TREAT-NMD Neuromuscular Network

24 April 2009

TREAT-NMD newsletter no. 53

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welcome

Welcome to the latest TREAT-NMD newsletter. This week's edition features two academic job/research opportunities in the UK and reports from a CMD consensus meeting in Newcastle and a Russian round table in Paris.

As always, we hope you enjoy the newsletter and look forward to hearing your comments - write to info@treat-nmd.eu with anything you'd like to say. Feel free to forward this message to anybody you think might find it of interest, or invite them to sign up to receive the newsletter by visiting our website. Back-issues of this newsletter can be found on our website at http://www.treat-nmd.eu/patients/news/ezine-archive/

Best wishes,

Katie, Volker, Hanns, Steve, Emma, Rachel, Michael and Sam: the Newcastle TREAT-NMD team

at a glance...

12-15 May 2009 The Nottingham Systematic Review Course 2009

21-23 May 2009 International conference in Ukraine: Recent standards in diagnosis, treatment and medical care for some rare neuromuscular diseases

01-03 Jun 2009 Update in Neuromuscular Disorders course in London

04-06 Jun 2009 TREAT-NMD workshop: clinical trial design in neuromuscular diseases

09-11 Jul 2009 "Therapeutic Targets in CMD", Emory University, Atlanta, Georgia

09-12 Sep 2009 IDMC-7 International Myotonic Dystrophy Consortium

17-19 Nov 2009 TREAT-NMD / NIH International Conference

CMD meeting makes progress on patient registry and more

TREAT-NMD hosted a conference with CMD expert neurologists and Cure CMD, an international CMD advocacy group based in the US. The meeting stressed the need for international consensus in building CMD infrastructure to support translational research and the goal of identifying drugs to slow disease progression.

Meeting participants focused on several key areas:

1. Application of TREAT-NMD tools and resources to CMD gaps of knowledge.
2. A definition of the CMDs.
3. The CMD International Patient Registry (CMDIR).
4. Placement of the CMDIR within existing infrastructure of current and planned locus specific databases (LSDB)
5. Harmonizing differences in national medical practice by pursuing consensus in launching the CMDIR with inclusion of both self report (patient directed) and physician report entries.

Outcomes include:

- Consensus that inclusion into the CMDs as a group is based on their current clinical definition as neuromuscular disorders with congenital and early childhood onset presenting with hypotonia, contractures, myopathic or dystrophic muscle biopsy finding and a variable CK. There is a recognition that the line between the CMDs, congenital myopathies and LGMDs is blurred with a gene classification approach demonstrating a gene specific spectrum of disease with clinical heterogeneity.
- A working group led by Dr. Susana Quijano-Roy and Dr. Susan Sparks to improve and standardize CMD online genetic resources on orphanet, genetests.org and wikigenetics. A desire to improve current OMIM classification and drive the report of both novel pathogenetic and sequences of unknown significance to both NCBI and Ensemble as well as Leiden and other locus specific databases will be stressed.
- Delineation of 9 core CMD questions that represent the core data elements of the CMDIR. These 9 core questions will be distributed to the 146 participating clinical trial and care sites within the TREAT-NMD registry for input by May 1st. A final core data set will be circulated amongst April participants with launch of CMDIR by June 2009.
- A working group led by Dr. Thomas Sejersen in conjunction with Dr. Ching Wang to establish current CMD care standards. An international steering committee will assist Drs. Sejersen and Wang in identifying discussion groups around various CMD subspecialty care areas: pulmonary, GI/nutrition, orthopedics, diagnostic access/workup, cardiac and psychosocial. A follow up conference to discuss CMD care standards will take place later this year.
- A working group led by Dr. Markus Ruegg to discuss current CMD animal models and methods used to evaluate their phenotype. The aim of this working group is to reach a consensus between the participants on the use of current animal models and the need to develop new ones. In a second step, protocols will be established that allow some standardization of the

preclinical evaluation of potential treatment options. A similar aim has recently been reached for preclinical research on DMD. The working group will utilize a breakout session led by Dr. Beth McNally, Dr. Jim Dowling and Dr. Yiumo Chan, during the July conference, “Therapeutic Targets in the CMDs”. Another opportunity for discussion will be the November, TREAT-NMD/NIH Translational Meeting.

- A discussion with the MDA to harmonize future MDA efforts around an MDA CMD registry platform with the CMDIR, with an acknowledgement that developing an online MDA resource for MDA clinicians including a list of US CMD expert neurologists would expedite and improve CMD genetic testing, streamlining expenses.
- Establishment of a plan to have a CMD global registry (CMDIR) with a portal through the Cure CMD website where core data elements will be posted. A CMD affected individual will enter through the portal, answer the questions and flag a genetic counselor. The genetic counselor will review the answers and request a fax either from the affected individual or their physician with a copy of their genetic test results if genetic testing has been done. The affected individual will then be contacted by the genetic counselor to re-enter the portal to update their profile and will be directed to the appropriate question set to be hosted on both a Cure CMD secure server and a locus specific database (LSDB). The LSDB will have a curator to assist with information curation of the more focused gene specific question set.
    - Individuals with a lamin A/C mutation or an FKRP mutation will be directed to the established lamin A/C and FKRP registry after answering the core data elements with confirmation of genetic mutation.
    - Individuals with an undiagnosed form of CMD will be eventually directed to a database (DB) for undiagnosed individuals with a specific question set to sub classify undiagnosed patients and recognize novel phenotypic patterns.
    - A LAMA 2 specific set of questions is currently being worked on by colleagues in Montpellier with the development of an LSDB. A future meeting to drive consensus around the question set will need to be established.
    - A col 6 specific question set will be discussed at the upcoming ENMD workshop with location of the col 6 LSDB to be decided at the workshop.
    - A gene specific LSDB for each dystroglycanopathy gene will need to be created with a question set patterned on the current FKRP registry questions.
- The launch of an initially informal CMD natural disease progression study led by Dr. Carsten Bonnemann in collaboration with selected centers to begin the process of identifying appropriate outcome measures and characterizing CMD subtype disease progression to build the infrastructure for CMD clinical trials to study medical, pharmacological, behavioral or other interventions.

CMD calendar of events:

- July 9-11th: “Therapeutic Target conference in the CMDs” at Emory University, organized by Dr. Carsten Bonnemann and Cure CMD, MDA and NIH grants pending.
- August 15th-16th: CMD Family and Affected Individual conference, Children’s Hospital of Philadelphia, organized by Dr. Bonnemann, Alan Tuttle, Marissa White and Cure CMD. Webex will allow for international remote conference participation.
- Fall 2009: CMD Standards of Care
- November 15-17th: TREAT-NMD/NIH Translational Meeting

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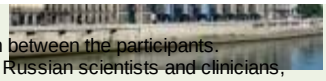
Russian round-table in Paris sets the scene for collaboration

The French Association Française contre les Myopathies (AFM), the Institut de Myologie and TREAT-NMD hosted a round-table meeting with representatives from clinical and research centres and patient organisations from Moscow, St Petersburg and Minsk in Paris from 9-11 April. The aim of the



meeting was to make progress on opportunities for collaboration between the participants. Discussions focused on training and education opportunities for Russian scientists and clinicians, grant submissions for joint EU-Russia calls, experience sharing between Russian patient organisations and the AFM, and opportunities for integration of Russian centres into TREAT-NMD activities, in particular the patient registries and care and trial sites initiatives. As well as receiving tours of the facilities at Genethon in Evry and the Institut de Myologie in Paris, participants shared experiences of the current situation regarding patient diagnosis and care in Russia and Belarus, current research, and training needs and opportunities. This meeting will be followed up by joint action in a number of areas, with training exchange visits and summer schools, Russian and Belarussian patient registries, and applications for funding opportunities all under consideration.

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Research opportunity in Newcastle: PhD studentship in medical research ethics

Newcastle University

Policy Ethics and Life Sciences Research Centre, School of Geography, Politics and Sociology

ESRC Collaborative (CASE) PhD Studentship 2009-2012

Research Decisions: Living with Duchenne Muscular Dystrophy
Information for Applicants.

Applications are invited for an ESRC Collaborative (CASE) PhD studentship under the supervision of Dr Simon Woods and Dr Janice McLaughlin of the Policy Ethics and Life Sciences Research Centre, School of Geography, Politics and Sociology, Newcastle University, in collaboration with TREAT-NMD (a network funded by the EU, which brings together people with neuromuscular diseases and specialists such as scientists, healthcare professionals and pharmaceutical companies who are working on treatments for neuromuscular diseases). The studentship is £18000 (tbc) per annum for 3 years (plus home fees). Preference will be given to applicants who have a Masters level degree and/or relevant research experience and training. Applicants should send their CV, letter of application and the names and addresses of two referees to Tom Martin, Policy Ethics and Life Sciences Research Centre, Citywall, St James Boulevard, Newcastle Upon Tyne, NE1 4JH tom.martin@ncl.ac.uk For further details contact Simon Woods simon.woods@ncl.ac.uk or Rob Walton rob.walton@ncl.ac.uk. Tel: 0191 222 3919

Closing Date for Applications is **Monday, 22nd June 2009.**

Interviews will be held on: **Monday, 27th July 2009**

If you are unable to attend on this date for any reason please indicate this on your application.

Duchenne Muscular Dystrophy (DMD) is one of the most common lethal genetic diseases of childhood and one of the most devastating of the muscular dystrophies. It affects all ethnicities, nationalities and socioeconomic groups, although it is almost exclusive to males. Important work is being done to develop effective clinical therapies; this research requires the recruitment of affected boys to participate in clinical trials of candidate drugs. We know from other research that many parents are keen to have their children participate (Henderson 2008), however little is known about the attitudes of the boys and young men themselves.

The principal objective of this studentship is to explore what frames the approach taken by boys and young men with DMD to participating in medical research.

Secondary objectives:

1. Identifying the social, cultural and familial contexts that influence their attitude to participating in medical research.

2. Drawing out the key processes and interactions they engage with when considering/making a decision to enter a clinical trial (for example with family, professionals and patient groups).

3. Exploring the resources, such as patient organisations, and sources of information, such as the internet, that they draw upon when considering participating in medical research.

Background:

DMD affects 1:3,500 live male births. It is clinically characterised by muscle weakness which becomes apparent between the ages of 3-5 and progresses to the point of preventing the child walking by about age 12. Few affected individuals survive beyond the age of 20 and only then with ventilator support. All current interventions are palliative or supportive.

Patient organisations such as Action Duchenne and the Muscular Dystrophy Campaign have become powerful lobbyists to improve services available to children and, more significantly to support research into therapies; these groups are driven by parents on behalf of boys affected by the condition. Parents

have a strong sense of urgency with regards to research and they are frequently frustrated by the various barriers to research. The medical research they promote and put forward their children to participate in will not provide a cure for their own children; instead they are seeking to create a future where Duchenne will not affect other children. This raises important questions regarding consent and children in clinical research; questions that have been explored in bioethics, but not with a sociological appreciation of the perspective of children themselves. There are a number of dynamics around consent, where we have limited knowledge about what children and young people, particularly those with such serious conditions, consider to be important.

First, it is parents, rather than those directly affected by the condition, who lead such groups and campaign for more research to be done, including more research using their children as the test subjects. This means there is the potential for conflict between the research aspirations of parents and the choices and priorities of their children. Do boys and young men affected by DMD feel the same about participating in the research as their parents? Do they value the principles of the greater good, which their parents appear to be driven by?

Second, while parents groups push for their children to be included in clinical trials, they face an increasing reluctance to include children in clinical trials. There is a high level of cautious paternalism within research ethics committees and implicit within the ethical guidance on research involving children. Are young people vulnerable human subjects in need of protection, or can they act as active agents, making choices, within the contexts of their lives, which they feel to be appropriate? Finally, a recently completed PhD (Alex Henderson supervised by Dr Simon Woods) has contributed to the growing body of evidence that parents who consent for children to enter clinical trials find it difficult to distinguish between treatment and therapy. This confusion thus poses a problem for the conventions of informed consent which require the person consenting to understand the information given to them and to have the capacity to weigh that information before coming to a decision. We are therefore concerned to explore whether young people with DMD make the distinction between therapy and treatment. Does their understanding differ from that of their parents? How may this influence possible differences in their approach to participating in research?

Approach and methods:

It is vital that the research seeks to involve young people via methods that bring to the fore their own perspectives and agency (Balen et.al,. 2006; Save the Children 1999, 2003). Doing so often troubles assumptions others make about what it is to be a disabled child or young person and who is a vulnerable human subject. PEALS, as a research centre specialising in exploring research ethics and the complex dynamics of consent; can draw upon a wealth of research expertise in developing appropriate methods for both working empirically on the ethics of consent and with working with children.

Access to boys and young men will be via the patient support groups who are partnered to TREAT-NMD or via the clinical data-base of the Newcastle Muscle Centre where the clinician co-ordinators of TREAT-NMD are based. We will seek to recruit between 20-25 boys and young men.

The age group we will work with will be 12 to 18. Our approach to introducing the research and obtaining consent will involve both parents and children and will be compliant with relevant law (Gillick Ruling and Mental Capacity Act 2005). The main research instrument will be qualitative semi-structured interviews with the participants, but drawing on narrative techniques to provide a space within which the boys and young men can articulate their lives, values and influences on their approach to potentially being involved in clinical research. The interviews will be conducted twice in order to provide a space for the participants to reflect on the narratives identified in the first interview; for the length of time taken in each interview to be shortened and for any issues created by the participants' health (for example communication difficulties that require the use of assistive technologies) to be factored into the interviews appropriately.

> **Year 1** - will include: orientation, methods training, literature review, refining research questions and methodology, networking with relevant organisations, applying for various permissions e.g. NHS Ethics approval.
>
> **Year 2** - Phase I data collection (interviews and transcription of data), Phase II secondary data collection (interviews and transcription of data), dissemination activities
>
> **Year 3** - Data analysis, writing thesis and partner reports, dissemination activities

Anticipated outcomes:

The CASE partnership will provide multiple dissemination opportunities for the outputs of the research. The new knowledge of young people's perspectives will be disseminated within the TREAT-NMD global network. In so doing it has the significant potential to influence consent approaches within international research. Further influence will be enabled through presentations at both academic and practitioner conferences, facilitated by PEALS connections.

References:

Balen, R.,et.al. 2006. Involving children in health and social research - 'Human becomings' or active beings? Childhood 13: 29-48.
Henderson, A. (2008) 'Consent, choice and children in research', PhD Thesis, Newcastle University
Save the Children (1999). Involving Young Researchers, http://www.savethechildren.org.uk/en/54_2334.htm, accessed 13th of January 2008
Save the Children (2003). Interviewing Children, http://www.savethechildren.org.uk/en/54_2333.htm, accessed 13th of January 2008

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Job opportunity in Oxford: Neuromuscular Research Fellow

Department of Clinical Neurology

Grade E71: £30,231 - £43,755 per annum

Applications are invited from registered medical practitioners for the post of neuromuscular research fellow in the Oxford Muscle & Nerve Centre, based in the University Department of Clinical Neurology.

The post is funded by the Muscular Dystrophy Campaign and is available for two years in the first instance. The appointee will be expected to undertake research suitable for a higher degree and will gain clinical experience in the management of neuromuscular disorders. The project will be looking at clinical and laboratory aspects of sporadic inclusion body myositis and will involve collaboration with other neuromuscular centres.

Further details about the project can be obtained from Dr Hilton-Jones (david.hilton-jones@clneuro.ox.ac.uk). Departmental and administrative particulars, including details of how to apply, are available from www.clneuro.ox.ac.uk/vacancies or e-mail moira.westwood@clneuro.ox.ac.uk, tel 01865 231909, quoting job reference HM/09/007.

The closing date for applications is **Friday 15 May 2009**.

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