the age of 13, and from the age of 14 underweight occurs among 50% of the boys. The reason for the development of underweight could be respiratory dysfunction that causes difficulty in breathing and fatigue at mealtime, poor appetite and incapacity to eat by themselves. Other reasons like depression, not to be able to visit the toilette by themselves, and the fact that they use food in a struggle for power might also lead to a decreased energy intake and malnutrition (2, 5, 6).

The resting metabolism is found to be significantly increased in the group of DMD-boys aged 11-29 compared to healthy controls. These boys also had a relatively high energy intake (110-115%) and protein intake (14,6% of the energy intake) when adjusted for bodyweight. The conclusion is that the underweight is due to an insufficient energy intake caused by hypercatabolism (7). The underweight could be improved by supplementary energy and protein and thereby also prolong life. Enteral nutrition should be considered in underweight DMD-patients. During the first period of malnutrition an enrichment of energy and protein in the usual food might help. The fluid intake tends to be low in high-energy regimes. That could cause or worsen constipation. Furthermore, intake of vitamins and minerals might be below the recommendations.

The easiest way for supplementary enteral nutrition is by gastrostomi during the night. At daytime the boys themselves can then decide what to eat and the size of portions.

In one study the DMD boys were given 1000 ml Osmolite during night (1000 kcal, 37,2 g protein). This led to a reduction of the energy intake with more than 40% during the day, but the total energy intake increased by 25%. The result after three month was a 4 kilos weight gain, and possible slower breaking down of muscle mass (8).

It is of great importance to continually take food anamnesis among these patients to be able to estimate the nutrient status. A food anamnesis should include what kind of food is eaten, portion size, appetite, how long time is needed to eat a full meal, difficulties in chewing and swallowing, obstipation, reflux, vomiting and other problems that might occur during

mealtime. It can also be an advantage at an early stage to prepare the patient and his family that enteral nutrition could be a necessary treatment of malnutrition later on. If possible, a regular indirect calorimetry is a good way to estimate energy allowance. An addition of 30% to the resting metabolic rate is needed to cover for the physical activity to get a more correct picture of the total energy expenditure. The total energy expenditure should be compared with the energy intake from 3-4 days diet record to estimate energy balance.

The boys with DMD should have an early established contact with a dietician to minimise the risk of overweight or malnutrition and to optimise the nutritional intake.

The chart for weight control in DMD could be an instrument to help estimate over- or underweight (9, 10).

In boys with chewing and swallowing problems a change in consistency of the food might be at hand. Also in reflux it might help. Otherwise the best way to handle with reflux is medical treatment and improved nutrition status.

Guidelines for energy allowance*

Overweight : 75-80% of RDA for age

Normal weight: 90-100% of RDA for age

Underweight: 125% of RDA calculated from kcal/kg bodyweight for age

*There are no documented energy recommendations for DMD in the literature.

Guidelines for dietary sources of energy in per cent of the energy, E%

	Protein	Fat	Carbohydrates
Overweight	10-15	25-30	55-65
Normal weight	10-15	30	60-65
Underweight	≥15	30-35	50-55

Recommendations

- The weight in boys without nutritional problems should be measured 1-2 times a year. In treatment of overweight or underweight the weight should be measured once a month initially. Situations where to expect changes in weight should also initiate weight measuring (e.g. loss of walking ability, before major surgery)
- To prevent overweight the dietician should be involved already at diagnosis, and when it is time for wheelchair. Dietician should also be contacted at tendency of underweight
- In overweight it is preferable with a weight loss of 0.5 kg per month or a stagnation of weight if there is a possibility to “grow in to” the weight within a year
- The first step in a minor underweight is to enrich the existing diet with energy and protein. Next step at more severe malnutrition is enteral nutrition during nighttime. In treatment of underweight the intake of energy and protein should be evaluated yearly
- Nutritional status should be examined before major surgery.

References

1. Hankard R, Gottrand F, Turck D, Carpentier A, Romon M Farriaux JP. Resting energy expenditure and energy substrate utilization in children with Duchennes muscular dystrophy. *Pediatr Res* 1996 Jul;40(1):29-33
2. Willig TN, Carlier L, Legrand M, Rivière H, Navarro J. Nutritional assessment in Duchenne muscular dystrophy. *Dev Med Child Neurol* 1993 Dec;35(12):1074-82
3. Okada K, Manabe S, Sakamoto S, Ohnaka M, Niiyama Y. Protein and energy metabolism in patients with progressiv muscular dystrophy. *J Nutr Sci Vitaminol (Tokyo)* 1992 Apr;38(2):141-54
4. Edward R, Round J Jackson M et al. Weight reduction in boys with muscular dystrophy. *Dev Med Child Neurol* 1984; 26: 384-390.
5. Tilton A, Miller M, Khoshoo V. Nutrition and swallowing in pediatric neuromuscular patients. *Semin Pediatr Neurol* 1998 June;5(2):106-115.
6. Willig TN, Paulus J, Lacau Saint Guily J, Béon C, Navarro J. Swallowing problems i neuromuscular disorders. *Arch Phys Med Rehabil* 1994 Nov;75:1175-1181
7. Okada K, Manabe S, Sakamoto S, Ohnaka M, Niiyama Y. Predictions of energy allowance of patients with Duchenne muscular dystrophy and their validity. *J Nutr Sci Vitaminol (Tokyo)* 1992 Apr;38(2):155-61
8. Goldstein M, Meyer S, Reund H. Effects of overfeeding in children with muscle dystrophies. *J Parenter Enteral Nutr* 1989 Nov-Dec;13(6):603-607
9. Griffiths RD, Edwards RH. A new chart for weight control in Duchennes muscular dystrophy. *Arch Dis Child* 1988 Oct;63(10):1256-8
10. Tanner JM, Whitehouse RH. Clinical longitudinal standards for height, weight, height velocity and weight velocity and stages of puberty. *Arch dis Child* 1976;

6. ORAL CARE

Background

Children with functional disabilities and their parents have the right to the security of knowing that the child with disability will receive special attention from an early age, be well looked after and receive highly-qualified care of all kinds, with particular consideration to each child's specific needs.

The objective of oral care is to keep the mouth as healthy as possible. Each patient should also be able to have positive expectations of a dental care appointment. Good oral health and function are also of significance for nutrition and communication. If it is difficult to maintain the individual's oral hygiene, supplementary prophylactic dental care will be needed. In order to avoid dental and oral mucosal diseases and to be able to follow the development of the individual's occlusion, it may be necessary to have relatively frequent dental appointments. In boys with Duchenne's muscular dystrophy (DMD) it is common to see a gradual development of occlusal malformation, with a successive reduction of the ability to chew, and increasing difficulty in maintaining oral hygiene.

Orofacial symptoms in DMD

There are very few studies on boys with DMD discussing the orofacial musculature of the oral cavity, jaws and face. In a longitudinal study, Eckhardt and Harzer (1) registered bite force and lip strength. Both these variables initially increased to a certain level, only to decrease successively afterwards, while the control group demonstrated continuous increases during the study period. The study also showed that the activity of the jaw muscles was reduced approximately two years prior to the corresponding reduction of the perioral musculature, where muscular force began to decrease at an average age of ten. The size of the tongue was also found to be larger than in the control group. Reductions in muscle tone and strength on masticatory muscles (musculi masseter) near the molars, in combination with the hypotonic, enlarged tongue and dominance of the less affected perioral musculature (musculi orbicularis oris) leads to transversal expansion of the dental arches, particularly in the lower jaw (See annex, figures 1 and 2).

The differences between the increased arch width of the lower and upper jaws give rise to conditions resulting in a posterior crossbite, which appears to be the most common malocclusion in boys with DMD. Furthermore frontal and/or lateral open bite occurs frequently (2). Other studies also show that half of the boys breathe through their mouths, and that the permanent teeth erupt on the average one year later than in others (2, 3). There is, of course, wide individual variation regarding the degree of occlusal malformation and other orofacial symptoms. A strikingly small number of these boys have eating difficulties, although they do tend to avoid certain foods. The slow course of the disease probably implies that they adapt in a natural way to their chewing difficulties. Clinical observations indicate that boys in late adolescence develop a successive reduction in mouth opening and greater chewing problems (4).

When there is major occlusal malformation, orthodontic treatment is considered. The prognosis for successful treatment is poor (5, 6), owing to the progressive development of the malocclusion and the progressively deteriorating course of the disease. It is doubtful if orthodontic treatment in boys with DMD will result in an improved ability to chew. However, Kawazoe et al (7) reported an improved ability to chew in six out of seven individuals (aged 16 to 24) with progressive muscular dystrophy who had trained with an orofacial exercise programme. Further studies are needed to provide adequate documentation of these claims (8)

Dental treatment

DMD is a rare disease with which most general dentists have little or no experience. For this reason, there is a point in centralising dental care of these boys at regional level. This does not necessarily mean that dental care is always provided by the same dentist, but the gathering of experience and deepening of knowledge of a dentist with special training, for instance at a specialist clinic, should lead to high quality care and provide a positive resource for the families of these boys and their local dentists in their home communities.

Annual dental examination

It is important that the patient's dentist, apart from dental caries and other oral infections, examines the following at individually adapted intervals:

- A thorough examination of the temporomandibular joint function, maximal jaw opening and tongue mobility.
- Occlusal development.
- Updating of patient records regarding respiratory function.
- Masticatory ability. Is the patient able to chew hard or tough food such as carrots, meat, etc.?
- Oral hygiene. Is the patient capable of brushing his teeth? What supplementary aids and devices are used?

The following should be kept in mind when dental treatment is carried out:

- Reduced ability to cough and swallow, breathing difficulties or cardiac disease may make it difficult for the patient to lie down in the dentist's chair. It may be possible in many cases to use the boy's individually adapted wheelchair or power-operated wheelchair, where he can sit safely and comfortably. (Annex, figure 3).
- There may be an increased risk of bleeding associated with major surgical interventions (9).
- Patients with DMD have an increased risk of problems related to cardiac and respiratory function. They also have an increased risk of malignant hyperthermia under general anaesthesia (10). Therefore preventive dental strategies are especially important.

Prophylactic dental care

Primary objective of prophylactic dental care is to prevent the most common dental diseases, caries and gingivitis/periodontitis.

- Clean teeth, good eating habits and supplementary fluoride are the cornerstones of such prophylaxis.

There should be an individually adapted prophylaxis programme as part of the dental therapy plan for each child from preschool age and upwards, and it should be updated annually.

Prophylactic dental care is essential for the prevention of diseases that would require treatment under general anaesthesia, as anaesthesia is a particular risk for boys with DMD.

Preventive measures should include the following:

- Planned prophylactic care both at the dental clinic and at home.
- Prescription of fluoride in an appropriate form.
- A suitable oral hygiene programme.

Personal care

One of the long-term consequences of DMD is difficulties to maintain good oral hygiene. One of the reasons for this is that it becomes increasingly difficult for the boy to keep his own oral cavity clean as the muscular weakness of the tongue, lips and cheeks progresses. Another reason is that tooth brushing becomes increasingly difficult due to general muscular weakness. It is important in terms of self-confidence that the individual be able to manage on his own for as long as possible. These patients should therefore clearly have the right to any aids and devices that can assist them.

When the boy no longer has the muscular strength in his hands and arms to raise the toothbrush to his mouth, a home visit is recommended. The dental hygienist and

occupational therapist should visit the patient together, so they can see the place where the patient normally carries out his daily dental care and give him the individual guidance he needs.

In the patient's bathroom, the following should be made available: (annex, fig 4)

- An adjustable sink that can be raised and lowered. It should also have a frame with a surface that can be used for arm support.
- The ability to access the sink from a wheelchair.
- A mirror at the right height.
- Good lighting.

Technical aids

Some suitable aids for oral hygiene, dental treatment and mouth motor exercises recommended for working with muscular weakness:

- Electric toothbrush. (Annex, fig 5).

An electric toothbrush is an excellent help as muscular strength in the arms and hands decreases and it becomes difficult to brush manually. With time, the patient will also require help to be able to lift the toothbrush to his mouth. A sink with adjustable height and a frame with a surface that can be used for arm/hand support will enable the individual to hold the battery operated toothbrush at a suitable height for cleaning the teeth.

- Bite support. (Annex, fig 6).

If it is tiring for the boy to keep his mouth open, a bite support between the upper and lower teeth may be useful.

- Cheek retractor. (Annex, fig 7).

A cheek retractor is an aid that can be used to improve access to the mouth both for the patient when brushing his teeth and in dental treatment.

- Jaw mobilizer. (Annex, fig 8)

Normal activity, exercising and stretching of the temporomandibular joint and masticatory musculature are encouraged with a view to maintaining orofacial function. This jaw mobilizer is made of wood and used to maintain mobility of the temporomandibular joint and stretch the jaw muscles after individual instruction.

Recommendations

- Boys with DMD should see a dentist with extended experience and detailed knowledge of the disease, preferably at a centralised or specialist clinic. The dentist's mission should be to strive for high-quality treatment, oral health and wellbeing and to function as a resource for the families and the boy's own dentist in his home community.
- For boys with DMD, oral and dental care is to be based on prophylactic measures with a view to maintaining good oral hygiene.
- For boys with DMD, individually adapted assistive devices and technical aids for oral hygiene are of particular importance when the muscular strength of the patient's hands, arms and neck begins to decrease.

References

1. Eckhardt L and Harzer W. (1996) Facial structure and functional findings in patients with progressive muscular dystrophy (Duchenne). *Am J Orthod Dentofacial Orthop*, 110(2): 185-190.
2. Ghafari J et al. (1988) Dental and occlusal characteristics of children with neuromuscular disease. *Am J Orthod Dentofacial Orthop* 93(2): 126-132.
3. Erturk N and Dogan S. (1991) The effect of neuromuscular diseases on the development of dental and occlusal characteristics. *Quintessence Int*, 22(4): 317-321.
4. Ahlborg B, Åhlander A-C (2003) Mun- och tandvård vid Duchennes muskeldystrofi. *Tandläkartidningen* 95(3): 38-43. (In Swedish. English equivalent title: Oral and dental care in Duchenne's muscular dystrophy).*
5. Matsson L, Bäckman B, Almer Nielsen L. Dental care for the disabled child and adolescent. In: Koch G and Poulsen S. 1st ed (2001) *Pediatric Dentistry – a clinical approach*, Munksgaard: 445-462.
6. Stenvik A, Storhaug K. (1986) Malocclusion patterns in fourteen children with Duchenne's muscular dystrophy. *ASDC J Dent Child*, 53(3): 215-218.
7. Kawazoe Y et al. (1982) Effect of therapeutic exercise on masticatory function in patients with progressive muscular dystrophy. *J Neurol Neurosurg Psychiatry* 45(4): 343-347.
8. Kiliaridis S and Katsaros C. (1998) The effects of myotonic dystrophy and Duchenne muscular dystrophy on the orofacial muscles and dentofacial morphology *Acta Odont Scand* 56(6): 369-374.
9. Nordeen MH, Haddad FS, Muntoni F, Gobbi P, Hollyer J, Bentley G (1999) Blood loss in Duchenne muscular dystrophy: vascular smooth muscle dysfunction? *J Pediatr Orthop B*; 8(3): 212-215.
10. Wedel DJ (1992). Malignant hyperthermia and neuromuscular disease. *Neuromuscul Disord* 2(3): 157-164.

7. Neuropsychological and educational aspects

Not yet translated – to be inserted later

8. Psychosocial aspects

Background

Duchenne muscular dystrophy is one of the most serious neuromuscular diseases characterised by progressive global muscle weakness, which considerably reduces or impedes the physical opportunities for development (1, 2). This implies an increased risk for DMD-boys to become isolated and experience psychological difficulties due to their limited ability to participate in many activities, and can also lead to emotional and behavioural problems. Furthermore, some DMD-boys have cognitive dysfunctions such as concentration and learning difficulties (3, 4).

Before the introduction of mechanical ventilation the life span of boys with DMD was considerably reduced, and there seemed to be no reason to prepare them for an adult life. Today, persons with DMD on assisted ventilation live longer, and therefore it is very important to prepare them for an independent life in their own home with personal assistants (5). This has caused the need for an entirely different kind of support, not only for the DMD-boys, but also for their parents, personal assistants and other professionals in this field.

Guidelines

When communicating diagnosis

The child is usually diagnosed at the age of 2 or 3. At that time the child has only few physical limitations, and the disease has no influence on the child's self-image. The parents, however, are often in severe crisis due to the bad prognosis of the disease and the limitations it will inflict on their child's possibilities for development.

Intervention

Parents should be offered support to overcome their crisis and deal with their grief. This can be accomplished by therapeutic sessions with the parents or by offering them participation in courses where they meet other families in the same situation, and where they are provided with information on possibilities for support, relief and development. Besides, it is important for the parents to become aware how to support their child in order that his possibilities for development and for active participation in social life are optimised.

Nursery school and pre-school

Gradually, the boy will need a practical helper to assist him in situations where he lacks strength. Usually, this happens without emotional problems for neither the child nor the helper.

Intervention

In some cases it will be necessary to inform the helper how to adequately support the child's emotional development. For example in the form of a meeting where the child's parents, helpers, teachers and special advisors are gathered. Furthermore, the parents can be supported through a follow-up family course aiming at strengthening their resources.

In connection with school start

Generally, the school age boy has acquired some knowledge about his own ability and disability compared to other children. Therefore the adults must support the child in enduring and mastering this knowledge adequately in order for him to develop a positive self-image. As a rule the boy has

a positive attitude towards starting school. Still, it is important that his teachers and the practical helper are carefully informed on the disability and compensatory possibilities, as well as the parents' expectations to the tasks and capacities of the school.

Intervention

In some cases the boy requires assistance from a psychologist in order to deal with his experiences of being different from other children. Generally, it will be appropriate to offer a course for his parents, teachers and practical helpers before the boy starts school. The purpose of this course should be to discuss the best way to arrange or organise the boy's education in order that it will offer him challenges and possibilities for development regarding the learning process, as well as social interaction with the other children. Such a course also offers an opportunity to inform the participants about the fact that some DMD-boys may have learning disabilities that require special tutoring (7, 8, 9, 10).

The age of 10 to 12

During this period children tend to manage by themselves at home or with friends after school rather than attending youth recreation centres. The DMD-boy at this age has become a severely disabled wheelchair user dependent on help from others and has to remain in the recreation centre with younger children. In this period the child experiences physical, psychological and social losses in comparison with his classmates. Moreover, during the same period his self-image develops considerably which among other things involves the fact that the boy to a large extent will compare himself with the others. The feeling of being different from others, of being excluded and losing contact to former friends is an emotionally painful experience for the boy. Some boys indicate that they do not want to continue life with muscular dystrophy.

Intervention

Provision of psychological support can be necessary; not only to the child but also to his parents who often find it difficult to support the boy during this period since they are often deeply affected themselves by the child's experiences and reactions, and fear where it is going to end. It can be beneficial to offer courses or supervision to the parents, other family members, teachers and personal assistants in order to ensure appropriate co-operation between home and school during the difficult period.

Teenagers

The adolescent has to relate to the fact that the need for personal assistance is increasing. At the same time the natural process of separation from the parents should be initiated (11). It is no longer adequate for the parents to help the boy with personal issues such as taking a bath or going to the toilet. The boy must learn to make use of his assistants for his personal care as well as other doings, which naturally leads to the development of an emotional relationship to his assistants. However, the boy should not let his assistants control his life, nor should they form his social network to such extent that he has no other friends. The adolescent should be prompted to lead an active, out-going life with natural social contacts to his surrounding world, and on the long view he should be prepared for an independent life in his own home with personal assistants.

Intervention

Courses where the DMD-adolescent meets others with the same disability are recommended. During such courses he is offered the opportunity of gathering experience how to manage the problems connected to being a young disabled wheelchair user, including the relationship to his parents, his independence, self-confidence, education, girlfriends, and the interaction with his personal assistants. Besides, courses should be arranged for the parents prompting them to support the adolescent's separation process. Some of the adolescents benefit from attending a boarding school for mainly able bodied adolescents; whereas others find it far more beneficial to

attend a special boarding school for disabled students where they do not differ from others as has been the case so far. In many cases there is a need for psychological support during this process for the adolescent as well as the parents in order for them to overcome these very difficult years with great changes, adjustments and critical health situations, for example connected to respiratory problems. These experiences can be very anxiety provoking for the whole family.

18-25 years

Some young DMD-persons arrange their own homes, including a room for personal assistants, in connection to the house of their parents. This makes the transition to an independent life more gradual. On the other hand it may retard the process and make it difficult for the young person if his parents are unable to withdraw in time and leave to the personal assistants all kinds of care taking, including possible difficulties in providing assistants and coping with acute situations. Young DMD-persons particularly have difficulties in having a girlfriend, or in getting a job or some other kind of meaningful occupation, as well as developing and maintaining a leisure activity and an active, out-going life with friends. Furthermore it is difficult for them to be responsible for housekeeping and to be the employer of a large group of personal assistants. In addition, the physical and emotional level can vary considerably, and daily chores such as bathing and dressing are time and energy consuming. On the whole, careful planning of everyday life is required.

Intervention

It is important for the young DMD-person to manage his situation in an active and constructive way so that his family, friends and personal assistants feel like keeping company with him. If he becomes too passive, guilty or controlling there is a risk of developing a self-increasing vicious circle where he becomes isolated and increasingly inhibited. It is important that the young person does not make use of avoiding reactions as models for solution whenever a difficult situation arises. In a transitional period, for example, he may need support in order to learn how to manage meetings with his staff of assistants.

Special courses for practising these skills or a sparring partner, for example a psychologist, can be of great help when finally the young man becomes independent and starts making his own life.

Recommendations

- The natural emotional reactions in DMD-boys should not be considered pathological
- The parents should be supported to endure the fact that their boys experience difficult problems
- The parents should be instructed to teach the boys how to manage their problems themselves
- DMD-boys should be guided how to manage emotional strain and problems
- DMD-boys, parents, family members and personal assistants should be offered psychological support in order to overcome crises and deal with grief.

References

1. Kroksmark, V; Thorén-Jönsson, A: At leve med Muskelsvind. Århus: Muskelsvindfonden 1989.
2. Steffensen, B m.fl.: Muskelsvind hos børn. Århus: Muskelsvindfonden 1996.
3. Polakoff, RJ; Morton, AA; Koch KD; Rios CM: The psychosocial and cognitive impact og Duchenne´s muscular dystrophy. Semin Pediatr. Neurol 1998 juni; 5 (2):116-23.
4. Cotten, S; Voudouris, NJ; Greenwood, KM. Intelligence and Duchenne muscular dystrophy. Developmental Medicine & Child Neurology 2001,43:497-501.
5. Kristensen, HS; Nielsen, TA; Nyholm G.: Danske respiratorbrugeres levevilkår. Århus: Muskelsvindfonden 1999.
6. Fyhr, G. Sorgens rum. København: Gyldendal 2000.
7. Greve, J. Drengene med Duchennes Muskeldystrofi, om forudsætninger – undervisning – fritid. Århus: Muskelsvindfonden 1993.
8. Billard, C; Gillet, P; Barthez, M; Hommet,C; Bertrand, P. Reading ability and processing in Duchenne muscular dystrophy and spinal muscular atrophy. Dev Med Child Neurol 1998. Jan;40(1):12-20.
9. Hinton, VJ; De Vivo, DC; Nereo, NE; Goldstein, E; Stern, Y. Selective deficits in verbal working memory associated with a known genetic etiology: The neuropsychological profile of Duchenne muscular dystrophy. J Int Neuropsychol Soc 2001 Jan;7(1):45-54.
10. Hinton;VJ; De Vivo, DC; Nereo, NE; Goldstein,E; Stern, Y. Poor verbal working memory across intellectual level in boys with Duchenne dystrophy. Neurology 2000 Jun 13;54(11):2127-32.
11. Reid, DT; Renwick, RM. Relating familial stress to the psychosocial adjustment of adolescent with Duchenne muscular dystrophy. Int J Rehabil Res 2001 Jun;24(2):83-93.

9. **Physiotherapy and occupational therapy** *Assessments and interventions*

Background

The aims of the interventions from physiotherapist and occupational therapist are:

- a) to delay or reduce complications due to the deterioration of muscle strength
- b) to give guidelines regarding activities, possibilities, adaptations and adjustments enabling the boys/men to live a socially active life together with family and friends

When muscle strength and functional abilities change over time, evaluations and interventions must continuously be adjusted in such a way that necessary interventions are performed and adjusted. To be able to provide optimal guidelines it is important for the therapists to be well informed about the course of the disease on individual basis.

The organisation of the health systems differs in Denmark, Sweden and Norway. In Denmark the therapeutic consultations are almost always performed in collaboration with the Institut for Muskelsvind (Danish Institute for Treatment of Neuromuscular Disorders) while in Norway and Sweden the consultations are managed in collaboration between habilitation teams in the communities and the neurology departments at the hospitals.

There are different traditions regarding which professional group is responsible for the evaluations, not only among the three countries but also within the same country. A schedule for the therapeutic evaluations and interventions is presented below. For clearness the schedule is divided into two parts, one for physiotherapy interventions, the other for occupational therapy interventions.

Guidelines for physiotherapy and occupational therapy evaluations

The ongoing progression of the disease and the boy's development demand frequent evaluations of functional abilities and possibilities for activities. Such an evaluation is performed through an interview with the boy himself, his family, local professionals, and through evaluation of function and other investigations. A thorough medical history/investigation with information concerning level of function and need for practical help at home, in leisure time, at pre-school/school forms part of every evaluation as the disease progresses.

Regular and systematic evaluations and documentation are vital to be able to follow the course of the disease and to be able to recommend the right intervention at the right time. It is important that the evaluation protocol used is as consistent as possible in order to make comparative investigations and perform joint Nordic projects.

The physiotherapist and occupational therapist evaluations will change through the course of the disease due to boy's level of function. The evaluations are divided into two sections; the first section, "Ambulant", when the boys are still ambulant, and the second section, "Non-ambulant", when the boys have lost independent ambulation.

Ambulant

Analysis of activities	Pedi (1), COPM (2)
Functional tests	Time tests, Hammersmith's scale (3), Brookes scale for upper extremities (4), Vignos scale (5), evaluation of hand function
Posture/investigation of the spine	Investigation of the standing posture Registration of the sitting posture (12)
Muscle test	Manual muscle test (9), dynamometry (8), Grippit (7)
Range of motion	Measurement of range of motion in upper and lower extremities and in the neck (10)
Vital capacity	Measurement of the forced vital capacity (FVC) (11)

Non-ambulant

Analysis of activities	COPM
Functional tests	Brooke, EK-scale (12), evaluation of hand function
Investigation of the spine/investigation of sitting posture	Analysis of sitting posture on a bench and in the wheelchair (13) Investigation of abilities to drive the electric wheelchair
Muscle test	Manual muscle test, dynamometry, Grippit
Range of motion	Measurement of the range of motion in the upper and lower extremities, in the neck and more comprehensive measurements of the range of motion of the hand.
Vital capacity	Measurements of forced vital capacity with and without spinal jacket

*Different tests of hand function are used in Norway, Denmark and Sweden.

** FVC is only measured when the boys are able to co-operate in the measuring procedure. Different lung function tests are used in the three countries. For that reason it is not yet possible to define which tests to use in a multicentre study in this field.

Guidelines for treatment

Few scientific studies exist on the effect of physiotherapy treatment in this disease. The interventions used are based on experience built up over many years of co-operation between therapists and people with the disease. It is important to continuously develop methods of measurements to be able to document the effect of treatment procedures. A Scandinavian programme of intervention can lead to a common assessment and treatment procedure and enhance the possibilities of future evaluations of the effect of treatment procedures.

The daily/weekly treatment should be done locally where the boy lives, with supervision to and in close co-operation with therapists who have specialised knowledge in this field. The organisation of both social and medical support is different in the three countries, and the implementation of the treatment varies accordingly.

It is important to give advice on positioning during rest, activity and play in order to prevent development of contractures. This must continue during the progression of the disease in order to optimise the use of steadily weakening muscles as well.

The boys stop walking because of a combination of weakening muscles and contractures in hip, knee and ankle joints. The development of contractures can be delayed by daily stretching and other measures, i.e. night splint, standing brace (14), and can, if successful, delay the time when walking/standing is no longer possible.

From an early age the boys depend on technical aids in their activities of daily living. Technical aids compensate lost functions for the grown-up as well (15). Technical aids can help the boys/men to continue in play and other activities with friends, and the adults to continue living independently and possibly also work. To do so both technical aids and other physical adaptations must be available in pre-school/school, at home, during play- and social time and at work.

The sitting position in the wheelchair is important in order to promote and optimise hand function. Correct sitting position is also important to prevent spinal curvature which, if developed, reduces lung function. Therapeutic intervention must include methods that promote coughing, mobilisation of secretion by different methods and optimal use of the steadily weakened respiratory muscles.

Recommendations

- From the time of diagnosis the boys must be assessed once to twice a year by therapists (physiotherapists and occupational therapists) with special experience in neuromuscular disorders. The interval between the assessments depends on the boy's age, the progression of the disease and his functional ability (see: Guidelines for therapeutic assessments in DMD)
- Boys with DMD should be referred to occupational therapist and physiotherapist at the time of diagnosis. Treatment should be planned and followed by therapists with experience in the field
- The therapeutic interventions must follow the principles described in the following: "Guidelines for physiotherapeutic intervention" and " Guidelines for occupational interventions"

Guidelines for Physiotherapy in Duchenne Muscular Dystrophy

	Time of diagnosis – ambulant	Slow and troubled ambulation	Non Ambulant	Wheelchair	
	3-6 years	7-11 years	12-15 years	> 15 years/respiratory aids	
Information about activities	<ul style="list-style-type: none"> – Activities at home and in the kindergarten, – Swimming once a week is recommended – Instruction on how to help (to lift) the boy from the ground is given to the parents and the kindergarten 	<ul style="list-style-type: none"> – As earlier – Ensure that the information is also given to the school – Swimming in warm water 	<ul style="list-style-type: none"> – Swimming in warm water – Information about possible sports 	<ul style="list-style-type: none"> – Swimming if possible 	
Preventing contractures	<ul style="list-style-type: none"> – Passive stretching for hip flexors, tensor fasciae latae, hamstrings and tendon Achilles – First as regular controls at the physiotherapist, but soon as daily exercises. – Few long stretches are better than many short stretches – Muscles working over two joints have to be stretched over both joints at the same time 	<ul style="list-style-type: none"> – As earlier, but now also with passive stretching for arms, hands and neck – Regular physiotherapy as treatment, control and supervision of the stretching performed by the parents or the helpers – Daily stretching exercises by the helpers or the parents 	<ul style="list-style-type: none"> – Daily exercises – Stretching is replaced by an increasing number of passive movements – continue treatment/exercises with the physiotherapist 	<ul style="list-style-type: none"> – Daily exercises by help from the assistant – Physiotherapy – according to the need 	
Standing	<ul style="list-style-type: none"> – the boy is recommended to stand at a table while he plays – If the boy is standing very asymmetrically – a standing frame is recommended one hour a day. 	<ul style="list-style-type: none"> – The ability to stand* is supported by long-leg calipers or a standing frame. – Recommended standing time: at least two hours a day if in calipers. / 30-60 minutes if in standing frame 	<ul style="list-style-type: none"> – As earlier with calipers or in a standing frame – The boy should cease to stand if he stands very asymmetrically because of joint contractures or scoliosis 	<ul style="list-style-type: none"> – as earlier 	
Sitting	<ul style="list-style-type: none"> – Awareness of the sitting position in his chair/wheelchair. – The chair must support his back in a lordotic position and prevent abduction of the thighs 	<ul style="list-style-type: none"> – The seat in his electric wheelchair must be adapted for the boy to sit symmetrically with lordosis. – Information about the importance of changing position regularly in the wheelchair – If the boy can no longer sit upright and tends to sit asymmetrically he should be referred to regular assessments at a department for orthopaedic surgery in order to follow a possible development in scoliosis 	<ul style="list-style-type: none"> – The boy's sitting position has to be assessed at regular intervals in order to support his back and his functions. – His wheelchair has to be equipped with side supports if he can not sit symmetrically without them – He is informed how to use an electrically operated belt as support in his wheelchair 	<p>The sitting position is corrected after spinal surgery but must be controlled at regular intervals to provide him the best possible functional abilities to manage his wheelchair</p>	
Respiratory function	<ul style="list-style-type: none"> – Instruction in deep breathing technique, exercises for the respiratory function, – Instruction in cough 	<ul style="list-style-type: none"> – As earlier – Dependent on his respiratory function and according to his needs the boy is instructed in 	<ul style="list-style-type: none"> – As earlier – Information about changing position, during lung infections – The boy has to be 	<p>Follow up on the respiratory problems: instruction and guidance in changing position, coughing etc.</p>	

	support	breathing against resistance, e.g. positive expiratory pressure or continuous positive airway pressure	referred to a respiratory department (according to their criteria for references)	
Splints and back-bracing	– Below knee night splints – when the tendo Achilles is beginning to become tight.	– Night splints – Long leg braces/calipers	– Below knee splints for daily use in the wheelchair. – Spinal brace when the boy is starting to sit asymmetrically, and/or he is not able to sit upright **	– Splints – Spinal brace, dependent on the degree of scoliosis

Comments on the guidelines above:

*** Standing**

The orthopaedic surgeons will have recommendations (see chapter 11) whether or when it is necessary to operate on contracted tendons in order to establish standing ability in long-leg calipers.

The optimal time to start standing with long-leg callipers is when walking is no longer possible, when the range of movement of the ankle joint is 90°, the knees can be fully stretched, and there is no tightness in tensor (according to international criteria)

This requires optimal timing to succeed.

**** Spinal-bracing.**

The orthopaedic surgeons set the criteria for when or whether bracing should be started. It is recommendable that these criteria will be the same in all three countries. Our suggestions are: when it is possible to observe back asymmetry, at the start of kyphosis and/or at Cobbs degree of >15° (when the boys are below 18 years of age)

Guidelines for Intervention for Occupational Therapy

	Time of diagnosis - ambulant	Slow and troubled ambulation	Wheelchair	Respiratory assistance
Age	3-6 years old	7-11 years old	12-15 years old	15 years old and more
Reduced activity and function	Reduced muscle strength in hand and arm. Shortening of the tendo achilles. Difficult to walk long distances, to climb stairs, to bicycle and to stand up from the floor	Difficult to lift arms against gravity, to get from lying down to sitting up, to get off a chair, to walk outdoors and to perform personal hygiene Reduced speed	Difficult to eat without assistance Unable to walk without support Unable to change position in bed or on chair	Very limited mobility
Interventions				
Mobility	Manual wheelchair for independent movement and transportation Pram Functional clothes Shoes with good stability Adjustments of car.	Electrical wheelchair with electrically operated belt for in/outdoor use Scooter. Mobile personal lift (electric) Wheelchair-ramp. Height adjustable bed with electric headrest.	Easy-glide. Electric blanket to change position in bed. Anti-decubitus mattress in bed	
Sitting and seating	Chair with footrest	Height adjustable chair Wheelchair with sitting support Electrical support-belt for the trunk	Wheelchair with good sitting support NB: Support for neck and trunk etc	Wheelchair with good sitting support Electric neck support

Arm- and hand-function	Adjustment of position for playing, and choice of lightweight toys.	Height adjustable table. Socks and gloves with heating elements. Lightweight pen and pencil. Computer.	Light cutlery with longer handles. Light drinking glass/cup.	Adjustment of the steering of the wheelchair. Switch-control to operate electric equipment, the environment and to call for assistance.
Bathing and toileting		Toilet-chair, bath-chair, bath-lift Adjust the toilet with foot-, trunk- and arm support "Closomat"-toilet with wash and wiping functions	Height adjustable shower bench Electric toothbrush	
Adjustment in the house	Secure and adjust entrance area of house. Remove thresholds Electric door opener Wheelchair accessibility inside the house.	Electrical wheelchair accessibility in the house (stair lift) Sufficient space for use of an electric wheelchair and a room for equipment and helpers. Ensure optimal independence (table, door, water tap) Ensure good working conditions for helpers.	Enough room/space for helpers in the house	Space for electrical wheelchair with ventilator
Transport	Taxi/own car	Apply for a van	Wheelchair-van	Van
School / institution	Give advice and consultation on adjustments for wheelchair accessibility. Select type of school Transport to school	Pedagogical and practical assistance. Double sets of school books Transport to school	Choice of school depends on educational systems and organisation in each country High school	Education? College/ University
Leisure		Hobby Handicap-sport Summer camp	Youth club Hobby Handicap sport Summer camp	Youth club Hobby Handicap sport Summer camp
Helpers	Helpers in school.	Helpers in school and social activities.	Helpers in school, at home and social life.	Helpers on a 24 hour basis
Social and economic regulations	Evaluate the family's increased expenses for - transport - helpers - clothes - electricity a. o. in the home Economic compensation for parents due to reduced job income.	Evaluate the increased expenses. Start and expand according to need the amount of and type of respite care (at home, in other peoples' homes or in institution).	Evaluate increased expenses to cover educational and living expenses. Increase time in respite care.	Evaluate increased expenses and ensure the boys'/men's independence socially and economically. At 18 years of age: Future economy? Independent living? Daily help and assistance on a 24 hour basis.

References

1. Pedi/Pediatric Evaluation of Disability Inventory – PEDI Research Group. Manual - Boston 1992
2. COPM/Canadian occupational Performance Measure. Manual - Nacka 1998
3. Scott OM, Hyde SA, Goddard, Dubowitz "Quantification and muscle function in children": a prospective study in Duchenne Muscular dystrophy. *Muscle & Nerve* 1982;5:291-301)
4. Brooke MH et al.: Clinical trial in Duchenne dystrophy. The design of a protocol. *Muscle & Nerve* 1983;6:91-102
5. Vignos PJ, Spencer GE, Archibald KC: Management of progressive muscular dystrophy in childhood. *JAMA* 1963;184:89-96
6. Nordenskiöld UM, Grimby G. Grip Force in patients with Rheumatoid arthritis and fibromyalgi and in helthy subjects, A study with the Grippit instrument. *Scan J Rheumatol.* 1993;22:14-19
7. Hyde SA et all.The Myometer, the development of a clinical Tool)
8. Brooke MH et all "Clinical trial in Duchenne dystrofi....., medicial Research Council og the United Kingdom. Aids to examination of the peripheral nervous system : memorandum No.45. palo Alto, Calif: Pendragon House; 1978)
9. American Academy of orthopedic surgeons. Joint motion;: Method of measuring and recording 1965 E&S Livingstone, Edinburgh and London
10. Lyager S, Steffensen B, Juhl B (1995) Indicators of need for mechanical ventilation in Duchenne muscular dystrophy and spinal muscular atrophy. *Chest* 108: 779-85)
11. Steffensen, Hyde, Lyager, Mattsson: "Validity of the EK scale: a functional assesment of non-ambulatory individuals with Duchenne muscular dystrophy or Spinal muscular atrophy.: *Physiotherapy Research International* 6(3) 119-134, 2001
12. Hyde et al. "A randomised comparative study of two methods for controlling TA contracture in Duchenne muscular dystrophy" – *Neuromuscular Disorders* 10(2000) 257-263

10. Medical management of muscular dystrophy

Background

Corticosteroids represent the only medical treatment that in a majority of studies have proved to delay the progressive muscle weakness which forms part of the natural history of Duchenne Muscular Dystrophy (1-14). Besides corticosteroids more than 30 different drugs have been evaluated in clinical trials, over the past 50 years without any proven positive effect. The lacking results of these early trials have been summarised by Emery (15) and Dubovitz and Heckmatt (16). Many of those trials, however, were designed in a way which made the results difficult to evaluate. (16). Few of them fulfilled the criteria of a clinical assessment with substantial reliability, which should include: A well defined group with a verified diagnosis, a matched control group (or cross-over design), a double-blind study, evaluation by methods with good reliability and validity, and an acceptable power of the trials to determine an effect. For Duchenne muscular dystrophy the latter has been carefully discussed by Brooke (17) and Stern (18). Several of the drugs that have formerly been tested, and new ones selected because of a beneficial effect on muscle strength in mdx-mice (mouse model for DMD), are now being tested, or being prepared for testing, in large worldwide clinical trials including several hundred DMD-boys (20).

Among the corticosteroids prednisone and prednisolone are the most frequently tested drugs (1-8, 11, 12). Fewer trials, though likewise with a proved beneficial effect, have been published about deflazacort (9, 13, 14), a corticosteroid with assumed fewer side effects, primarily with regard to demineralisation. Still, for deflazacort a greater share of side effects in the form of asymptomatic cataract have been recorded. It is not clear whether in DMD the delaying effect on the progress of the disease from corticosteroids is due to their immunosuppressive effect, or to their effect on regulation of genes of importance for the dystrophic processes. – See appendix for table summarizing the results of clinical trials of the three corticosteroids.

Prednisone, the corticosteroid used in a majority of the trials, has, compared with placebo, proved to improve muscle strength, muscle function, and retard the loss of ambulation by up to 2.5 years (4, 8, 14). This positive effect, as well as the side effects, is dose dependent (6). At a dose of 0.7 mg/kg/d prednisone causes 18% kg gain of weight as a substantial side effect (5, 6, 14) Approaches to reduce the side effects include alternate day medication (1, 2, 4), altering 10 days with corticosteroids and 10-20 without (11), and reducing the daily dose (12). Side effects in the form of weight gain have turned out to be considerably less marked with deflazacort than with prednisone (13). Despite the most convincing advantage of corticosteroids to delay the course of the disease during the trials, there is no international consensus to recommend cortisone medication in DMD (20, 21) because of an uncertainty about the effect of cortisone in a longer perspective than so far examined. The concerns include the effect on heart, osteoporosis, and possible negative long-term effects on skeletal muscles. A retrospective long term follow-up up to 6.5 years showed that respiratory function was significantly better among those at the age of 15 who had been treated with deflazacort than among those who had placebo (14). One case has reported an adolescent who owing to asthma had been medicated with high dose prednisone over many years and still maintained partial ambulation (22). These reports, however, lack high scientific value, and knowledge about the effect of corticosteroids after the loss of ambulation is still lacking. Nor is there scientific evidence about the optimal time to start medication with corticosteroids. Still, there are many indications that it is best to start soon after diagnosis in order to delay the muscle deterioration.

In the Nordic countries corticosteroid medication in Duchenne muscular dystrophy has been most frequent in Sweden, mostly due to a clinical study performed by Bäckman & Henriksson (12) proving positive effect on muscle strength. In Sweden this study has had a great impact and forms the basis of the instructions given to the majority of Swedish families which is reflected by the fact that about 50% of DMD boys are medicated with Prednisolon or deflazacort. In Norway, and particularly in Denmark, the use of corticosteroids in DMD has been more restrictive. This difference to some extent is due to the degree of scientific documentation considered to be required in order to advocate for the use of cortisone, the end-point chosen (e.g. prolongation of ambulation), and evaluation of side effects. Besides, there is a probable individual difference in response to corticosteroid medications, the causes of which seem unknown for the time being. An evidence-based Cochrane review of corticosteroid medication in DMD is being planned (24).

If initiation of corticosteroids is decided, it is of vital importance from a quality assurance point of view to accurately follow their efficacy and side effects. This must be done systematically and include parameters which can be compared between different clinics, above all in the Nordic countries. A proposal like that would also make it possible to evaluate the effect of treatment in a larger material in a joint Nordic study.

Recommendations

On initiating corticosteroid medication prednisolone in a dose of 0.35 mg/kg/day is recommended. Medication can be started early after diagnosis or later.

Deflazacort can be recommended as an alternative drug in case Prednisolone has given / is expected to give non tolerable side effects.

Before initiation of corticosteroid medication the following assessments must be done: blood pressure, b-glucosis, s-Na, s-K, weight/length, echo cardiography, vital capacity, time test walking 10 meters, time test Gower's manœuvre, fuctional test and test of muscle strength (see assessments by PT and OT, chapter 9).

In case of significant overweight, hyperglychemia / glycosuria, cataract, fractures, gastrointestinal bleeding, hypertonia (blood pressure above 97 percentile for the age group), behavioural changes, tuberculosis should be considered as relative or absolute contraindications for medication with corticosteroids.

References

1. Drachman, D.B., K.V. Toyka, and E. Myer. Prednisone in Duchenne muscular dystrophy. *Lancet*, 1974. **2**(7894): p. 1409-12.
2. Siegel, I.M., J.E. Miller, and R.D. Ray. Failure of corticosteroid in the treatment of Duchenne (pseudo- hypertrophic) muscular dystrophy. Report of a clinically matched three year double-blind study. *IMJ Ill Med J*, 1974. **145**(1): p. 32-3 passim.
3. Brooke, M.H., et al. Clinical investigation of Duchenne muscular dystrophy. Interesting results in a trial of prednisone. *Arch Neurol*, 1987. **44**(8): p. 812-7.
4. DeSilva, S., et al.. Prednisone treatment in Duchenne muscular dystrophy. Long-term benefit. *Arch Neurol*, 1987. **44**(8): p. 818-22.
5. Mendell, J.R., et al. Randomized, double-blind six-month trial of prednisone in Duchenne's muscular dystrophy. *N Engl J Med*, 1989. **320**(24): p. 1592-7.
6. Griggs, R.C., et al. Prednisone in Duchenne dystrophy. A randomized, controlled trial defining the time course and dose response. *Clinical Investigation of Duchenne Dystrophy Group. Arch Neurol*, 1991. **48**(4): p. 383-8.

7. Fenichel, G.M., et al. Long-term benefit from prednisone therapy in Duchenne muscular dystrophy. *Neurology*, 1991. **41**(12): p. 1874-7.
8. Fenichel, G.M., et al. A comparison of daily and alternate-day prednisone therapy in the treatment of Duchenne muscular dystrophy. *Arch Neurol*, 1991. **48**(6): p. 575-9.
9. Mesa, L.E., et al. Steroids in Duchenne muscular dystrophy--deflazacort trial. *Neuromuscul Disord*, 1991. **1**(4): p. 261-6.
10. Griggs, R.C., et al. Duchenne dystrophy: randomized, controlled trial of prednisone (18 months) and azathioprine (12 months). *Neurology*, 1993. **43**(3 Pt 1): p. 520-7.
11. Sansome, A., P. Royston, and V. Dubowitz. Steroids in Duchenne muscular dystrophy; pilot study of a new low- dosage schedule. *Neuromuscul Disord*, 1993. **3**(5-6): p. 567-9.
12. Backman, E. and K.G. Henriksson, Low-dose prednisolone treatment in Duchenne and Becker muscular dystrophy. *Neuromuscul Disord*, 1995. **5**(3): p. 233-41.
13. Bonifati, M.D., et al. A multicenter, double-blind, randomized trial of deflazacort versus prednisone in Duchenne muscular dystrophy. *Muscle Nerve*, 2000. **23**(9): p. 1344-7.
14. Biggar, W.D., et al. Deflazacort treatment of Duchenne muscular dystrophy. *J Pediatr*, 2001. **138**(1): p. 45-50.
15. Emery, A.E. Drug therapy, in Duchenne muscular dystrophy. 1993, Oxford University Press: Oxford. p. 282-290.
16. Dubowitz, V. and J. Heckmatt. Management of muscular dystrophy. Pharmacological and physical aspects. *Br Med Bull*, 1980. **36**(2): p. 139-44.
17. Brooke, M.H., et al. Clinical investigation in Duchenne dystrophy: 2. Determination of the "power" of therapeutic trials based on the natural history. *Muscle Nerve*, 1983. **6**(2): p. 91-103.
18. Stern, L. Criteria for therapeutical trials in Duchenne muscular dystrophy, in *Neuromuscular diseases*, G. Serratrice, Editor. 1984, Raven Press: New York. p. 525-528.
19. www.dmdrc.org/cinrg/.
20. Urtizberea, J. Therapies in Muscular Dystrophy: Current Concepts and Future Prospects. *Eur Neurol*, 2000. **43**: p. 127-132.
21. Dubowitz, V. Special Centennial Workshop-- 101st ENMC International Workshop: Therapeutic Possibilities in Duchenne Muscular Dystrophy, 30th November- 2nd December 2001, Naarden, The Netherlands. *Neuromuscul Disord*, 2002. **12**(4): p. 421-31.
22. Carter, G.T. and C.M. McDonald. Preserving function in Duchenne dystrophy with long-term pulse prednisone therapy. *Am J Phys Med Rehabil*, 2000. **79**(5): p. 455-8.
23. Dubowitz, V., et al. Remission of clinical signs in early duchenne muscular dystrophy on intermittent low-dosage prednisolone therapy. *Eur J Paediatr Neurol*, 2002. **6**(3): p. 153-9.
24. www.cochrane.org/cochrane/revabstr/g410index.htm.

11. ORTHOPAEDIC TREATMENT IN DUCHENNE MUSCULAR DYSTROPHY (DMD)

Introduction

The orthopaedic treatment in muscular dystrophies includes both orthotic (splint) and surgical treatment of spine and extremity deformities. Treatment indications as well as type of orthoses and extent and timing of surgery vary. In spite of very common splint prescriptions to the majority of Duchenne patients, there are very few studies on the efficacy and outcome of orthotic treatment (3). Splint prescription frequencies are given in literature as follows: AFO (ankle-foot orthosis) in 91 %, standing device in 61 %, KAFO (knee-ankle-foot orthosis) in 22 % according to Bakker et al (1), and a common use of spinal orthosis according to Heller et al (2). Due to a small number of cases in treating units, health care organisational problems, and ethical reasons, it has not been possible to run prospective randomised studies on treatment as compared to the natural history in Nordic countries.

A study from Germany (4) demonstrated that an early, at the age of 4-8 years, multisegmental surgical release of incipient deformities in a DMD population of 87 boys prolonged the walking ability more than a year as compared to a non-surgically treated control group of 100 Duchenne boys. All surgically treated boys were independent walkers at the age of 6-8 years as opposed to the non-surgically treated ones. Goertzen et al found (5) that all 32 early surgically treated Duchenne boys were still walkers at a 3.4 years follow-up. Which overall importance can be counted on this extended ambulation can be discussed from different perspectives. An important clinical observation might be that spine deformity hardly ever is seen in walking DMD patients. In a retrospective study Furderer et al (6) report on 45 Duchenne boys that none of the ambulatory ones had scoliosis, whereas 96 % of the wheelchair dependents had a spine deformity. It is also shown that therapy standing postpones the occurrence of spine deformity (7).

Surgical treatment of neuromuscular spine deformities is combined with a high risk for complications such as respiratory, implant related, infections and pseudo arthrosis. In the literature, complication rates vary from 10 to 60 % as compared to a risk rate of 5 % when surgically treating idiopathic scoliosis (8). In spite of high risks a high patient satisfaction is reported, up to 96 %, and good functional outcomes, such as body balance in sitting (9-13). The respiratory function, however, does not improve post surgery (14, 15) as opposed to the findings in long term follow-up of surgically treated adolescent idiopathic scoliosis.

Clinical practice and recommendations

Orthosis treatment - Splinting

As valid in other orthotic treatment, only stretchable deformities can be treated with orthoses.

A walker without any tendon tightness and with a normal walking strategy, heel contact and toe off, is not in need of splints.

In DMD walking on toe is a strategy to facilitate walking, to keep upright position and to locate the centre of mass when hip and knee extensor muscle strength is weak. The foot plantar flexion can improve the extending moment in the knee joints. An increased lumbar lordosis can improve the extending moment in hip joints. Thus, the centre of mass moves dorsally and enables walking in spite of extensor muscle weakness.

As soon as contractile signs are present, a preventive splint treatment is recommended with dynamic AFO:s. When standing balance starts to deteriorate, though, before the walking ability is lost, the introduction of load bearing orthoses is recommended. To begin with it might be possible to use AFO:s, though KAFO:s supporting ischial tuberosity are most often the treatment of choice. KAFO:s without tuberal support can come into question if the construction and orthosis-patient interface considers the specific needs of support. An experienced and enthusiastic orthopaedic engineer can create a combination of low-weight, stability, and enhancement of useful motion strategies.

Spinal orthosis, brace, can hardly ever prevent progression of spine deformity in DMD. The role of brace is to improve body balance and sitting stability. Bracing can be used when the surgery is not chosen or when waiting for spine surgery. The need of diaphragma breathing should be considered when bracing.

Please, see the attachment on orthosis treatment.

Surgical treatment – lower extremity

The aggressiveness of surgical treatment varies and is moderated by the long term natural history of DMD. Some recommendations can be given, though:

Increasing outward rotation and abduction in hip joints:

Early release of tractus iliotibialis/tensor fascia lata.

Increasing hip flexion contracture:

Early release of flexor muscles at spina.

Increasing toe walking:

Early achilles tendon release with or without tibialis posterior tendon transfer.

Additional foot deformities:

If early release is practised, arthrodesis is seldom indicated. A non-ambulant person with an advanced handicap does not benefit from a major corrective foot surgery.

Increasing hamstring tightness:

Not indicated for walkers to prevent additional anterior pelvic tilt.

Progressing knee flexion contracture:

Release can be indicated in wheelchair bound persons.

Surgical treatment – spine

While surgical treatment of lower extremities in DMD is discussed and recommendations can be contradictory, the indication for fusion surgery of a progressing spine deformity in DMD is generally accepted, and the outcome is generally good with an improved sitting stability and body balance. A progressing spine deformity is not seen in walkers, whereas at least 80 % of non-walkers develop a scoliosis, commonly a lordoscoliosis with an increasing thorax deformity and an increasing restrictive respiratory insufficiency.

Preoperative examination and treatment of cardiopulmonary status and nutrition are mandatory. A severe cardiomyopathy should be identified and constitutes a contra-indication for major surgery. A patient with decreasing body weight and deteriorating respiratory capacity forms a very high risk for postoperative complications, whereas a patient with a normal and stable body weight and preoperatively well introduced respiratory training/assistance can leave the hospital after a few days after spine surgery and experience an improvement. A prophylactic tracheotomy is hardly ever needed, if the respiratory assistance is individualised before surgery and applied immediately after.

In most cases, a standard posterior approach with multisegment fixation and long fusion from upper thoracic spine to L5 or sacrum is appropriate and enough. DMD spine deformity presents an onset in the early teens, when remaining growth no more needs to be considered when choosing the surgical approach. A fusion surgery can be recommended as soon as there is a clear progress and the Cobb angle passes 25 – 30 degrees. Thus, the surgery time, tissue damage and depending postoperative risks are minimised as compared to late surgery of a major rigid curve and severe muscular as well as restrictive respiratory insufficiency.

Recommendations in conclusion

- A walker without any tendon tightness and with a normal walking strategy, heel contact and toe off as well as normal spine configuration – expectation.
- Incipient contractile signs – prophylactic splinting.
- Obvious contractile signs – early soft tissue surgery.
- Progressing spine deformity – early surgery.
- Before surgery – check cardiopulmonary function and nutrition.

References

1. Bakker JP, De Groot IJ, De Jong BA, Van Tol-De Jager MA, Lankhorst GJ. Prescription pattern for orthoses in The Netherlands: use and experience in the ambulatory phase of Duchenne muscular dystrophy. *Disab Rehab.* 19:318-25, 1997.
2. Heller KD, Forst R, Forst J, Hengstler K. Scoliosis in Duchenne muscular dystrophy: aspects of orthotic treatment. *Prosth Orthotics Int.* 21:202-9,1997.
3. Hyde S, Flöystrup I, Glent S, Kroksmark A-K, Salling B, Steffensen B, Werlauf U, Erlandsen M. A randomized comparative study of two methods for controlling tendo achilles contractures in Duchenne muscular dystrophy. *Neuromuscular Disorders* 10:257-263, 2000.
4. Forst J, Forst R. Lower limb surgery in Duchenne muscular dystrophy. *Neuromuscul Disord.* 9:176-81, 1999.
5. Goertzen M, Baltzer A, Voit T. Clinical results of early orthopaedic management in Duchenne muscular dystrophy. *Neuropediatrics.* 26:257-9, 1995.
6. Furderer S, Hopf C, Zollner J, Eysel P. Scoliosis and hip flexion contracture in Duchenne muscular dystrophy. *Zeitschrift für Orthopädie und Ihre Grenzgebiete.* 138:131-5, 2000.
7. Galsasko CSB, Williamson JB, Deleney CM. Lung function in Duchenne muscular dystrophy. *Eur Spine J* 4:263-267, 1995.
8. Fox HJ, Thomas CH, Thompson AG. Spinal instrumentation for Duchenne´s muscular dystrophy: experience of hypotensive anaesthesia to minimise blood loss. *J Ped Orthop.* 17:701-2, 1997.

9. Yazici M, Asher MA, Hardacker JW. The safety and efficacy of Isola-Galveston instrumentation and arthrodesis in the treatment of neuromuscular spinal deformities. *J Bone Joint Surg Am.* 82:524-43, 2000.
10. Bridwell KH, Baldus C, Iffrig TM, Lenke LG, Blanke K. Process measures and patient/parent evaluation of surgical management of spinal deformities in patients with progressive flaccid neuromuscular scoliosis (Duchenne's muscular dystrophy and spinal muscular atrophy). *Spine.* 24:1300-9, 1999.
11. McCarthy RE. Management of neuromuscular scoliosis. *Orth Clin North Am.* 30:435-49, 1999.
12. Matsumura T, Kang J, Nozaki S, Takahashi MP. The effects of spinal fusion on respiratory function and quality of life in Duchenne muscular dystrophy. *Clinical Neurology.* 37:87-92, 1997.
13. Ramirez N, Richards BS, Warren PD, Williaams GR. Complications after posterior spinal fusion in Duchenne's muscular dystrophy. *J Ped Orthop.* 17:109-14, 1997.
14. Chataigner H, Grelet V, Onimus M. Surgery of the spine in Duchenne's muscular dystrophy. *Rev Chir Orth.* 84:224-30, 1998.
15. Gayet LE. Surgical treatment of scoliosis due to Duchennemuscular dystrophy. *Chirurgie.* 124:423-31, 1999.
16. Alman BA, Kim HK. Pelvic obliquity after fusion of the spine in Duchenne muscular dystrophy. *J Bone Joint Surg Br.* 81:821-4. 1999.

12. Treatment of respiratory insufficiency

Background

The general progressive deterioration of the muscles in boys suffering from Duchenne's muscular dystrophy affect all three types of muscle found in the body: striated muscle, smooth muscle and cardiac muscle. The chronology of the natural history is typically that symptoms from failure of the striated muscles are the first to appear, followed by insufficient function of the smooth muscles and finally by cardiac affection (1).

The consequences of failure of the striated muscles initially originate from the arms and leg and later on from the respiratory muscles (1,2).

The respiratory development in the DMD-boys is characterized by an increase in vital capacity (VC) (the maximal expired volume following a maximal inspiration) for a number of years as a consequence of the child's growth. This is followed by a plateau phase where the growth related increase of pulmonary function is balanced by the progressively weakened muscle strength, and finally the muscle deterioration dominates resulting in a decrease of pulmonary function. Respiration typically becomes insufficient around the age of 14-17 years and lethal around the age of 20, although considerable individual variations can be found. In a minority of the boys the insufficient respiration mainly originates from a failing heart (2-4). VC is the best predictor of survival (5). Concomitant presence of $FEV_1 < 40\%$ of predicted value and daytime hypercapnia is predictive of nocturnal hypoventilation (6) and an expected survival of 9.7 months if no respiratory support is initiated.

Symptoms

As respiration is most vulnerable during sleep, sleep related symptoms will often be the first signs of respiratory insufficiency detected. Symptoms usually include restless sleep and a need for frequent change of position, an increasing amount of dreams, sometimes nightmares, nocturnal awakenings with dyspnea, nocturia, night sweats and palpitations. Getting up in the morning can be difficult and slow and accompanied by morning headaches that will not disappear until maybe after an hour or sometimes even later. Fragmented sleep can result in tiredness, daytime somnolence, no energy, changes in mood and a reduced ability to concentrate. Obviously dyspnea may be a complaint, initially related to meals, speech or (in particular in the case of significant dysfunction of the diaphragm) supine position. The weakened respiration can – in particular when associated with an insufficient cough – be complicated by an increased propensity for pulmonary infections. Advanced respiratory insufficiency is often associated with loss of weight (7).

Diagnosis

There is no global agreement on the precise diagnosis and treatment of respiratory insufficiency nor are there any recommendations based on randomized trials. However, some degree of consensus and examples of the practice from experienced clinicians do exist.

The diagnosis of respiratory insufficiency in boys suffering from DMD can preferably be established from the following four categories:

1. knowledge of the respiratory natural history of the condition
2. a thorough anamnesis
3. pulmonary function test and continuous respiratory monitoring
4. complete polysomnography (PSG).

As the categories 1 and 2 have already been mentioned, only 3 and 4 will be dealt with in a more detailed manner.

Ad 1 and 2: The parents and the boys must be informed about the symptoms and signs of respiratory insufficiency.

Ad 3: It is recommended that VC is measured annually from the time when the child can cooperate, or at least from the age of 10 years. When $VC < 50\%$ of predicted value, the child can be referred for PSG. When VC is reduced to 1.5 L, and/or day time $PaCO_2 \geq 6.0$ kPa (45 mmHg), and/or BE is elevated (typically > 4.0), and/or relevant symptoms are found (vide supra) the boy should be referred for PSG. Following this PSG should be performed every 6th month or more frequently depending on the condition of the child (8,9).

Ad 4.: PSG can *ideally* include continuous registration of EEG, EOG, EMG, SaO_2 , $PtcCO_2$ or end-tidal CO_2 or another quantitative measure of the sleep related ventilation, oro-nasal flow, thoracic and abdominal excursions and body position, and should *as a minimum* include a continuous registration of a measure of oxygenation, of ventilation and of respiratory movements.

When VC is reduced to $< 50\%$ of predicted value it is recommended that pulmonary function tests and PSG are performed by persons/centers with experience in diagnosis and treatment of respiratory problems in boys suffering from DMD.

Treatment

Respiratory muscle training has shown conflicting results, but over all no convincing effect (10). Periodic hyperinflation improves lung function (11), and CPAP used by DMD-boys has resulted in reduced amounts of secretion after 72 hours compared to a control group (12). Cough-assisting devices have produced an increase in peak cough flow (13). Actual respiratory support is applied invasively, and increasingly non-invasively. The majority of non-acute non-invasive treatments have via a nasal mask used positive pressure, while a few have used volume targeted machines (14). Negative pressure ventilation has been applied (15), but in some cases followed by obstructive apneas.

There are no hard data on types of machines and masks, but nasal masks are often preferred for long term use and full-face masks for acute respiratory failure.

It is unclear when it is indicated to change from non-invasive ventilation to ventilation via a tracheostomy. Many clinicians will suggest this change when the ventilator assisted individual (VAI) requires respiratory support for most of the day (around 12-18 hour/day) (16,17), when the VAI wants it, when non-invasive ventilation is no longer able to sustain acceptable oxygenation and/or

ventilation (CO₂-removal), or when secretions in the airways become a problem (18). The degree of motor handicap and of impaired lung function has been found to be predictive for when ventilatory support via tracheostomy is initiated. Survival data have shown surprisingly short survival of 4-10 years and a mean survival time of 3.6 years, not quite in agreement with clinical experience. The advantage of ventilation via tracheostomy is that it is often more efficient than non-invasive ventilation, in particular in the case of problems with swallowing and secretions as seen in case of bulbar dysfunction. In addition it allows oral and facial communication.

Treatment should as a first step include thorough information about effects, consequences and complications of the planned treatment (10).

Generally it is recommended to start treatment when the conditions mentioned in “ad 3)” are apparent. Treatment will often as a first option include non-invasive positive pressure ventilation (NIPPV), often via a nasal mask, using BiPAP®, VPAP® or a similar product (10,19,20). Full face masks and oral interfaces are other possibilities. If treatment is extended to more than ½-2/3 of the day, if non-invasive ventilation is insufficient, if unacceptable complications are present or if the VAI does not want to use non-invasive ventilation, ventilation via tracheostomy will often be chosen (10,19). This latter mode of ventilation can utilize pressure targeted ventilators, but most frequently volume targeted devices have been used, usually via an uncuffed or fenestrated tube in order to preserve the ability to speak (10,19).

It is very important that a thorough, structured and well monitored education of the attendants and the VAI has taken place before long-term home mechanical ventilation is initiated.

After discharge regular follow-up visits should take place to monitor and if necessary adjust the treatment. In case of non-invasive treatment possibly every 3rd to 6th months, and in case of invasive ventilation once a year or every other year, depending on the condition.

It is important to recognize that in each case a comprehensive evaluation of the individual's total situation should be performed, and treatment should be tailored specifically according to that. It is thus perfectly possible that the course of events may vary from what has been outlined above.

It would be practical and desirable that regional data-bases concerning DMD are formed according to a common data-base format, so that data immediately can be added to a Scandinavian pool, preferably with the possibility to be integrated into a larger European data-base.

Vaccinations

There are no data that directly visualize the effect of vaccination against influenza among DMD-boys. Studies including other groups of patients show that the vaccination results in a reduction of morbidity as well as mortality, and that the intervention is cost-effective (21,22). The American Muscular Dystrophy Association (MDA) recommends in addition that the whole family of the child should be vaccinated against influenza (23).

Whether it generally should be recommended that individuals with DMD should be vaccinated against pneumonia (*pneumococci*) is still a matter of debate. Available data suggest a beneficial effect of vaccination against infection with *pneumococci* in individuals suffering from reduced pulmonary function. MDA recommends that all DMD-individuals above 10-12 years of age and the closest family should be vaccinated against infection with *pneumococci*, and before school age also against chicken pox (23).

Recommendations

- VC should be measured annually once ambulation is lost
- The boy should be referred for nocturnal monitoring of respiration at experienced centres when VC < (30)-50% of predicted value
- Intermittent CPAP treatment and possibly cough augmentation should be offered at the latest when VC < (30)-50%
- Treatment of respiratory insufficiency for instance using bilevel respiratory assist devices via non-invasive interfaces **or** volume or pressure targeted ventilators via tracheostomy should be initiated when signs or symptoms of respiratory insufficiency are present
- Structured education of the ventilator user and the attendants and regular follow-up should be an integral part of the treatment
- Vaccination against infection with influenza and *pneumococci* should be offered once respiratory insufficiency is present.

References:

1. Emery AEH. Duchenne and Becker muscular dystrophy. In: Emery AEH. Ed. Neuromuscular Disorders. Clinical and molecular genetics. Chichester, England. Wiley 1998, p. 59-85
2. Boland BJ et al. Skeletal, cardiac and smooth muscle failure in Duchenne muscular dystrophy. *Pediatr Neurol* 1996;14:7-12
3. Bach JR et al. Management of end stage respiratory failure in Duchenne muscular dystrophy. *Muscle Nerve* 1987;10:177-82
4. Ishikawa Y et al. Cardioprotection for Duchenne's muscular dystrophy. *Am Heart J* 1999;137:895.
5. Phillips MF et al. Nocturnal oxygenation and prognosis in Duchenne muscular dystrophy. *Am J Respir Crit Care Med* 1999;160:198-202
6. Hukins CA et al. Daytime predictors of sleep hypoventilation in Duchenne muscular dystrophy. *Am J Respir Crit Care Med* 2000;161:166-170
7. Guilleminault C et al. Sleep and neuromuscular disease: bilevel positive airway pressure by nasal mask as a treatment for sleep disordered breathing in patients with neuromuscular disease. *J Neurol Neurosurg Psychiatry* 1998;65:225-32.
8. Respiratory insufficiency and ventilatory support. 39th ENMC international workshop. *Neuromusc Disord* 1996;6:431-5.
9. Gozal D. Pulmonary manifestations of neuromuscular disease with special reference to Duchenne Muscular Dystrophy and Spinal Muscular Atrophy. *Pediatr Pulmonol* 2000;29:141-50

10. Vignos PJ et al. The effect of exercise in muscular dystrophy. *JAMA* 1966;197:843-8
11. Sinha R et al. Prolonged alteration of lung mechanics in kyphoscoliosis by positive pressure hyperinflation. *Am Rev Respir* 1972;106:47-57.
12. Klefbeck B et al. Lung clearance in children with Duchenne muscular dystrophy or spinal muscular atrophy with and without CPAP. *Exp Lung Res* 2001 ;27:469-84.
13. Chatwin M et al. Cough augmentation with mechanical insufflation/exsufflation in patients with neuromuscular weakness. *Eur Respir J* 2003;21:502-8
14. Niranjana V et al. Noninvasive management of pediatric neuromuscular ventilatory failure. *Crit Care Med* 1998;26:2061-5.
15. Curran FJ. Night ventilation by body respirators for patients in chronic respiratory failure due to late stage Duchenne muscular dystrophy. *Arch Phys Med Rehabil* 1981 ;62:270-4.
16. Robert D et al. Permanent mechanical ventilation at home via a tracheotomy in chronic respiratory insufficiency. *Rev Fr Mal Respir* 1983;11:923-36
17. Robert D et al in: Kryger, Roth and Dement. *Principles and Practice of Sleep Medicine*. Saunders, Philadelphia 2000
18. Baydur A et al. Long term non-invasive ventilation in the community for patients with musculoskeletal disorders: 46 year experience and review. *Thorax* 2000;55:4-11.
19. Make B (Ed) *Mechanical ventilation beyond the intensive care unit: Report of a Consensus Conference of the American College of Chest Physicians*. *Chest* 1998;113(Suppl. 5):S289-S349.
20. Clinical indications for Noninvasive Positive Pressure Ventilation in Chronic Respiratory Failure Due to Restrictive Lung Disease, COPD and Nocturnal Hypoventilation - A Consensus Conference Report. *Chest* 1999;116:521-34.
21. Reichert TA et al. The Japanese experience with vaccinating school children against influenza. *N Engl J Med* 2001;344:889-96.
22. White T et al. Potential cost savings attributable to influenza vaccination of school-aged children. *Pediatrics* 1999;103:A1273
23. Muscular Dystrophy Association. Home page: www.mdaua.org

13. Diagnosis and Treatment of Cardiac Disease

Background

Patients with muscular dystrophy (MD) can develop cardiac disease (1-3). The spectrum of possible cardiac manifestations is wide. However, the most common and serious are dilated cardiomyopathy (DCM) with or without symptoms and clinical signs of heart failure, and AV conduction disturbances. To a high degree the risk for a cardiac complication and its nature is related to the type of muscular dystrophy. The risk is great in patients with Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD). In DMD boys older than 12 years of age, more than half will have evidence of cardiomyopathy (3). ECG abnormalities, which are common, are not closely related to the presence of or the degree of DCM, and the same goes for the severity of the muscular dystrophy. The progression of the cardiac involvement is not related to changes in or the extent of the underlying MD. The only certain way to make a diagnosis of DCM and to quantitate the severity of the cardiac involvement is by echocardiography (4). In boys with severe deformation of the chest it is not possible to obtain so called standardized parameters for left ventricular dimensions and function (4). However, in almost all cases it will be possible, by eyeballing, to decide whether left ventricular systolic function is normal or abnormal (light / severe).

Heart failure can have severe impact on the quality of life, due to symptoms like dyspnoea, fatigue and oedema (4). These classical symptoms of heart failure are only present in a minority of MD patients. DMD patients do often present atypical symptoms such as uneasiness, cough, changed respiration, sweating and palpitations (5). This probably relates to the reduced cardiovascular demands caused by the severely reduced muscular mass and the wheelchair dependent condition. In BMD patients heart failure is the most common cause of death (6).

In some MD patients the most common cardiac complication is AV conduction disturbances. In particular this is the case in Limb-Girdle type 1B. Conduction disturbances can cause symptoms such as sudden loss of consciousness, palpitations and syncope, which are always preceded by symptoms of neuromuscular disease. Some families have such a high prevalence of malignant AV conduction disease that prophylactic implantation of a pacemaker may be warranted, despite lack of symptoms (7). Generally the diagnosis is based on a 12 lead ECG and 24-hour Holter monitoring. It is recommended, in all MD patients, to record an ECG each year.

The aim of the treatment in DCM is to reduce or stop the progression of the cardiac disease and thereby prolong life (4). In case of symptoms the treatment additionally has the purpose of reducing or eliminating these. There are no randomised studies, which specifically have addressed the effect of ACE inhibition, diuretics, digoxin or betablocker treatment in MD patients with DCM. Only one observational investigation of full heart failure treatment in 11 DMD patients with reduced left ventricular function and presumed symptoms of heart failure has been published (5). All patients had abnormally elevated levels of neuroendocrine hormones, which indicates a high probability of heart failure. In all cases symptoms were relieved by treatment, clinical signs of heart failure disappeared, and levels of neurohormones were normalised. During the observation period of 36 months cardiac function was improved.

On the other hand, large randomised studies of the effects of ACE inhibitors, digoxin and betablockers on adult patients with DCM, but without MD, are available (4,8). It must be assumed that the beneficial effects on symptoms, and in case of ACE inhibitors and betablockers also on survival, are also valid for MD patients, as the underlying causes for DCM in non-MD patients are many. It is assumed that about 30% of DCM cases, without MD, are hereditary (9). Probably there is a significant overlap in gene defects and associated abnormal proteins which causes dysfunction of the cardiac myocyte in DCM patients with and without MD.

In patients with reduced left ventricular systolic function ($EF < 45\%$), but without symptoms or clinical signs of heart failure, there is evidence and consensus that ACE inhibitor treatment prolongs time before the first appearance of symptoms and improves survival (4,10). It is therefore recommended that MD patients with an $EF < 45\%$ should receive ACE inhibitor treatment, regardless of symptoms or not.

Female carriers of the gene defect for DMD and BMD have an increased occurrence of DCM (11). The majority appears to be completely without symptoms and have only minor cardiac involvement. As the natural history of this condition is unknown and may have a good prognosis, it is not indicated to recommend screening.

Due to the rarity and the special conditions of the disease, MD patients should generally be offered cardiac examinations and follow-up at tertiary centers.

Recommendations

- DMD patients on broad clinical suspicion (symptoms, abnormal ECG) should be offered cardiac examination by echocardiography and 24-hour ECG monitoring
- DMD and BMD patients at the age of 12 should be offered yearly echocardiography
- All MD patients with evidence of cardiomyopathy (EF<45%) should be offered ACE inhibitor treatment
- In case of symptoms indicating heart failure treatment, if needed, should be supplemented by diuretics, digoxin and betablocker, according to ordinary guidelines.

References

- 1) Cox GF, Kunkel LM. Dystrophies and heart disease. *Current opinion in cardiology*. 1997;12:329-343.
- 2) Finstrerer J, Stöllberger C. Cardiac involvement in primary myopathies. *Cardiology* 2000;94:1-11.
- 3) Bäckman E, Nylander E. The heart in Duchenne muscular dystrophy: A non-invasive longitudinal study. *Eur Heart J* 1992;13:1239-1244.
- 4) Guidelines for the diagnosis and treatment of chronic failure. Task force for the diagnosis and treatment of chronic heart failure. European Society of Cardiology: WJ Remme and K Swedberg. *Eur Heart J* 2001;22:1527-1560
- 5) Ishikawa Y, Bach JR, Minami R. Cardioprotection for Duchennes muscular dystrophy. *Am Heart J* 1999;137:895-902.
- 6) Stöllberger C, Finstrerer J, Keller H et al. Progression of cardiac involvement in patients with myotonic dystrophy, beckers muscular dystrophy and mitochondrial myopathy during a two-year follow-up. *Cardiology* 1998;90:173-179.
- 7) Bécane H-M., Bonne G, Varnous S et al. High incidence of sudden death with conduction system and myocardial disease due to lamins A and C gene mutation. *Pace* 2000;23:1661-66.
- 8) Kober L, Torp-Pedersen C, Carlsen JE et al. For the Trandolapril Cardiac Evaluation (TRACE) study group. Effects on mortality by trandolapril after myocardial infarction. *N Engl J Med* 1995;333:1670-1676
- 9) Graham RM, Owens WA. Pathogenesis of inherited forms of dilated cardiomyopathy. *N Engl J Med* 1999;341:1759-1762.

10) The SOLVD investigators. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fraction. N Engl J Med 1992;327:685-69

11) Hoogerwaard EM, van der Wouw PA, Wilde AAM et al. Cardiac involvement in carriers of duchenne and becker muscular dystrophy. Neuromuscular disorders 1999;9:347-351.

14. Rehabilitation of adult persons with DMD

Background

Adulthood is defined as the period of life starting at the age of 18 and onwards (though for many reasons it should be fixed at the age of 20 for this group). The life span of a DMD-person is expected to be prolonged by mechanical ventilation (1, 2, 3, 4).

Whereas earlier, before 1990, the estimated life expectancy for persons with DMD was about 20 years it is unknown today, but several DMD-persons are assumed to become more than 40 years old.

At the age of 18-20 the young man with DMD will be characterised by:

- I. Generally reduced strength in the striated and smooth muscles, and in the cardiac muscle (13). - The reduced strength of the striated muscles implies that merely the hands, feet, face and the muscles of mouth, tongue and speech are capable of functioning (5,6,7,8,9,10). The reduction of strength also includes the respiratory muscles so that the respiration and the ability to keep the airways free from mucus is severely reduced, thus causing a high risk of the development of pneumonia, fatigue and loss of appetite. The reduced strength in the smooth muscles can cause gastrointestinal problems (15). Reduced function of the cardiac muscle (16, 17, 18) is described in chapter 13.
- II. Contractures in most joints (19), scoliosis (20) and hip subluxation can compromise the person's ability to sit in his wheelchair (22, 23), control his head (24), lie comfortably and perform activities with his hands and feet. Spinal fusion is an intervention that contributes to the ability of the adult DMD person to preserve his sitting position. However, there is contradictory information whether the rods should be fixed to os sacrum or not (27, 28, 29) in order to achieve an acceptable seated position.
- III. Total dependence of assistance involving the risk of social isolation (30, 31, 32), loss of possibilities of controlling life (33) and of making the most of one's capabilities which again causes depression and reduced quality of life.

The aim of the rehabilitation process is to enable the young person to take control of his own life and provide him with the possibilities for compensating his loss of abilities through assistive devices and personal assistance.

An important precondition for a successful rehabilitation process is information to the DMD-person about all aspects of the disease (34, 35), the availability of a clinic for seating adaptation (36, 37, 38, 39, 40, 41), equipment for the preservation of functional abilities (42), availability of counselling about nutrition (43, 44, 45, 46), counselling about medical treatment (47, 48), counselling about participation in medical trials (49), emotional problems (50, 51, 52), sexual questions (53), and contact to other persons with a neuromuscular disease.

Special aspects about adulthood in DMD persons are:

- I. They are all treated with mechanical ventilation, non-invasive or invasive
- II. Their condition is merely slowly progressive

III. On the whole, the course of adulthood is unknown this one being the first generation; all kinds of information are lacking.

Ad I. Mechanical ventilation is described in chapter 12. Continuous, centralised outpatient assessments are necessary.

Ad II. After the implementation of mechanical ventilation DMD seems stationary since the rate of the further weakening of the striated muscles is very slow.

Regular outpatient assessments at a cardiological unit should be maintained for the prevention of cardiac insufficiency, medical or surgical.

The ability to speak and swallow is important for the quality of life, and therefore oculopharyngeal functions should be followed. The seated position and the hand function must be frequently assessed since even slight changes can cause loss of functions reducing the possibilities for making use of assistive devices for communication and transport.

The total dependence on the assistance of other persons demands functional rehabilitation that provides support for the administration of an assistant's scheme, adaptation of housing and social life, including sufficient network in daily life.

Recommendations

- Annual neurological, respiratory and cardiological assessments at a centralised DMD rehabilitation unit
- Annual home visit / assessments performed by an interdisciplinary team from a special DMD rehabilitation unit (in Denmark Institut for Muskelsvind)
- Annual, centralised weekend or one week's course for adult DMD persons arranged by the NMD-association in co-operation with the centralised rehabilitation unit.

References

1. Mukoyama M, Kondo K, Hizawa K, Nishitani H. Life spans of Duchenne muscular dystrophy patients in the hospital care program in Japan. J Neurol Sci 1987; 81:155-8.
2. Johnsen EW, Reynolds HT, Stauch D. Duchenne muscular dystrophy: a case with prolonged survival. Arch Phys Med Rehabil 1985; 66:260-1.
3. Bach JR, O'Brien J, Krotenberg R, Alba AS. Management of end stage respiratory failure in Duchenne Muscular dystrophy. Muscle Nerve 1987; 10:177-82.
4. Alexander MA, Johnson EW, Petty J, Stauch D. Mechanical ventilation of patients with late stage of Duchenne muscular dystrophy: management in the home. Arch Phys Med Rehabil 1979; 60:289-92.
5. Boland BJ, Silbert PL, Groover RV, Wollan PC, Silverstein MD. Skeletal, cardiac, and smooth muscle failure in Duchenne muscular dystrophy. Pediatr Neurol 1996; 14:7-14.

6. Wagner MB, Vignos PJ Jr, Carlozzi C. Duchenne muscular dystrophy: a study of wrist and hand function. *Muscle Nerve* 1989; 12:236-44.
7. Lord JP, Portwood MM, Liebermann JS, Fowler WM Jr, Berck P. Upper extremity functional rating for patients with Duchenne muscular dystrophy. *Arch Phys Med Rehabil* 1987; 68:151-4.
8. Morita H. A functional and anatomical study of finger deformities in Duchenne muscular dystrophy. *Nippon Seikeigeka Gakkai Zasshi* 1986; 60:989-1002.
9. Willig TN, Paulus J, Lacau Saint Guily J, Beon C, Navarro J. Swallowing problems in neuromuscular disorders. *Arch Phys Med Rehabil* 1996; 75:1175-81.
10. Nagaoka M, Minami R, Wakai S, Okabe M, Kameda K, Annaka S, Tachi N, Shinoda M. Enlargement of the tongue and a deformity of the oral cavity in patients with Duchenne muscular dystrophy. *No To Hattatsu* 1987;19:422-4.
11. Morimoto T, Takebe H, Hamada T, Kawamura Y. Oral kinesthesia in patients with Duchenne muscular dystrophy. *J Neurol Sci* 1981; 49:285-91.
12. Steffensen BF, Lyager S, Werge B, Rahbek J, Mattsson E. *Dev Med Child Neurol* 2002; 44:623-32.
13. Yasuma F, Kato T, Matsuoka Y, Konagaya M. Row-a-boat phenomenon: respiratory compensation in advanced Duchenne muscular dystrophy. *Chest* 2001; 119:1836-9.
14. Gibson B. Long-term ventilation for patients with Duchenne muscular dystrophy: physician's beliefs and practices. *Chest* 2001; 119:940-6.
15. Mohr CH, Hill NS. Long-term follow-up of nocturnal assistance in patients with respiratory failure due to Duchenne-type muscular dystrophy. *Chest* 1990; 97:91-6.
16. Lunshof L, Schweizer JJ. Acute gastric dilatation in Duchenne's muscular dystrophy. *Ned Tijdschr Geneeskde* 2000; 144:2214-7.
17. Malacini P, Vianelle A, Villanova C, Fanin M, Miorin M, Angelini C, Dalla Volta S. Cardiac and respiratory involvement in advanced stage Duchenne muscular dystrophy. *Neuromuscul Disord* 1996; 6:367-76.
18. Heymsfield SB, McNish T, Perkins JV, Felner JM. Sequence of cardiac changes in Duchenne muscular dystrophy. *Am Heart J* 1978; 95:283-94.
19. Matsuoka S, Ii K, Akita H, Tomimatsu H, Kurahashi Y, Nakatsu T, Miyao M. Clinical features and cardiopulmonary function of patients with astrophic heart in Duchenne muscular dystrophy. *Jpn Heart J* 1987; 28:687-94.
20. Lehman M, Hsu AM, Hsu JD. Spinal curvature, hand dominance and prolonged upper-extremity use of wheelchair-dependent DMD patients. *Dev Med Child Neurol* 1986; 28:628-32.
21. Chan KG, Galasko CS, Delaney C. Hip subluxation and dislocation in Duchenne muscular dystrophy. *J Pediatr Orthop B* 2001; 10:219-25.

22. Hsu JD. The natural history of spine curvature progression in the nonambulatory Duchenne muscular dystrophy patient. *Spine* 1983; 8:771-5.
23. Sussman M. Duchenne muscular dystrophy. *J Am Acad Orthop Surg* 2002; 10:138-51.
24. Granata C, Merlini L, Cervellati S, Ballestrazzi A, Giannini S, Corbascio M, Lari S. Long-term results of spine surgery in Duchenne muscular dystrophy. *Neuromuscul Disord* 1996; 6:61-8.
25. Kiliaridis S, Katsaros C. The effects of myotonic dystrophy and Duchenne muscular dystrophy on the orofacial muscles and dentofacial morphology. *Acta Odontol Scand* 1998; 56:369-74.
26. Matsumota S, Morinushi T, Ogura T. Time dependent changes of variables associated with malocclusion in patients with Duchenne muscular dystrophy. *J Clin Pediatr Dent* 2002;27:53-61.
27. Rice JJ, Jeffers BL, Devitt AT, McManus F. Management of the collapsing spine for patients with Duchenne muscular dystrophy. *Ir J Med Sci* 1998;167:242-5.
28. Gayet LE. Surgical treatment of scoliosis due to Duchenne muscular dystrophy. *Chirurgie* 1999; 124:423-31.
29. Alman BA, Kim HK. Pelvic obliquity after fusion of the spine in Duchenne muscular dystrophy. *J Bone Joint Surg Br* 1999; 81:821-4.
30. Harper DC. Personality correlates and degree of impairment in male adolescents with progressive and nonprogressive physical disorders. *J Clin Psychol* 1983; 39:859-67.
31. Bach JR, Campagnolo DI, Hoeman S. Life satisfaction of individuals with Duchenne muscular dystrophy using long-term mechanical ventilatory support. *Am J Phys Med Rehabil* 1991; 70:129-35.
32. Siegel IM. Update on Duchenne muscular dystrophy. *Compr Ther* 1989; 15:45-52.
33. Miller JR, Colbert AP, Osberg JS. Ventilator dependency: decision-making, daily functioning and quality of life for patients with Duchenne muscular dystrophy. *Dev Med Child Neurol* 1990; 32:1078-86.
34. Madorsky JG, Radford LM, Neumann EM. Psychosocial aspects of death and dying in Duchenne muscular dystrophy. *Arch Phys Med Rehabil* 1984; 65:79-82.
35. Konagaya M, Sakai M, Kuru S, Kato T, Yasuma F, Matsuoka Y. Evaluation of cranial CT findings of patients with muscular dystrophy: with a reference to cerebral vascular disease and cardiac complications. *No To Shinkei* 1999; 51:621-6.
36. Strobl W. Neurogenic spinal deformities. II. Sitting and seating devices: principles and indications. *Orthopade* 2002; 31:58-64.
37. Duport G, Gayet E, Pries P, Thirault C, Renardel-Irani A, Fons N, Bach JR, Rideau Y. Spinal deformities and wheelchair seating in Duchenne muscular dystrophy: twenty years of research and clinical experience. *Sermin Neurol* 1995; 15:29-37.
38. Shapiro F, Sethna N, Colan S, Wohl ME, Specht L. Spinal fusion in Duchenne muscular dystrophy: a multidisciplinary approach. *Muscle Nerve* 1992; 15:604-14.

39. Seeger BR, Sutherland AD, Clark MS. Orthotic management of scoliosis in Duchenne muscular dystrophy. *Arch Phys Med Rehabil* 1984; 65:83-6.
40. Heller KD, Forst R, Forst J, Hengstler K. Scoliosis in Duchenne muscular dystrophy: aspects of orthotic treatment. *Prosthet Orthot Int* 1997; 21:202-9.
41. Koreska J, Albisser AM. A new foam for support of the physically handicapped. *Biomed Eng* 1975; 10:56-8, 62.
42. Bach JR, Zeelenberg AP, Winter C. Wheelchair-mounted robot manipulators. Long term use by patients with Duchenne muscular dystrophy. *Am J Phys Med Rehabil* 1990; 69:55-9.
43. Lynch GS. Therapies for improving muscle function in neuromuscular disorders. *Exerc Sport Sci Rev* 2001; 29:141-8.
44. Willig TN, Carlier L, Legrand M, Riviere H, Navarro J. Nutritional assessment in Duchenne muscular dystrophy. *Dev Med Child Neurol* 1993; 35:1074-82.
45. Okada K, Manabe S, Sakamoto S, Ohnaka M, Niiyama Y. Protein and energy metabolism in patients with progressive muscular dystrophy. *J Nutr Sci Vitaminol (Tokyo)* 1992; 38:141-54.
46. Moriuchi T, Fujii Y, Kagawa N, Hizawa K. Autopsy study on the weight of the heart, liver, kidney and brain in Duchenne muscular dystrophy. *Tokushima J Exp Med* 1991; 38:5-13.
47. Iannaccone ST, Nanjiana Z. Duchenne Muscular Dystrophy. *Curr Treat Options Neurol* 2001; 3:105-117.
48. Fanin M, Melacini P, Angelini C, Danieli GA. Could utrophin rescue the myocardium of patients with dystrophin gene mutations? *J Mol Cell Cardiol* 1999; 31:1501-8.
49. Rosenberg LT. We have a prejudice against ourselves – sentiment, ethics, and reason. *J Med Humanit* 1993; 14:5-14.
50. Raphael JC, Dazord A, Jaillard P, Andronikof-Sanglade A, Benony H, Kovess V, Charpak Y, Auriant I. Assessment of quality of life for home ventilated patients with Duchenne muscular dystrophy. *Rev Neurol* 2002; 158:453-60.
51. Annane D, Chevrolet JC, Chevret S, Raphael JC. Nocturnal mechanical ventilation for chronic hypoventilation in patients with neuromuscular and chest wall disorders. *Cochrane Database Syst Rev* 2000; CD001941.
52. Prigent H, Samuel C, Louis B, Abinum MF, Lejaille M, Raphael JC, Lofaso F. Comparative Effects of Two Ventilatory Modes on Speech in Tracheostomized Neuromuscular patients. *Am J Respir Crit Care Med* 2002;
53. Thompson CE. Reproduction in Duchenne dystrophy. *Neurology* 1978; 28:1045-7.

15. Patients' organisations

Norway

Foreningen for Muskelsyke
Kjelsåsveien 174 B
Boks 4395 Nydalen
0402 Oslo
e-mail: ffm@ffm.no

Sweden

Riksförbundet för Rörelshindrade Barn och Ungdomar (RBU)
Box 6607
SE-113 84 Stockholm
e-mail: mail@riks.rbu.se

Neurologiskt Handikappades Riksförbundet (NHR)
Box 3284
SE-103 65 Stockholm
E-mail: nhr@nhr.se

Denmark

Muskelsvindfonden
Kongsvang Alle 23
8000 Århus C
E-mail: msfoplys@post1.tele.dk

So far, there exists no cure for Duchenne muscular dystrophy; the disease is an inevitable condition for the person and the family involved.

But the fact that Duchenne muscular dystrophy is incurable does not mean that it can not be treated. Over the past 10 years significant advances have been made within various methods of treatment, among others respiration, cardiology and spinal fusions. Therefore, today DMD-persons live longer than formerly, which we regard as a gift.

There is no ready-made recipe available for a good life. It is entirely up to the individual person to define what a good life is and how it should be lived. In the patients' organisations priority is given to develop possibilities and conditions for the good life. WHO worded this as follows: Add life to years, not years to life.

Foreningen for Muskelsyke (N), RBU and NHR (S), and Muskelsvindfonden (DK) do not compete with the public health care system. We consider ourselves to be a positive supplement and a progressive and necessary partner in co-operation. Our aim is to ensure that existing and future possibilities for treatment are offered to people with Duchenne muscular dystrophy. Therefore, our organisations closely follow the development in medical research and gene therapy, and we do not turn down new methods of treatment beforehand.

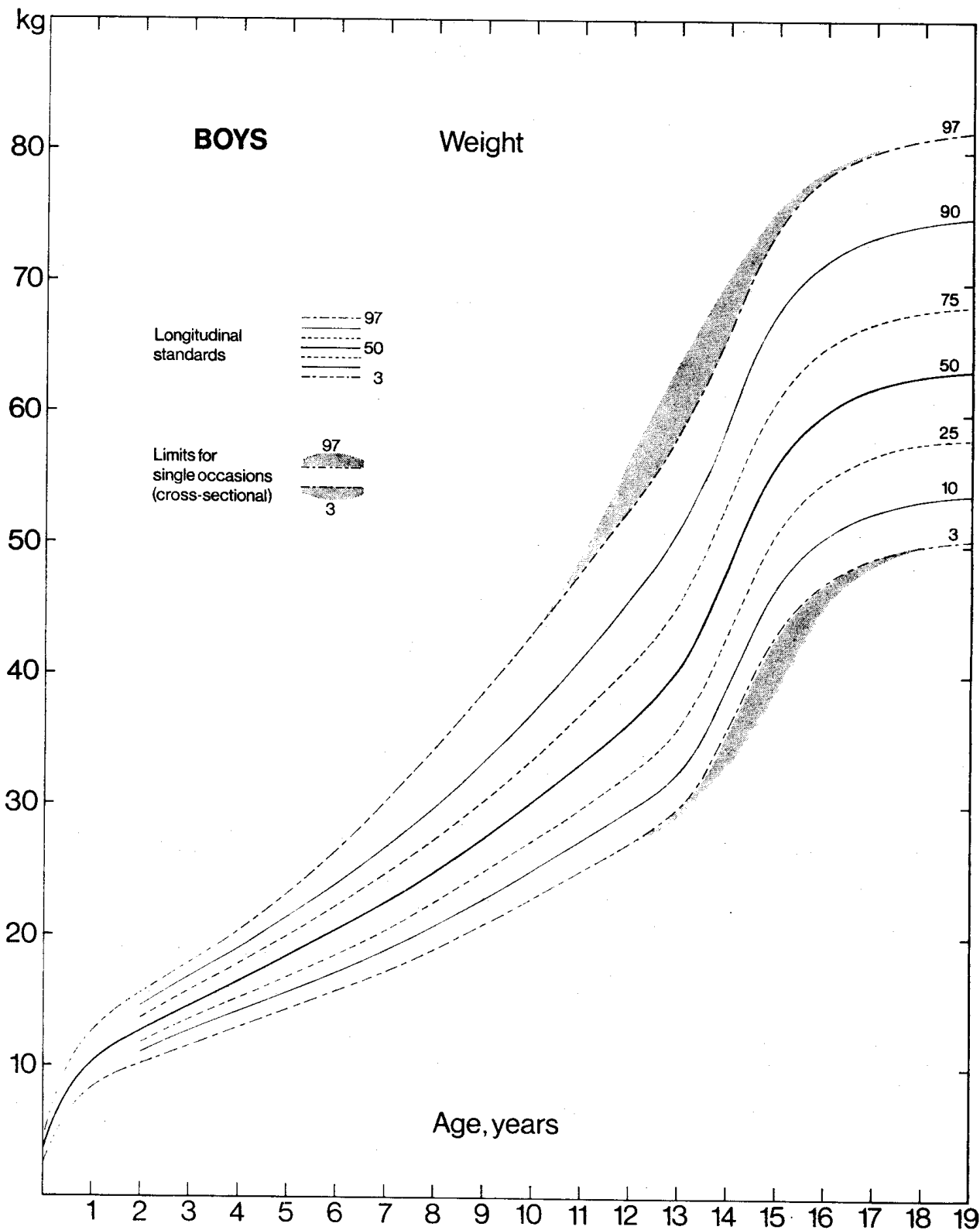
Muskelsvindfonden makes knowledge and information available, thus providing the individual person the opportunity to make his own choice.

Nowadays, it is not a disaster to be disabled in Scandinavia – but to have a neuromuscular disease could be perceived like that. We steadily endeavour to make life with a neuromuscular disease good and rewarding, and we therefore explore possibilities rather than limitations. We believe in rendering possible what seems impossible.

Recommendations

- At diagnosis the hospital unit should inform about the patients' organisation and recommend the patient to take contact
- Hospital units treating neuromuscular diseases should keep contact to the patients' organisation and particularly inform it about the introduction of new methods of treatment.

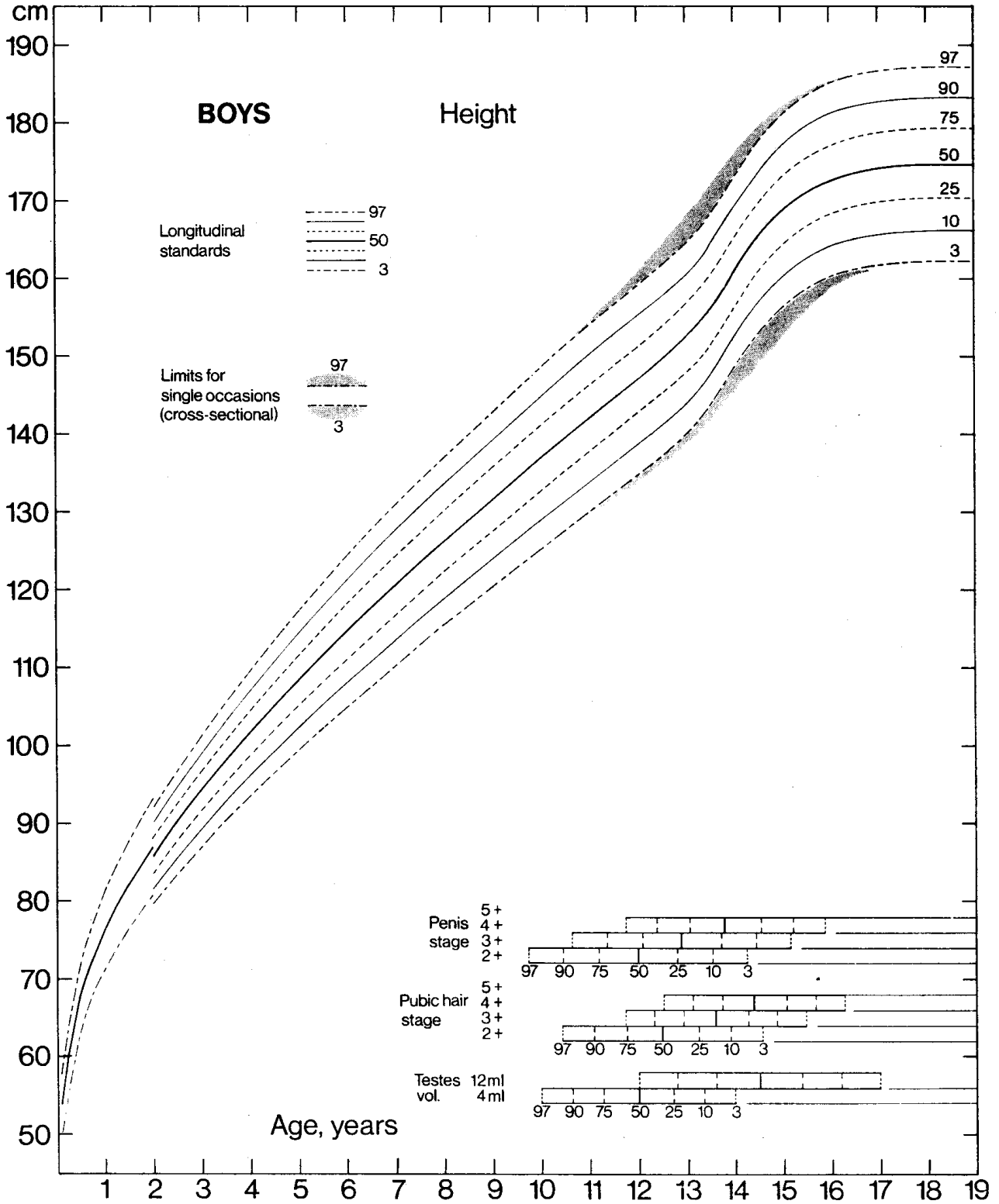
Bilaga Nutrition



Bilaga Nutrition

172

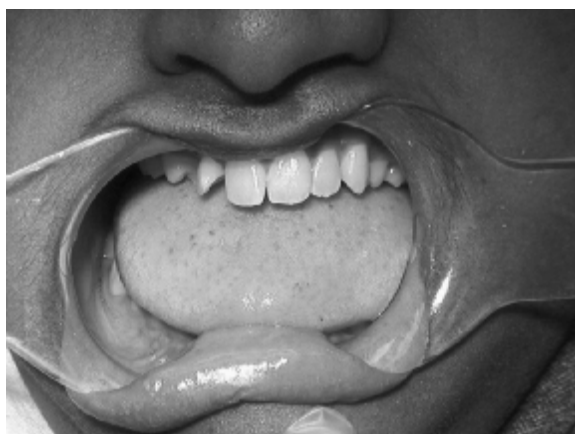
Tanner and Whitehouse



App.: ORAL CARE



Caption figure 1:
Boy (age 16) with DMD. Crossbite. Lateral open bite. When the mouth is closed normally, the only contact is between the front teeth.



Caption figure 2:
Hypotonic tongue.



Caption figure 3:
The individually adapted wheelchair or power-operated wheelchair can be used by the dentist when treating these boys.



Caption figure 4:
The bathroom must be adapted to enable day-to-day oral hygiene to be maintained.



Caption figure 5:
An electric toothbrush is an excellent aid when the muscle strength of the arms and hands decreases.



Caption figure 6A:
When keeping the mouth open wide is tiring; a bite support between the upper and lower teeth may be useful.



Caption figure 6B:
Bite supports.



Caption figure 7:

A cheek retractor is an aid that may be used by both the patient and the dentist to facilitate access to and examination of the mouth.



Caption figure 8:

A jaw mobilizer is an aid that can be used to maintain temporomandibular joint mobility and stretch the cheek muscles.

Corticosteroid treatment of DMD; a simplified summary

<u>Authors</u>	<u>Design</u>	<u>No of patients</u>	<u>Follow-up time</u>	<u>Dosage</u> PRD = Prednisone PRL = Prednisolone DFZ = Deflazacort	<u>Results</u> Motor function, muscle strength
Drachman (1974)	Open	14	28 months	PRD 2 mg/kg/d After 2-3 mo alt day + reduced dose	Improvement
Siegel (1974)	Double-blind	14	3 yrs	7 on PRL 5 mg/kg alt day, 7 placebo	"Transient and minimal slowing of process" Not eff treatment
Brooke (1987)	Open	33	6 mo	PRD 1.5 mg/kg/d	Improvement
DeSilva (1987)	Open	16	>1 yr (1-11 yrs)	PRD 2 mg/d, after 2-3 mo alt day, red dose	Improvement, slowing of deterioration
Mendell (1989)	Double-blind	36 placebo 33 low dose 34 high dose	6 months	PRD 0.75 mg/kg/d (low) and 1.5 mg/kg/d (high)	Improvement
Griggs (1991)	Random selection Double-blind	32 placebo 33 on 0.3 mg/kg/d 34 on 0.75 mg/kg/d	6 months	PRD 0.3 mg/kg/d and 0.75 mg/kg/d	Improvement, more on 0.75 mg/kg than on 0.3 mg/kg
Fenichel (1991a)	Doouble-blind	49	1 yr	PRD 0.65-0.75 mg/kg/d	Improvement
Fenichel (1991b)	Doouble-blind	40	3 yrs	PRD <0.65 mg/kg/d	Improvement, less than with higher doses
Mesa (1991)	Double-blind controlled	28	9 months	DFZ 1 mg/kg/d	Improvement
Griggs (1993)	Randomized controlled	107	6 months placebo, 0.3 mg/kg/d, 0.75 mg/kg/d	PRD 0.3 mg/kg/d, 0.75 mg/kg/d	Improvement, more with 0.75 mg/kg/d than with 0.3 mg/d
Sansome (1993)	Randomized open	32	18 months	PRL 0.75 mg/kg/d 10 first day of month	Improvement at 6 mo, declining at 12 and 18 mo
Bäckman (1995)	Double-blind Cross-over	38	6 months placebo, 6 months PRL	PRL 0.35 mg/kg/d	Improvement
Bonifati (2000)	Double-blind, randomized	67	3-12 months	DFZ 0.9 mg/kg/d vs PRD 0.75 mg/kg/d	Improvement, similar both groups, less weight gain DFZ
Biggar (2001)	Retrospective	54; 30 DFZ 24 placebo	1.6.5 yrs	DFZ 0.9 mg/kg/d	Improvement of motor + respiratory function

App.: ORTHOSES

Attachment to Orthopaedic treatment of DMD

ORTHOSES - SPLINTING

Non load bearing orthoses

The most common first orthosis is a night time ankle-foot orthosis (AFO) to stretch the achilles tendon. AFO can be static with a fixed angle or dynamic allowing some joint movement as shown in Figures 1 and 2.

KAFO

The opinions vary when it is time with orthoses to support the whole leg. A boy who is still walking, will easily experience knee-ankle foot orthoses as an impairment, whereas it is very difficult to start training to walk with KAFO:s (knee-ankle-foot orthosis) if there is no more any walking ability at all. Latest when the boy still can stand without support, but no more can stand up neither elevate the head when lying, it is time to start with KAFO:s. The KAFO:s, alike all loaded orthoses, should improve and not deteriorate the location of center of mass in balancing the body during standing and walking.

KAFO:s should support the ischial tuberosity to compensate for weak hip extensors. They also should have a possibility to lock the knee in extended position to prevent knee deformities. The sole should leave the forefoot free to facilitate the toe off and foot progression. The shoes should not have rigid soles either. An ischial tuberosity supporting KAFO is shown in Figure 3.

If a surgery for lower extremity deformities is planned, the plaster cast modelling for custom made orthoses should be planned a couple of weeks/days before to provide orthoses as soon as the post operative mobilisation is allowed.

Spinal orthosis – brace

Bracing the spine can be indicated to improve the body balance in sitting in spite of commonly occurring progress of an existing spine deformity even if braced. Best support is achieved if the brace opening is on back and if the brace is taken on in lying position. An opening covered with an elastic material should be provided on front over diaphragm to facilitate breathing and eating. A prefabricated symmetric module is preferred except in cases with a major, rigid deformity.

Standing device

To keep up standing in non-ambulators a standing wheelchair with KAFO:s is an alternative. However, it can be difficult to support the body upright and symmetrically in a standing wheelchair. A custom made whole body standing scale in polypropylene plastic material is the most supporting alternative.

TEXT TO FIGURES

Night time bracing in Duchenne muscular dystrophy

1. Static unloaded AFO made to keep the ankle joint in 90 degrees angle.
2. Dynamic AFO with a free or chosen range of motion in the ankle joint, dynamic loading is regulated by an elastic band.

Orthoses are perforated and lined for better ventilation and comfort. There is an opening to see/feel the position of the heel.

3. Load bearing KAFO with support on ischial tuberosity – JF PP KAFO.

- support under ischial tuberosity;
- knee front support for stable extension;
- aluminium splint for low weight, lock frame in front to give a better control for the patient;
- reinforcement in polypropylen;
- free forefoot for better balancing, toe off and foot progression.

Nattortoser till patienter med Duchennes muskeldystrofi

Statisk nattortos



Ortosen görs så att foten hamnar i 90 graders vinkel i vristen

Ortoserna perforeras med lufthål samt kik- eller kännhål i hälen så att man kan kontrollera att foten är på plats i ortosen.

Polstring i hela ortosen i mjuk aliplast

Ortoserna är klädda inuti med frotté för att minska de vanligt förekommande värmeproblemen

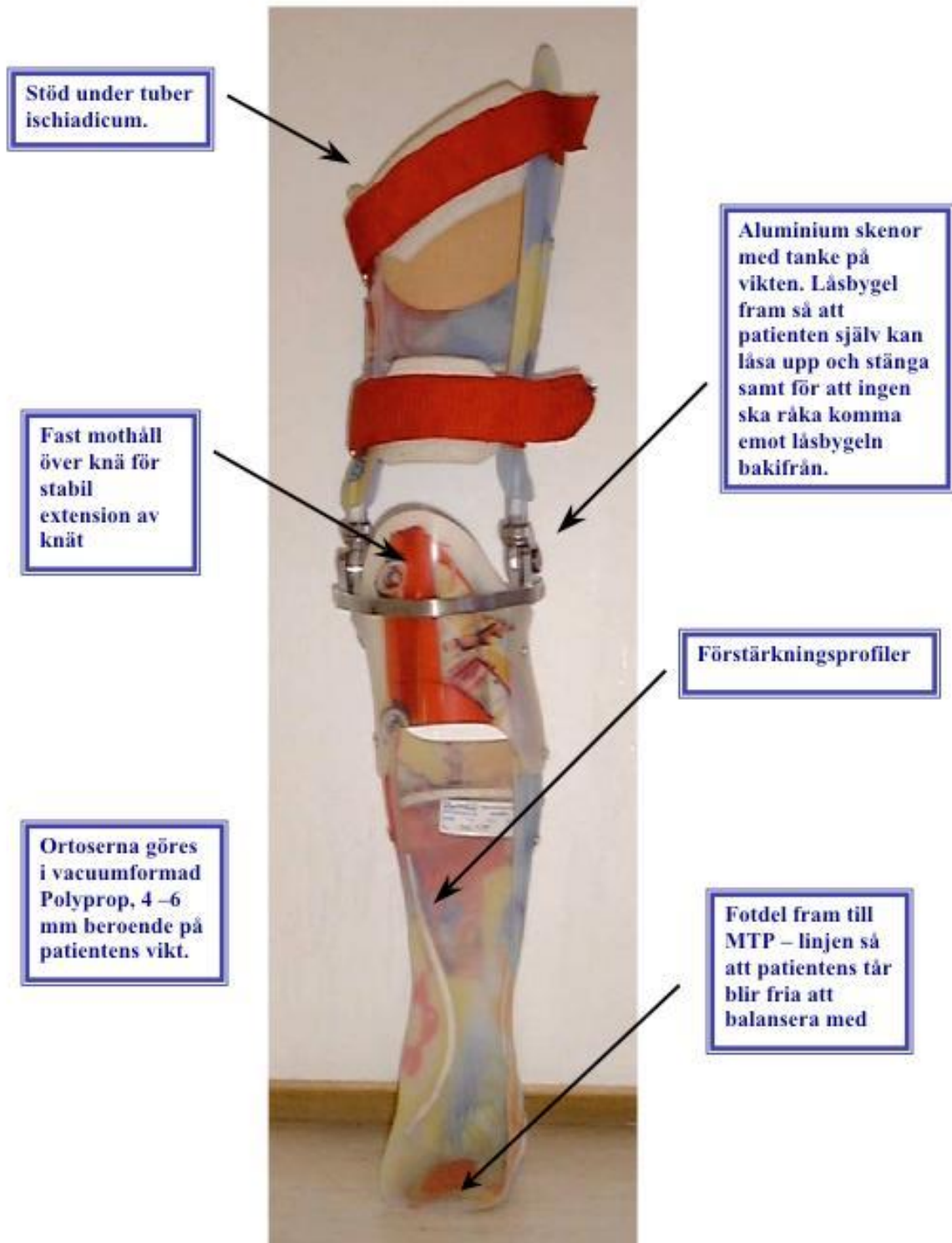
Dynamiska nattortoser

Elastiska dragband så att man kan ställa in den vinkel man önskar i fotleden.



Ylva Hägglund och Åsa Eliasson 2000 - 01-11

Helbensortos till patient med Duchennes
muskeldystrofi
JF PP KAFO



App.:

Management and Co-ordination in a Multi-centre cross border project.

Background

The importance of sound management and the role of the co-ordinator in the organisation of cross border multi-centre projects and co-operation is easily overlooked. Attention is focused on developing the protocol, deciding on the methodology, recruiting participants and staff, in fact on all those areas that are rightfully seen as central to the project. However all of this effort can be wasted and the study in jeopardy if the organisational and management structure has not received as much thought and been agreed before the project begins. There is always an expectation by clinicians / researchers that the interest of the work and the enthusiasm and goodwill of staff at all levels in all the participating centres can be relied upon and will lead to a successful outcome. However these attributes need harnessing and direction in order to maximise effectiveness. Further it is important to recognise that the greater the number of centres involved the greater is the need for co-ordinated effort. This should not be confused with administration.

In the following paragraphs some of the issues and factors relating to the above will be explored. The ideas, suggestions are largely drawn on the experience gained through the Nordic Contracture Study (NCS) (1,2) placed into the context of management theory. The NCS was a multi-centre, cross border study involving Denmark, Norway and Sweden, five main centres were used but in Sweden many peripheral clinical facilities were also used. It should be remembered that the more centres used the 'flatter' the organisational structure will be.

There are three main issues to be dealt with, namely, **methodological**, **people/organisational** and **data handling**. In cross border studies all must be seen in the context of differing cultures and differing healthcare delivery provision. To neglect addressing these aspects may impair compliance with the project, reduce co-operation and ultimately make assimilation of the results of the study into change in clinical practice more difficult.

Methodological issues

The detailed methodology has been dealt with in other sections. Therefore it is only necessary to state that staff training in the precise techniques to be used is essential before and during the project to ensure that there is standardisation. It is essential to document carefully and thoroughly the methods and precise techniques that have been agreed and each examiner must have a copy of the document to refer to.

Inter-observer and intra-observer error must be considered. This presented an organisational problem in the NCS because of the number of subjects available for test retest and the logistical difficulties of the distances that separated both examiners and subjects. We were forced to compromise and settled for a 'gold' standard and consistency testing but this is less than ideal.

Ideally train and accredit more therapists in the methodology than you think you need so that you have staff available for any contingency, (e.g. Maternity leave, job change, long term study leave). **Agree, document, train/revise, validate**

People / Organisational Issues

Multi-centre studies demand clear lines of responsibility and accountability to be effective. The very term 'multi-centre' implies that the project will create an interdependence of one centre on another. Failure to comply with the agreed protocol or level of agreed resource by one participating centre may adversely affect the work of other teams. This does not mean that the management structure has to be hierarchical or bureaucratic but there must be one in place!

At the very least there should be a project Manager who has the authority to commit resources at levels that have been agreed prior to the commencement of the study. This person should be close to the study and may also have a role as a co-ordinator. It is unlikely that a departmental Director will be close enough to the project or have time to assume this role, so there must be delegation .

Funding once agreed should be '**ring fenced**' and not be at the mercy of competing needs of other sections of the department / larger organisation. This approach also provides more security for staff and reduces stress on them, particularly where they are only seconded to the project for some hours of a week.

Cross border projects are particularly vulnerable to national government initiated **changes in the delivery of healthcare** resulting in changes of patient flow to particular hospitals, changes in the place and quantity of resources and the redeployment of staff. It is probably advisable to have written agreements with senior medical and administrative staff to avoid the project being compromised, for example, ensuring continued use of facilities, support staff (e.g. clerical).

Other factors to be considered

- **Impact of the study and its organisation on the participant**, for example ensuring clear lines of communication between project staff and those responsible for day to day care of the participant, clear definition of line of responsibility for delivery of care and agreed sharing of information.
- **The professional staff undertaking the study** must receive regular feed back on the progress of the project and their job satisfaction must be a consideration. It is also essential that other staff with whom they work, but who may not be involved in the project, are made aware of the purpose of the study. Non project staff should also be assured that they are not having to do extra tasks to support the project. Attention to this prevents interpersonal jealousies that can be less than constructive and isolate the researcher, as well as creating disharmony within a department.
- **Other professionals not actively involved in the study but responsible for the participant.** Depending on the type of intervention or project those staff responsible for the day to day care of the participant can feel threatened by projects feeling that they are themselves under scrutiny. This is more important where the project centre is geographically removed from the study centre. Participants are quick to recognise this and may become confused, dissatisfied or even take advantage of the situation. **Effective communication and liaison** is essential to prevent problems.

- **Cultural differences and language barriers** to communication have to be considered. It is not enough to assume that thoughts communicated in a second language can be taken at face value. Understanding must be checked, it is not just semantics.

Data Handling

Regardless of whether the data gathered is to be used for a specific research project, or simply used for clinical decision making in the management of a specific child a research discipline should prevail. All data should be **screened before and after entry to a common database** according to the agreed protocol. Experience showed that the greatest errors arose from the method of recording results.

Brooke et al (3) used an ‘expert’ computer software programme, menu driven to screen data for errors. This can be expensive to install and is still subject to error. I suggest that screening of data is done by a suitably qualified professional person.

I have had some experience of electronic menu driven programmes where non-professional members of staff are responsible for entering the data. In these systems ranges of data are usually identified so that an entry falling outside the pre-set limits produces a warning.

The structure of the database should be available at the start of the project.

Sustained **vigilance** is required to prevent the database becoming corrupted. **Agree** beforehand who has access to, **ownership** of the database, and that it complies with Data Protection legislation.

Outcomes and change management

The underlying purpose of consensus programmes or clinical research is to improve the treatment of the patient whether this is achieved by expanding the knowledge base or treatment strategy. Participants in such studies usually agree to take part in the study because they believe it will improve their own care or that of others suffering the same condition. It is in many respects an unspoken contract between researcher and subject.

Effective management of the study will greatly influence the ease with which any resultant change in clinical practise is implemented. One of the greatest barriers to change is when long established practices are challenged or the power of a practitioner(s), which has been based on, is threatened. Ensuring that communication has been inclusive, that even those who have not had an active part in the study feel a sense of ownership and have collaborated will do much to reduce this problem.

Possible benefits of collaborative studies

- Improved patient care
- Pooling of validated data to permit quantitative analysis
- Early identification of any problem areas
- Provide baseline data on outcomes as a standard against which any future developments could be evaluated
- Formulation of hypotheses for future research

Recommendations

Clinical Consensus Programme

- Negotiate with all participating centres
 - Agree assessment / protocol
 - Document
 - Communicate effectively
 - Train staff in use of agreed procedures
 - Accredit staff
- Preferrably enter data into common database

Clinical Research

- Build team and appoint manager/ co-ordinator
- Agree protocol
- Train staff / accredit
- Communicate
- Contingency plan for staff migration / change
- Contracts

Ring Fence Funding

References

1. Hyde SA, Floytrup I, Glent S, Kroksmark AK, Salling B, Steffensen BF, Werlauff, Erlandsen M. Arandomised comparative study of two methods for controlling Tendo Achilles contracture in Duchenne muscular dystrophy. *Neuromuscular Disorders* 10 (2000) 257-263.
2. Hyde SA. et al. Longitudinal data analysis : an application to construction of a natural history profile of Duchenne muscular dystrophy. *Neuromuscular Disorders* 11 (2001) 165-170.