Neuromuscular disorders
Development of consensus for diagnosis and standards of care

Thomas Sejersen, Pediatric neurology
• What are neuromuscular disorders?
• How does the field of neuromuscular disorders deal with networking?
• What guidelines exist on standards of diagnosis and care?
Neuromuscular disorders affect the motor unit

Motor unit: motor neuron and its innervated muscles
Neuromuscular disorders affect the motor unit

Motor neuron
- SMA, polio

Axon
- Guillain-Barré, HMSN

Neuromuscular junction
- Myasthenia

Muscle fiber
- Muscular dystrophies
- Myopathies
Neuromuscular disorders affect the motor unit

Motor neuron
- *SMA*, *polio*

Axon
- *Guillain-Barré*, *HMSN*

Neuromuscular junction
- *Myasthenia*

Muscle fiber
- *Muscular dystrophies: DMD, CMD*
- *Congenital myopathies*
Neuromuscular disorders in children: -how common?

- 1:1500 at school age (enrolled Habilitation Center)
- Most hereditary (>200 neuromuscular disorders)

In Stockholm:
- 30 DMD
- 10 DM1
- 20 SMA
- 20 AMC
Neuromuscular disorders in children: symptoms

- muscle weakness
  - sequelae: breathing problems, contractures, scoliosis
- myotonia, paralysis, pain, cramp
- symptoms from other organs (heart, smooth muscle, CNS)
Neuromuscular disorders frequently present as "Floppy infant"
Neuromuscular disorders frequently present as "Floppy infant"

e.g. in SMA, congenital myopathies, congenital dystrophies
• What are neuromuscular disorders?
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• What guidelines exist on standards of diagnosis and care?
Working together to accelerate treatments for Neuromuscular Disorders -

The TREAT-NMD model of networking
TREAT-NMD: a network of excellence in the neuromuscular field

- €10 million funding from the European Union
- linking clinicians and researchers across Europe and worldwide in a network designed to reduce fragmentation, share good practice and improve global standards of care
- working closely with industry, providing expert backing to accelerate clinical trials of the most promising new treatments
- creating international patient databases and biobanks as specialist resources for research and future trials
- strong transatlantic and global links with clinicians, researchers, patient organisations, regulatory bodies and industry
- facilitating training for the next generation of neuromuscular specialists
- coordinated by Newcastle University; 21 partners in 11 European countries and a worldwide club of interest
Selection of partners: excellence, representation

Backup from international scientific advisory board
TREAT-NMD collaborations – a global network
TREAT-NMD offsprings:

- NMD-CHIP (genetic diagnosis)
- CARE-NMD (spread of care standards)
- BIO-NMD (Biomarkers)
NMD-Chip

EU-projekt för “high throughput diagnosis of Neuromuscular disorders”
• All known genes analyzed at once
• 2,100,000 spots, 250 kb DNA-sequence
• Total cost reduced
What are neuromuscular disorders?
How does the field of neuromuscular disorders deal with networking?
What guidelines exist on standards of diagnosis and care?
Why Standards of Care?

Reasons:
1. Joint basis for diagnostics and care prerequisite for future international treatment studies
2. Low prevalence of the disorders necessitates expert advice on management being collated on a multinational level
3. Families should be offered the most informed treatment and counselling regardless of where (in Europe) they live
Standards of care activities in TREAT-NMD

- SMA collaboration with ICC
- DMD- working with CDC led initiative
- CMD- working with CURE-CMD
- Congenital myopathies consortium
Principles of generation of care standards similar

• How?
  – Gather evidence from literature where this exists
  – Assemble expert panels
  – Ensure representation as broad as possible
  – Use an unbiased method for building consensus
    • RAND/ UCLA appropriateness method (RAM)
    • Delphi methodology
  – High profile academic publication
  – “Joined up thinking” for dissemination and implementation
  – Consistent message
Motoneuron degeneration in Spinal Muscular Atrophy (SMA)
SMA - great variation in severity:

Type 1

Type 2

Type 3
ICC Consensus statement for Standards of care in SMA:

Journal of Child Neurology
http://jcn.sagepub.com

Consensus Statement for Standard of Care in Spinal Muscular Atrophy
Ching H. Wang, Richard S. Finkel, Enrico S. Bertini, Mary Schroth, Anita Simonds, Brenda Wong, Annie Aloysius, Leslie Morrison, Marion Main, Thomas O. Crawford, Anthony Trela and Participants of the International Conference on SMA Standard of Care
J Child Neurol 2007; 22; 1027
DOI: 10.1177/0883073807305788

The online version of this article can be found at:
http://jcn.sagepub.com/cgi/content/abstract/22/8/1027

Standard of care committee (SCC) formed 2005
to establish guidelines
12 core members, 56 experts
How to reach consensus? Delphi technique
ICC Consensus statement for Standards of care in SMA

**Five areas addressed:**
- diagnosis
- pulmonary care
- GI and nutritional care
- orthopedics and (re)habilitation
- palliative care

**Three functional levels:**
- non-sitter
- sitter
- walker
Standards of care for spinal muscular atrophy

TREAT-NMD worked with the authors of the international consensus statement on care for patients with spinal muscular atrophy to create useful summary factsheets based on the full published document. A TREAT-NMD working group is continuing to develop the standards for care on SMA in areas such as physical and occupational therapy, orthopaedics, nutrition and psychosocial implications.

We are very interested in talking with patients and clinicians about these recommendations and suggestions for their future improvement. If you're interested, please email the TREAT-NMD team at info@treat-nmd.eu.

Document downloads

Individual documents are available for download in a number of languages, along with the original published journal article, the "Consensus Statement for Standard of Care in Spinal Muscular Atrophy" - see the downloads section to the right.

Click here to download the English text as a PDF brochure with pictures.

Translations

We believe it is crucial to have this type of information about standards of care available in patients' and clinicians' native languages, and we are therefore in the process of translating it into a number of languages with the generous help of multilingual staff within the TREAT-NMD network and colleagues from patient organisations. If you are interested in translating our factsheets into your language for hosting on our website, please contact the TREAT-NMD team at info@treat-nmd.eu - we'd love to hear from you!

Recently added translations include: Polish, Dutch, Italian and Turkish.

Translations that are currently in progress include: Slovenian

www.treat-nmd.eu
# SMA care guidelines
## -key recommendations

<table>
<thead>
<tr>
<th>Care Area</th>
<th>Recommendations for Clinicians</th>
</tr>
</thead>
</table>
| **Diagnosis and Care for the Newly Diagnosed Patient** | - If SMA is suspected, order a blood test to confirm or rule out the disease (SMN gene deletion test can confirm 95% of all SMA cases)  
- If SMA is confirmed, develop a care plan with the patient and family and collaborate with a multidisciplinary care team |
| **Pulmonary Care**          | - Routinely perform pulmonary assessments  
- Teach caregivers techniques to assist with airway clearance  
- Practice vigilance and plan carefully to prevent problems  
- Work with the family to develop a plan for routine care & care for acute respiratory illness |
| **GI and Nutritional Care** | - Monitor growth velocity  
- Evaluate patient for swallowing difficulties and problems with reflux or constipation  
- Work with family to develop a personalized feeding plan |
| **Orthopedic Care and Rehabilitation** | - Develop a physical/occupational therapy plan to help patient achieve and maintain highest level of function and independence  
- Consider use of assistive devices, tools, and exercise to support breathing, eating, work, and play and slow or prevent complications of SMA  
- Evaluate and treat scoliosis before severe respiratory complications develop |
| **Palliative Care**         | - Work with patient and family to develop a plan for medical emergencies |
Duchenne muscular dystrophy

- Progressive muscle weakness
- X-linked recessive inheritance (1:4000 boys)
- Symptoms from age 4
- CNS + heart engaged
- Wheelchair from age 10
- Death at early age if untreated

*From Erb et al, Nervenheilkd 1:13, 189.*
How reach consensus?

- RAND, combines scientific evidence with consensus opinion among experts

- 84 experts

- 489 articles selected

- Rating of ”signs and symptoms”

- Rating of ”assessment tools / interventions”

- 2 anonymous ratings with in-person meeting in between
Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management

part 2: implementation of multidisciplinary care

Katharine Bushby, Richard Finkel, David J Birnkrant, Laura E Case, Paula R Clemens, Linda Cripe, Ajay Kaul, Kathi Kinnett, Craig McDonald, Shree Pandya, James Poysky, Frederic Shapiro, Jean Tomezsko, Carolyn Constantin, for the DMD Care Considerations Working Group*

www.treat-nmd.eu/patients/DMD/dmd-care/
Follow stages of disease:
### DMD Stages of Disease:

<table>
<thead>
<tr>
<th>Stage 1: Presymptomatic</th>
<th>Stage 2: Early Ambulatory</th>
<th>Stage 3: Late Ambulatory</th>
<th>Stage 4: Early Non-ambulatory</th>
<th>Stage 5: Late Non-ambulatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>May be diagnosed at this stage if CK found to be elevated by chance or if positive family history</td>
<td>Gowers maneuver</td>
<td>Increasingly labored gait</td>
<td>May be able to self propel for some time</td>
<td>Upper limb function and postural maintenance increasingly limited</td>
</tr>
<tr>
<td>May show developmental delay but no gait disturbance</td>
<td>Waddling gait</td>
<td>Losing ability to climb stairs and rise from the floor</td>
<td>Able to maintain posture</td>
<td></td>
</tr>
<tr>
<td></td>
<td>May be toe walking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Can climb stairs</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

- **Stage 1:** Presymptomatic
- **Stage 2:** Early Ambulatory
- **Stage 3:** Late Ambulatory
- **Stage 4:** Early Non-ambulatory
- **Stage 5:** Late Non-ambulatory
Figure 1: Interdisciplinary management of DMD
DMD care standards

Introduction

A major international consensus document setting out best practice in care for Duchenne muscular dystrophy (DMD) was published in the *Lancet Neurology* journal in January and February 2010. The product of an extensive review process by 84 international experts in DMD diagnosis and care, this document is a unique guide to expert recommendations on the care that all individuals with DMD should receive.

The document is available in the January and February editions of the printed journal, online from the journal’s website, or here on this page, with special permission from the journal’s publisher Elsevier.

Click here to download the full document (parts 1 and 2 combined)*.

Katharine Bushby, Richard Finkel, David J Birnkrant, Laura E Case, Paula R Clemens, Linda Cripe, Ajay Kaul, Kathi Kinnett, Craig McDonald, Shree Pandya, James Poysky, Frederic Shapiro, Jean Tomezsiko, Carolyn Constantin and for the DMD Care Considerations Working Group

The Diagnosis and management of Duchenne muscular dystrophy

Part 1: diagnosis, and pharmacological and psychosocial management*
PMID: 19945913, DOI: 10.1016/S1474-4422(09)70271-6

Part 2: implementation of multidisciplinary care*
PMID: 19945914, DOI: 10.1016/S1474-4422(09)70272-8

*If you downloaded your copy of the second article BEFORE Jan 18th 2010, please download it again! The new version contains an important correction.

Downloads

- DMD - Interim Recommendations - Czech
- DMD - Interim Recommendations - Dutch
- DMD - Interim Recommendations - English
- DMD - Interim Recommendations - French
- DMD - Interim Recommendations - German
- DMD - Interim Recommendations - Italian
- DMD - Interim Recommendations - Serbian
- DMD - Interim Recommendations - Polish
THE DIAGNOSIS AND MANAGEMENT OF DUCHENNE MUSCULAR DYSTROPHY

A guide for families
Workshop report

Best Practice Guidelines on molecular diagnostics in Duchenne/Becker muscular dystrophies

Stephen Abbs, a, Sylvie Tuffery-Giraud, b, Egbert Bakker, c, Alessandra Ferlini, d, Thomas Sejersen, e, Clemens R. Mueller f

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Congenital muscular dystrophies and congenital myopathies:

- Online survey of experts’ opinion
  1. Key symptoms/problems?
  2. Assessments recommended?
  3. Interventions recommended?

- Workshops, Brussels -09 (CMD) & Stanford -10 (CM) for building consensus:
  - Literature review
  - Survey discussion
  - Specialist group discussion
  - General discussion
  - Guideline summary

- 2 manuscripts (diagnosis, care)
Conclusions:

• Guidelines for Standards of care for SMA, DMD, and CMD published
• User-friendly versions of guidelines available in several languages
• Ongoing work to produce guidelines for Standards of care for Congenital Myopathies
• Full documents and (translated) user-friendly versions available at www.treat-nmd.eu
Thank you!