

British Myology Society
Third Annual Meeting

6th – 7th September 2011
St Anne's College, Oxford

MRC | Centre for Neuromuscular Diseases

Registered Charity No. 1142966

Contents

Welcome from the BMS organising Council

Dear Member,

We are delighted to welcome you to this third meeting of the British Myology Society at St Anne's College in Oxford.

The BMS background

The object of the BMS is to act as an independent multidisciplinary professional body of experts to promote the clinical practice, education and advancement of knowledge relating to muscle diseases, myasthenia gravis and spinal muscular atrophy in the British Isles and Ireland. The BMS was established in London in April 2008 and has registered for charitable status (number 1142966). Some rules have been drawn up and are contained in this brochure. We are very pleased that over 70 members are attending this third meeting in Oxford.

The specific aims of the BMS include:

- Agreeing best practice and standards of care for clinical and diagnostic pathology services
- Agreeing standards for training in clinical myology and clinical muscle pathology
- Promoting translational research
- Establishing clinical networks to improve standards of care and promote registries and clinical trials.
- Facilitating collaborations with patient organisations
- Providing a forum to improve recognition of rare conditions or their complications

Running the BMS

The BMS is a new venture which is untested. It has come together as a result of discussions and some meetings of the colleagues listed at the end of this introduction. At present the secretariat for the BMS is located at and sponsored by the MRC Centre for Neuromuscular Diseases in London. At the second annual BMS a brief AGM was held - see minutes. Since this was a new venture, and we needed to assess if it will be useful to colleagues, we considered it reasonable to simply ask colleagues if they were content for the initial organising group to continue to organise the next meeting and to have a show of hands. This was agreed as indicated in the minutes. It was also agreed that a subscription of £25 per year would be charged for the year 2011 – 2012.

The second BMS meeting

We devised a programme of interactive sessions for the second annual BMS meeting.

The key themes that were covered in interactive sessions included:

Commissioning neuromuscular services in the UK
Planning muscle pathology services
Developing networks for clinical practice and clinical trials
Update on UK neuromuscular workshops and clinical trials
Interesting-difficult cases supported by the NCG services

The invited guest speaker was Professor Marianne de Visser from the Academic Medical Centre, University of Amsterdam department of Neurology.

This year the council have devised a programme which builds on the themes covered in the first two meetings, and we will also report on progress in the UK in each of these areas. This year we are delighted that Dr Michael Hubank has agreed to be our guest speaker, and we are very pleased that Professor Alan Emery will be our guest after-dinner speaker.

We hope you have an enjoyable, stimulating and useful time at this third annual BMS meeting in Oxford!

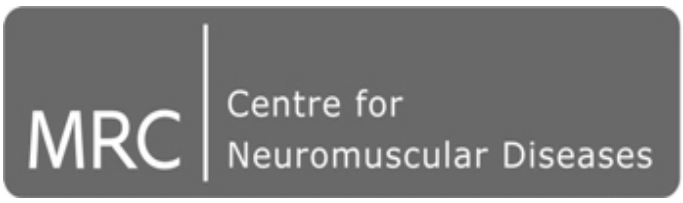
Michael Hanna, David Hilton-Jones, Francesco Muntoni, Kate Bushby,

Doug Turnbull, Janice Holton, Caroline Sewry,

Helen Roper, Mike Rose, Peter Baxter, Doug Wilcox

Professional Academic sponsor

The Secretariat for the BMS has been provided by the MRC Centre for Neuromuscular Diseases.



About the MRC Centre for Neuromuscular Diseases

Genetic and acquired neuromuscular diseases represent an important cause of mortality and morbidity in children and adults. In the UK there is a large gap between major science discoveries and patient benefit in these important disorders. This gap is larger in the UK than in other countries such as Germany, France and the USA who have already moved forward with translational research initiatives. The new MRC Centre aims to reduce this gap by establishing a multidisciplinary translational research activity in these disabling diseases.

This is a joint centre between the UCL Institute of Neurology and the UCL Institute of Child Health, London and the University of Newcastle. The Centre is building on long-established UCL-Newcastle research and clinical links. ***The centre is committed to form reciprocal clinical and research links with other neuromuscular research groups and patient organisations throughout the UK.***

Our mission is to translate basic science findings into clinical trials and new treatments for children and adults with disabling neuromuscular diseases. Current world-class science programmes in London and Newcastle attracting in excess of £20m of grant income underpins the activities of the Centre. The Centre aims to develop new cross-cutting collaborations. We have identified five key areas which we consider to be current obstacles to effective translation of basic science findings into patient benefit. These are: clinical trials support/networks, availability of patient tissues and cells, assessing animal models, applying MRI to humans and animals and developing expertise capacity for the future.

Professional and patient organisation partners

Programme

TUESDAY 6th SEPTEMBER - Day 1

14:15 – 14:20	**Welcome and Introduction** The BMS progress to date	**Prof Michael Hanna**
14:20 – 15:25	**Commissioning**	**Chair: Prof Mike Hanna**
14:20 – 14:50	Update on national commissioning and neuromuscular disease	Teresa Moss
14:50 – 15:00	Discussion	
15:00 – 15:15	Commissioning update & the MDC	Robert Meadowcroft
15:15 – 15:25	Avoidable emergency admissions project update and discussion	Prof Michael Hanna
15:25 – 17:00	**Registries, Databases and Networks**	**Chair: Prof Francesco Muntoni**
15:25 – 15:45	Update on National Neuromuscular Database	Dr Adnan Manzur
15:45 – 15:50	Discussion	
15:50 – 16:15	UKCSG paediatric cancer network	Dr Bruce Morland
16:15 – 16:25	Discussion	
16:25 – 16:50	Medicines for Children Network and Cystic Fibrosis network/registry	Prof Warren Lenney
16:50 – 17:00	Discussion	
17:00 – 17:30	**Coffee break**	
17:30 – 18:45	**Registries, Databases and Networks continued**	**Chair: Dr Adnan Manzur**
17:30 – 17:50	Myotonic Dystrophy workshop/ database	Dr Chris Turner
17:50 – 18:10	IBM-Net	Dr Matt Parton
18:10 – 18:30	FKRP Registry/TREAT-NMD update	Prof Kate Bushby
18:30 – 18:45	Discussion	

18:45 – 19:35	**Patient Organisation Update**	**Chair: Dr David Hilton-Jones**
18:45 – 19:05	SMA Trust update	Lucy Blyth/ Prof Angela Vincent
19:05 – 19:10	Discussion	
19:10 – 19:30	Myotubular Trust update	Anne Lennox
19:30 – 19:35	Discussion	
19:35 – 20:15	**Controversies in Neuromuscular Diseases**	Chair: Dr David Hilton-Jones
19:35 – 20:05	3,4-diamonopyridine and orphan drugs – major lessons for the myologist	Dr David Nicholl/ Dr Daphne Austin
20:05 – 20:15	Discussion	
20:15 – 22:00	**Dinner at St Anne's College** Ruth Deech Building Foyer Guest after-dinner speaker: Professor Alan Emery	

WEDNESDAY 7th SEPTEMBER – Day 2

07:30 – 08:15	**Breakfast** Main Hall	
08:15 – 08:35	**AGM**	Prof Mike Hanna
08:35 – 09:20	**Keynote Speaker: Dr Mike Hubank** Next generation sequencing	Introduced by Professor Francesco Muntoni
09:20 – 12:10	**Muscle Interest Group**	**Chair: Dr Helen Roper**
09:20 – 10:35	MIG unsolved cases	
10:35 – 10:55	**Coffee break**	
10:55 – 12:10	MIG solved cases	
12:10 – 13:10	**Lunch** Main Hall	
13:10 – 13:55	Round table discussion	Chair: Dr Ros Quinlivan

13:55 – 15:05	**Studies updates**	**Chair: Dr Ros Quinlivan**
13:55 – 14:15	Update on Muscle Quality of Life Study in the UK	Chris Graham
14:15 – 14:35	Update following national physiotherapy workshop	Dr Gita Ramdharry
14:35 – 14:55	Paediatric physiotherapy update	Elaine Scott
14:55 – 15:05	Discussion	
15:05 – 16:25	**Myasthenia Interest Group**	**Chair: Dr David Hilton-Jones**
15:05 – 15:25	Revised target for K-channel antibodies	Dr Camilla Buckley
15:25 – 15:45	MG management guidelines in pregnancy	Dr Fiona Norwood
15:45 – 16:05	Detection of low-affinity antibodies causing MG by cell-based assay	Dr Isabel Leite
16:05 – 16:25	LEMS: the other myasthenic syndrome	Dr Beth Lang
16:25 – 16:30	**Conclusion and next steps**	**Prof Michael Hanna & Dr David Hilton-Jones**

Speaker Abstracts

The Paediatric Cancer Network

Dr Bruce Morland
Birmingham Children's Hospital

The centralised care of children with cancer in the UK has been the envy of many clinical groups over the years. Evidence suggests that standardisation of care and routine adoption of clinical trial entry as the norm for front line therapy has delivered successful outcomes in terms of improved survival. Little coincidence then that the first National Cancer Plan focused very heavily on increasing trial recruitment for adults with cancer too.

The children's cancer network has evolved over time. The formation of the United Kingdom Children's Cancer Study Group in 1977 was the first step. This group, along with the UK Childhood Leukaemia Working Party were instrumental in setting the scene for delivery of clinical trial protocols as "standard of care". Other key functions including collection of detailed registry data and providing professional support to clinicians involved with cancer care were deemed invaluable. Key to the success of this strategy was the invaluable support from CRUK and MRC who provided funding and infrastructure to allow the network to develop and expand.

More recently UKCCSG evolved to become CCLG (Children's Cancer and Leukaemia Group), reflecting a desire to become truly multidisciplinary and encompass both solid tumour and leukaemia activities under one umbrella organisation. The impact of the EUCTD and greater regulation, linked to the maturing adult national cancer networks, resulted in a further major restructuring of CCLG activities in 2008. Under the auspices of the National Cancer Research Institute but with continuing support from CRUK and MRC and DoH we have 3 major strategic arms. The clinical trials portfolio is distributed to NCRI Clinical Study Groups, some child-specific but some (e.g. sarcoma) shared with adult CSGs. Our network of 21 principal treatment centres is supported and performance managed through the National Cancer Research Network. CCLG now has no clinical trial remit but continues to provide professional support, a range of disease-focused interest groups to develop guidelines, and perhaps most importantly a valuable source of information and publication material aimed at parents and patients. Transition has not been easy but we now feel we are once again "fit for purpose" to deliver 21st Century care to children with cancer.

Update on National Neuromuscular Database

Dr Adnan Manzur on behalf of North Star, SmartNet, MD-CORE and IBM Networks
Great Ormond Street Hospital for Children

The National Neuromuscular Database (NaNDa) project was established in 2009 with the MDC UK funding and support. This project fosters the development of

national neuromuscular clinical networks, and has funded the development and maintenance of neuromuscular disease specific databases. This contribution reports the progress in the first two years and developments and challenges in the coming years.

The nidus of this project, the North Star Clinic Network was established in 2004 with MDC support and funding and the network database went online in 2006. The North Star Network was successful in consensus on assessment & clinical management of ambulant boys with Duchenne muscular dystrophy, and allowed completion of three national audits and two publications on development on motor assessment scales. This success led to further paediatric and adult disease specific networks and databases and National Neuromuscular Database was set up in collaboration with MRC Muscle Centre, BMS and MDC. The aim was to allow an organisational structure which allows inclusivity and optimal governance and to foster durability of clinical networks by identifying the resources and streamlining the process of data entry and registry links.

I am pleased to report the progress over the two years. The North Star Duchenne Muscular Dystrophy Database now has over 500 DMD patients. The SmartNet SMA Database and Inclusion Body Myositis IBMnet Network and its registry are actively recruiting. The MDCORE Network for congenital muscular dystrophies and congenital myopathies has agreed upon the clinical assessments and the physiotherapy protocol is being developed.

One of the achievements of the network has been the implementation of scannable forms, for “automatic” data upload, starting with the ambulant Duchenne muscular dystrophy patients, in summer 2011. It is anticipated that this will allow automated data entry and the scannable form project will be extended to the other disease specific databases. Registry links with SMA and DMD registries are being developed.

The challenges for the coming year are two fold: maintenance of funding, and database developments. Unfortunately, two grant applications seeking support for the clinical networks with development of relevant research projects have not been successful. We recognise the impact of this project in improving and implementing standardised assessments in the individual neuromuscular disorders. We need to work towards full patient ascertainment & data entry, and audit of clinical practice, and in particular ongoing efforts for securing funding for the infrastructure and development for the clinical networks and databases.

Children, databases and research

Warren Lenney
Professor of Respiratory Child Health
Keele University & University Hospital of North Staffordshire

One of the accepted constraints in our society is that, for its future survival, focus on children is imperative. Despite this, medical research in children has often been undervalued and emphasis has usually been directed to adults with established

disease. Given that prevention is better than cure we need to reappraise our priorities, highlight the advantages of early diagnosis and careful long-term monitoring together with a national and international plan for research, involving children at an early stage. We must maintain long-term health whilst simultaneously reducing the social, financial and psychological burden of chronic disease.

Cystic fibrosis (CF) and many neuro-muscular diseases have much in common. There is a genetic basis with the possibility of newborn screening. The disease population can be well defined. Early diagnosis and prevention of disease progression is becoming increasingly realistic and development of specific databases is necessary to record and publicise the health improvements which have, and are continuing, to occur.

The CF database has been a great success and now forms the basis of clinical knowledge nationwide which will be used to inform the Payments by Results funding scheme which is about to come into force. There are still some unanswered questions but the CF model could well be used as a basis for similar developments in other chronic disease states.

Without the development, over the last 6 years, of the paediatric research networks for both medicines and non-medicines research, research into children's medical disorders within the UK would have virtually disappeared. My talk will illustrate how the CF database and MCRN have thrown essential lifelines to children within the UK.

IBM-Net
Dr Matt Parton

MRC Centre, National Hospital for Neurology and Neurosurgery

IBM-Net is a clinical project studying the natural history of inclusion body myositis (IBM).

IBM offers several challenges: while, in its purest form, it demonstrates clearly recognisable and distinctive clinical and pathological features, its diagnosis relies on an overall assessment of the patient and muscle biopsy findings, with no conclusive diagnostic test. IBM can overlap with other conditions and also be hard to differentiate from features of normal aging. The aetiology of IBM is uncertain, as both inflammation and degeneration of muscle have been proposed as the primary mechanism of muscle damage, and a complex interplay between the two processes appears to be involved.

Moreover, to date the largest published series of IBM cases is limited to eleven patients followed for only six months. Thus the information given to patients on the pattern and progression of IBM is based on clinical experience and expectation, rather than on firm scientific data.

To better characterise IBM, this project gathers serial data (annual) from as many cases as possible. This generates information on natural history and establishes a cohort of reliably-defined patients, forming a valuable resource for future studies.

An update on the project will be presented, including some preliminary analysis of the cases seen at Queen Square.

3,4-diamonopyridine and orphan drugs – major lessons for the myologist
Dr David Nicholl & Dr Daphne Austin
City Hospital Hospital & Queen Elizabeth Hospital, Birmingham & West Midlands Specialised Commissioning Team

Dr David Nicholl is a Consultant Neurologist at City Hospital Birmingham and University Hospital Birmingham. When it was clear in 2010 that there would be significant problems obtaining 3,4 DAP for Lambert Eaton Myasthenic syndrome due to the availability of a much more expensive licensed alternative, Dr Nicholl organised an open letter to the BMJ highlighting the problems of so called orphan drugs. Dr Nicholl will provide an update on the 3,4 Dap/Firdapse/LEMS story. Dr Daphne Austin is lead commissioner for specialty services in the West Midlands and developed the commissioning policy for orphan drugs in LEMS and will detail how these issues are relevant to many other rare neurological disorders.

Dr Daphne Austin is a consultant in public health working in the West Midlands. She has 20 years commissioning experience within the NHS and has developed particularly expertise and national recognition in priority setting.

Update on Muscle Quality of Life Study in the UK
Chris Graham
King's College London

In muscle disease (MD), Quality of Life (QoL) has been related to aspects of disease severity with variable results: QoL either shows a moderate association with disease severity or only relates to the physical sub-scales of QoL measures. This mismatch may be due to individual differences in patients' understanding of their illness, degree of optimism, coping skills, or mood; meaning that even those with similar disease severity may have widely different QoL. We aimed to understand how these variables, in addition to measures of disease severity and demographics, predicted QoL in MD.

The analyses included 226 participants with MD who completed a questionnaire booklet containing measures of: disease severity, illness perceptions, coping, mood, and optimism. These scores, alongside demographic variables, were entered into multiple step-wise regressions as predictor variables, the dependent variable being QoL as measured by the INQoL questionnaire. We observed that models containing psychosocial variables, in addition to a disease severity measure, predicted moderate to large amounts of the variance in QoL score. The variance in the score of some QoL domains was best predicted by psychosocial variables alone. Results will be discussed in relation to the utility of a cognitive intervention aimed at retaining QoL in MD. Limitations and future analysis of the data will also be discussed.

Update following the national physiotherapy workshop
Dr Gita Ramdharry
SGUL/Kingston University & UCL Institute of Neurology

On the 28th March 2011, the MRC Centre for Neuromuscular Diseases hosted a meeting of physiotherapists across the UK working with adults with neuromuscular diseases. Two guest physical therapists from the USA were also invited. The meeting was sponsored by the Muscular Dystrophy Campaign.

The purpose of the meeting was to bring together the experience and knowledge from specialist physiotherapists involved in the clinical management and research of adults with NMDs. The aim was to create a forum to discuss and evaluate the efficacy of current physical therapies and discuss research priorities.

Topics discussed were standardisation of assessment, exercise prescription, orthotic interventions, fatigue management and IBM assessment. A number of actions were agreed:

The group agreed on increased use of the Adult Ambulatory Neuromuscular Assessment (AANA) to provide feedback to Anna Mayhew who will go on to refine the scale using Rasch analysis.

The group agreed that guidelines on exercise prescription should be produced for patients and physiotherapists. Funding for this work has been pursued and part agreed to date.

A forum for sharing best practice for orthotic management was discussed. Options for a web based forum are to be investigated.

The group discussed the topic of fatigue as a common problem and its management. With little research evidence available, it was agreed that established services that manage fatigue for conditions such as multiple sclerosis would be appropriate for people with NMDs.

Increased therapy based assessment of people with IBM was considered important to increase understanding of the progression of the disease and its impact on functional abilities. The group recommended that this would be beneficial at initial visits and follow up sessions in IBM clinics.

Finally, an invited lecture by Shree Pandya, Rochester, USA, outlined her extensive experience of conducting research in people with NMD. This was invaluable knowledge shared with the group.

It is the intension of this group to meet annually to monitor the progress of proposed work and continue to set priorities in the light of developing knowledge.

Paediatric Neuromuscular Physiotherapists Network

Elaine Scott
Muscular Dystrophy Campaign

The physiotherapy network forms part of the North Star Clinical Network for Paediatric Neuromuscular Disease, working in partnership with our clinical colleagues. The network was initiated in 2004. 23 specialist neuromuscular centres currently participate. Work undertaken to date includes the development of standardised assessment techniques for ambulant and non-ambulant DMD, type II and III SMA. Substantive review of outcome measures led to the definition of test method and production of test manuals and standardised assessment forms. Data from these assessments are entered onto the National Neuromuscular Database, as part of the comprehensive longitudinal clinical dataset. Work to standardise assessments for congenital muscular dystrophy and congenital myopathy is underway. The North Star Ambulatory Assessment1 (NSAA), a functional scale for ambulant DMD, was developed by the group and has been in clinical use since 2005. Initial Rasch evaluation of the psychometric properties of the scale have been positive2, and further work with a view to converting data gained to a linearised, parametric scale for use in clinical trials is underway. This scale has also been adapted for ambulant patients with SMA. North Star and SMARTnet physiotherapy data have been presented as part of the work of the clinical network at international meetings. Work continues on evaluating and adapting assessment techniques in line with international developments.

Scott E, Eagle M, Mayhew A, Freeman J, Main M, Sheehan J, Manzur A, Muntoni F, the North Star Clinical Network for Paediatric Neuromuscular Disease. **Development of a functional assessment scale for ambulatory boys with Duchenne muscular dystrophy** - Phys Res Int – in press

Mayhew A, Cano S, Scott E, Eagle M, Bushby K, Muntoni F, The North Star Clinical Network for Paediatric Neuromuscular Disease. **Moving towards meaningful measurement: Rasch Analysis of North Star Ambulatory Assessment in Duchenne muscular dystrophy**. Dev Med Child Neurol. 2011 Mar 17. doi: 10.1111/j.1469-8749.2011.03939.x. [Epub ahead of print]

Detection of low-affinity antibodies causing MG by cell-based assay

Dr M Isabel Leite
Neuroimmunology Group and Neurosciences Group of the Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, University of Oxford.

It is well known that around 80% of patients with generalized myasthenia gravis (MG) and around 50% of those with ocular MG have serum antibodies to acetylcholine receptor (AChR-Abs), which are usually detected by radioimmunoprecipitation. Much rarer is the MG mediated by antibodies to muscle specific kinase (MuSK-Abs); its frequency is variable, and goes up to around 8% of the total number of generalised MG patients. The patients with neither AChR nor MuSK antibodies are known as seronegative (seronegative MG, SNMG).

The diagnosis of SNMG is usually difficult to achieve, because of the often mild clinical manifestations, similarities between MG and other conditions such as congenital myasthenic syndromes, particularly in children, co-existence of risk

factors to other non-related disorders, such as vascular diseases in older patients, frequent mild or inconsistent electrophysiological test results and variable response to treatments. Therefore, improvements in the methods of detection of AChR and MuSK antibodies would have relevant clinical implications in SNMG patients.

We have recently demonstrated that using rapsyn-clustered AChR expressed on the surface of human embryonic kidney cells improves the detection of AChR-Abs. A significant proportion of patients with SNMG have been found to have antibodies to clustered AChR. Using similar approach (cell-based assay) we have also found MuSK-Abs in a smaller proportion of SNMG patients. This technique is also very useful in the detection of antibodies to the fetal form of AChR, which has been very relevant in studies of patients with arthrogryposis and their mothers (with or without MG).

In conclusion, cell-based assays constitute new methods for detection of antibodies in MG, which have allowed us to improve the diagnosis and management of patients with myasthenic features, but without detectable antibodies.

LEMS: the other myasthenic syndrome

Dr Bethan Lang
University of Oxford

The Lambert-Eaton myasthenic syndrome (LEMS), like myasthenia gravis (MG), is an autoimmune disorder of the peripheral nervous system. Patients with LEMS often present with proximal muscle weakness, and dysarthria that may be mistaken clinically for MG. However, LEMS has clinical features which distinguishes it from MG: autonomic dysfunction is common and (in over 90% of cases) tendon reflexes are diminished on examination. Neurophysiologically it is distinguished by cMAP increment on high frequency repetitive stimulation. In MG antibodies directed against the postsynaptic acetylcholine receptors (AChR) have been detected in about 80-85% of patients, however in LEMS the antibodies are directed against a presynaptic protein, the voltage-gated calcium channels (VGCC) in over 90% of cases.

Approximately 60% of all LEMS cases are found in association with a small cell lung carcinoma (SCLC). SCLC is known to express functional VGCC on their surface and it is thought that these VGCC may `trigger the antibody response in the paraneoplastic patients (P-LEMS); virtually all (>98%) of P-LEMS patients are VGCC-antibody positive. However the antigenic stimulus that initiates the immunological response in the non-paraneoplastic patients (NP-LEMS) is as yet unknown. Patients with P-LEMS and NP-LEMS have similar clinical features. However P-LEMS progresses more rapidly with earlier weakness in distal muscles and early erectile dysfunction in men. P-LEMS will often have other antibodies directed to additional intracellular antigens, e.g. SOX1 (60%) and/or Hu (30%).

SCLC is a fast-growing tumour, of neuroendocrine origin, that metastasises early and has a poor prognosis (median survival 8.9 months). To the contrary, SCLC patients with concomitant LEMS appear to have a much better prognosis, with a median survival of 19.6 months. The reason for this is currently unknown.

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Rules of the BMS

Name

1. The Society shall be called the British Myology Society.

Object

2. The object of the Society is to act as a multidisciplinary professional body of experts to promote the clinical practice, education and advancement of knowledge about muscle disease, myasthenia gravis and spinal muscular atrophy in the British Isles.

This will include:

- Agreeing best practice and standards of care for patients with muscle disease
- Agreeing standards for training in clinical myology and clinical muscle pathology
- Promoting translational research
- Establishing clinical networks to facilitate and promote clinical trials and patient registries
- Facilitating collaborations with patient organisations

Membership

3. The Society shall consist of Ordinary, Associate and Honorary Members.

4. Those appointed to consultant posts, or senior lectureships or equivalent, in the neurological sciences, genetics, paediatrics, physiotherapy, nursing and neurorehabilitation who undertake specialised muscle clinics or pathological examination of biopsy material from muscle shall be eligible for Ordinary Membership.

5. Persons of distinction in Medicine or related paramedical disciplines who have contributed to the advancement of muscle disease shall be eligible for the Honorary Membership. Foreigners of similar distinction shall be eligible for the Honorary Foreign Membership. The number of Honorary Members shall be limited to 10 and of Honorary Foreign Members to 10; they shall be elected by the Society on the recommendation of the Council.

6. All specialist registrars and others pursuing clinical practice or research in muscle disease within the British Isles or the Republic of Ireland shall be eligible for Associate Membership. On appointment to substantive consultant or senior lecturer posts, Associate Members will automatically become Ordinary Members at the next Annual General Meeting.

8. Ordinary members on reaching the age of 65 or on prior retirement from paid employment , shall cease to be Ordinary Members at the next Annual General Meeting, and may become Senior Members, enjoying benefit of membership without payment of subscription.

9. Candidates for Ordinary, Membership shall be nominated by at least two members of the Association in writing to the Honorary Secretary by the time of the last Council Meeting prior to the Annual General Meeting.

10. The Council shall recommend candidates from those nominated as Ordinary or Honorary Members to the Annual General Meeting.

Subscription

11. The annual subscription shall be decided by Council on a yearly basis in the light of the financial situation of the Society and after taking advice from the Treasurer. The subscription shall then be ratified at the next Annual General Meeting of the Association. It shall be paid by Deed of Covenant, or Direct Debit, or Banker's Order.

12. Non-payment of the subscription within twelve months may be considered by Council as equivalent to resignation.

Officers and Councillors

13. The Council shall consist of the Chairman, Honorary Secretary, Honorary Treasurer, and eight council members. All members of Council shall be Ordinary Members of the Society. Officers of the Society shall be elected at the Annual General Meeting. The chairman shall be responsible for organizing a suitable secretariat.

14. Council may co-opt others, without voting rights, to attend its meetings.

15. A quorum of four voting members will be necessary for decisions made by Council to be valid.

16. The Councillors shall hold office for three years following which there will be re-election. In order to avoid a complete change of council members at once a staggered re-election of council members will be agreed.

17. If an Officer or Councillor of the Society be unable to continue in office for any reason the Council shall have the power to nominate a successor to hold office until the next Annual General Meeting.

Meetings and the Annual General Meeting

18. At least one and usually two or more meetings shall be held each year, one of which shall include the Annual General Meeting. Associate members shall be entitled

to attend these meetings and the Annual General business meetings of the Association as non-voting members. 19. At least two months prior to the meetings the Honorary Assistant Secretary shall send a notice to each member and shall invite communications to be presented at the scientific meetings.

20. At each clinical meeting time there will be time available for members to discuss management and research issues of general interest to the Society. The agenda for these items will be decided by the Council and will generally focus on the main aims of the Society across all muscle diseases.

21. The programme for the Meetings of the Society will be organised by the local organiser in discussion with the Honorary Secretary and Chairman.

22. The programme for each clinical meeting shall be sent by the Honorary Secretary to each member of the Society at least one week before the meeting is held.

23. The agenda for the Annual General Meeting of the Association shall be sent to Ordinary and

Honorary Members by the Honorary Secretary at least one week before the meeting is held.

24. A majority vote of those members present will be required to ratify decisions at the Annual General

Meeting.

Other Rules

24. No alteration shall be made in the rules except at the Annual General Meeting and unless proposed by the Council or by at least ten members in writing. In the latter case, the proposal must reach the Secretary at least four weeks before the date of the meeting. Notice of the proposed change shall be circulated to each member at least one week before the meeting at which it is to be brought forward, and it shall be decided by vote of those present at the meeting.

25. The income and property of the Society, whencesoever derived, shall be applied solely towards the promotion of the objects of the Society as set forth in the Rules, and no portion thereof shall be paid or transferred directly or indirectly, by way of dividend or otherwise howsoever by way of profit to members of the Society. Provided that nothing herein shall prevent the payment, in good faith, of reasonable and proper remuneration to any officer or servant of the Society, or to any member of the Society, in return for any services rendered to the Society.

26. If upon the winding up or dissolution of the Society there remains, after the satisfaction of all its debts and liabilities, any property whatsoever, the same shall not be paid or distributed among the members of the Society, but shall be given or transferred to some other institution having objects similar to the objects of the

Society, and which shall prohibit the distribution of its or their income and property among its or their members to an extent at least as great as is imposed on the Society under or by virtue of the last preceding Rule, such institution or institutions to be determined by the members of the Society at or before the time of dissolution, and if and so far as effect cannot be given to such provisions, then to some charitable object.

27. The Association shall be independent and its views shall not be compromised as a consequence of its relationships with commercial sponsors or any other organisation.

Minutes from previous council meetings 2008 - 2011

Monday 28th April 2008

Present:

Mike Hanna, Francesco Muntoni, Caroline Sewry, Janice Holton, Doug Wilcox, Michael Rose, Helen Roper, Peter Baxter, David Hilton-Jones

Apologies:

Doug Turnbull, Kate Bushby

The following points were agreed:

All people present agreed to the establishing the BMS on the 28th April 2008.

All present agreed to act on the initial council of the BMS.

Mike Hanna will amend the rules of the society to incorporate the provision of staggered re-election of council members.

All present agreed the preferred meeting arrangement was to hold an annual BMS meeting over two days, with an overnight stay. It was anticipated that this meeting would cover a BMS specific agenda including reports from BMS working groups and workshops.

All present agreed to MH amending the rules to correct the error and add consultant paediatricians in the list of eligible people to be members.

It was agreed that the BMS will collaborate with charities and patient organizations but it is very important the society should be an independent professional society.

It was recognised that although there are many scientific and clinical muscle meetings held in the UK, there is currently no forum to address the specific aims of the BMS as outlined in the rules including implementation.

It was agreed that the first annual meeting should be held at the end of March/start of April 2009 to avoid the school half-term breaks, and that Mike Hanna and David Hilton-Jones would look at venue options.

It was agreed the initial secretariat would be provided by the Senior Administrator at the MRC Centre for Neuromuscular Diseases in London.

It was agreed that Mike Hanna would contact the appropriate professional associations to seek affiliation including BPNA, ABN and BSHG.

It was agreed that the BMS would not supplant current muscle meetings. Thus for example the Muscle Interest Group would continue unchanged as a diagnostic forum for paediatric adult muscle disease and the Oxford summer meeting would also continue unchanged. There would be a series of Disease related workshops held by the MRC centre and summaries of key outcomes from such workshops will be made available at the annual BMS meeting (the first workshop on IBM will be held on 13th June 2008). BMS working parties might be set up to tackle specific issues such as agreeing standards of care relating to diagnosis, treatment and training.

It was agreed that the BMS would potentially be a valuable implementation forum for standards of care.

It was agreed the BMS should include all acquired and genetic muscle disease and acquired and genetic myasthenia gravis and spinal muscular atrophy.

It was noted the BPNS addressed all peripheral nerve diseases.

4th July 2008, Worcester College Oxford

Present

Mike Hanna-MH, Helen Roper, Caroline Sewry, Janice Holton, David Hilton-Jones

Apologies

Doug Wilcox, Kate Bushby, Michael Rose-MR, Francesco Muntoni, Peter Baxter, DougTurnbull

Previous meeting minutes

Minutes of the meeting 28th April 2008 London, as updated 18th May 2008 were accepted as a correct record.

Matters arising

Rules adjustments:

MH had updated the Rules as agreed and minuted 28th April.

MH gave a brief update on the recent IBM workshop organized by MH, DHJ, Matt Parton and MR and held in the MRC Centre Queen Square 13 June 2008.

The workshop was attended by 49 colleagues, mainly adult neurologists, interested IBM. There was agreement to establish an IBM database, an IBM DNA bank and natural history studies. Revised clinical and pathological criteria were discussed. A workshop report is in progress. The BMS was discussed and 37 written expressions of interest to join were received on the day.

MH had met with ABN representatives who were supportive of the BMS initiative and agreed to advertise the first annual meeting in ABN newsletter.

Membership of the BMS

It was agreed that this should be an expert professional body that includes ordinary members as outlined in the revised rules.

It was agreed that trainees in myology should be associate members.

It was agreed that the BMS should be an independent professional body.

It was agreed that an annual BMS meeting would take place at which there would be an AGM.

Invitation to be members:

It was agreed that a standard email should be sent to all colleagues potentially interested in being members of the BMS.

This email should be accompanied by the latest version of the rules.

Actions

MH will draft an invitation from council with instructions to reply to Zoe Scott [MRC Centre administrator]. MH will circulate the invitation to all members of the council for approval and so they can invite colleagues who they consider might be interested.

HR will circulate to the MIG members

JH will circulate to members of the RCP who might be interested [neuropathologists]

MH will circulate to all adult neurologists through the ABN, to the BPNS membership and to MDC colleagues.

MH will ask FM to circulate to BPNA members and BSHG members.

All present agreed they would let MH know if there were other groups of colleagues that should be invited.

It was agreed that a subscription would not be requested for the first year.

Replies to the invitations for membership will be collated by Zoë Scott

Annual BMS meeting possible date: 23rd and 24th April 2009

An annual meeting of the BMS over two days with an overnight stay for socialising and networking was agreed as the preferred format.

Broad discussion took place about the content and aims of the annual meeting which would be within the remit of the aims outlined in the rules. DHJ indicated it should be a varied format including service issues, training issues, interesting cases and difficult diagnoses, as well as updates on trials and clinical research. MH and HR suggested that parts of the meeting could be given over to specific topics/mini-workshops.

It was agreed that the BMS meeting should stand alone from science meetings such at the MRC centre annual meeting.

The provisional date set in the previous meeting was agreed ie 23 and 24th April 2009.

It was agreed that costs would be covered by individual attendees.

Action

MH will identify venue in Cambridge. DHJ had obtained details of Clare College and MH will pursue this and other Colleges.

AOB

None

Date of next meeting

It was agreed this should be during the WMS in Newcastle in October 2008. Date to be confirmed.

WMS meeting of BMS council Newcastle 1 October 2008

Present: David Hilton-Jones, Caroline Sewry, Mike Hanna, Helen Roper, Francesco Muntoni.

Apologies: all other council members

Main action point agreed- No availability identified in Cambridge. The first annual BMS meeting would be Oxford on 2nd and 3rd July 2009 and Mike Hanna would take forward the organizational details.

BMS council telephone conference 11 March 2009

All council members called in and programme agreed.

Minutes of 2009 meetings

Conference call, 30 September 2009

Present: Peter Baxter, David Hilton Jones, Mike Hanna, Caroline Sewry, Doug Wilcox, Helen Roper, Ros Quinlivan

Apologies: Doug Turnbull, Mike Rose, Francesco Muntoni, Katie Bushby, Janice Holton, Mike Rose

The following points were agreed:

A single annual joint BMS-MIG meeting would be held over two days on a Tuesday and Wednesday, with overnight accommodation and dinner on the Tuesday.

This clinical/practical meeting would complement the annual MRC MDC UK translational research scientific conference held on a Thursday and Friday end of March each year.

It was agreed the meeting would start mid-morning on the Tuesday and finish around 4pm on Wednesday.

The purpose of the meeting is to

1)continue with the BMS agenda and initial workstreams generated from the original BMS meeting including, supporting commissioning efforts, developing muscle pathology serves, training and education, promoting UK databases, networks and registries and supporting clinical trials. The meeting would be an opportunity for continuing implementation of national initiatives to be discussed such as NorthStar, IBM-net, Smart net, UK MRC mitochondrial cohort and other planned natural history databases supported by the MRC Centre including the national neuromuscular databases in collaboration with MDC etc.

2) Create a relaxed forum to enable full discussion about difficult and unsolved cases.

3) Colleague networking

It was agreed that this BMS-MIG meeting would incorporate one of the MIG meetings. It was considered ideal that the second MIG meeting would be linked to the MRC MDC scientific meeting. In that way there would only be two key meetings per year.

Action Mike David Helen and Francesco would consult with colleagues about feasibility of incorporating MIG into annual MRC MDC scientific meeting.

The venue was discussed. It was recognised no venue is perfect geographically. The general view, including form Doug Wilcox travelling from Scotland, was that given this was a two day and not a one day meeting, it was reasonable to continue to have the meeting in Oxford. It was also pointed out that Oxford was convenient for those travelling from the west and southwest.

It was agreed that an Oxford college, out of term time, provided good value for money accommodation and the right atmosphere. It was recognised it was most likely that the meeting would attract more than 50 delegates and therefore a large college would be required. It was commented that the St Anne's College lecture theatre and accommodation was superior to Worcester College.

The timing of the meeting in the year was discussed. There was agreement that early September was preferred to July or to later in the year given the need for college availability. However, it was considered sensible to undertake a Doodle date exercise offering July and September as the options

Action Mike and Zoe to do a Doodle Date choice

Administration of the meeting was discussed. It was agreed Mike would provide admin support and organize the meeting through the MRC Centre administrator Zoe.

Relationship to the Oxford Summer Muscle meeting was discussed. David explained that he had no direct involvement with the organisation and running of this meeting but that Chris Fursdon Davis had approached Mike to consider linking with the BMS.

All present at the conference call agreed that the new meeting planned ie the BMS MIG meeting would have quite a different format [with aims as described above] to the existing Oxford muscle meeting. It was agreed that the planned BMS-MIG meeting was mainly aimed at UK muscle specialists and to consider UK issues, although all colleagues attending the Oxford muscle meeting would be welcome and invited to attend the BMS-MIG meeting. It was not clear if Chris had started to plan for the next 2010 Oxford muscle meeting or not.

Action- Mike will speak to Chris and explain the agreed plan for the new BMS-MIG meeting and that we were now planning this for next year and that we would be happy for this to incorporate the oxford meeting if he wished.

Minutes of 2010 meetings

Conference call, 8am, 14th April 2010

Present: Helen Roper, David Hilton-Jones, Janice Holton, Caroline Sewry, Katie Bushby, Mike Hanna, Michael Rose

Apologies: Doug Turnbull, Doug Wilcox, Peter Baxter, Francesco Muntoni

1. Minutes of the BMS meeting debrief 30th September 2009 were accepted as a correct record.
2. It was noted that the doodle preferred date exercise indicated that the BMS meeting should be held the first week of September each year, preferably on a Tuesday and Wednesday or Thursday and Friday to avoid other meetings. It remained unclear whether there would be union with the Oxford summer muscle meeting, and after the September 2010 BMS meeting in Oxford, it is proposed that there will be a Doodle ballot members vote regarding members' preference for the location of future meetings.
3. The provisional draft programme for the BMS meeting 2-3 September 2010 was discussed in detail.

The following was agreed in relation to the programme:

i Mike Hanna would contact Rita Barresi to confirm the exact timing of the NCG and Neuromuscular Disorders consortium meeting which will be held in Oxford earlier on the 2nd September, precise time to be confirmed.

ii. David Hilton-Jones will contact Marguerite Hill and offer the Myasthenia Interest Group the opportunity to have a meeting in St Anne's College prior to the commencement of the BMS meeting at 4pm on 2nd September, and will also offer the Muscle Interest Group a slot to update the BMS of their activities, beginning the afternoon session of 3rd September.

iii. Mike Hanna will invite Marianne de Visser to lecture on the Netherlands' experience of developing a national neuromuscular database

iv. First session: Neuromuscular Services in the UK will contain the following components:

A presentation by Robert Meadowcroft regarding the progress in commissioning by discussion.

A session on national commissioned services with very brief updates about each service, to include the rare neuromuscular service, the mitochondrial service, the Myozyme enzyme replacement service.

A session on muscle pathology service developments and tissue pathways building on the presentation from 2009 at the BMS.

The second half of the neuromuscular service session will involve brief updates and a panel format to encourage maximum interactive discussion. The brief presentations will include an update on UK training (Mike Hanna will liaise with Mary

Reilly and Chris Turner and Colin Ferrie, paediatrics in Leeds, regarding progress of the national UK neuromuscular training curriculum).

The topics will include the national neuromuscular database – Adnan Manzur, the Scottish muscle network – Doug Wilcox and TREAT-NMD. The afternoon session will end with an AGM in which Mike and the others will update the BMS members about charitable status, to meeting locations, future administration of the BMS.

Dinner will commence at 8pm and at the moment there is no planned after-dinner speaker.

Day two 3rd September will commence at 8.30am and will comprise a Muscle Interest Group session which will initially be presentation of unsolved cases followed by a presentation of solved cases which will be chaired by Helen Roper.

Following lunch will be an optional Myasthenia Interest Group update.

There will then be a session of about 45 minutes on update on UK trials co-led by Mike Hanna and Kate Bushby.

There will be a lecture on quality of life measures in myasthenia.

At the end of the afternoon session there will be a lecture on enzyme replacement therapy in the UK. Robin Lachmann will be invited by Mike.

The meeting will close at 16.00.

4. It was agreed that secretarial support needed to be identified by the BMS which would be the responsibility of the Chairman. It was agreed that Mike Hanna would pursue the possibility of Genzyme funding secretarial support for twelve months.

5. Mike Hanna has made an application for charitable status for the society.

6. The BMS has been approached by the Joint Neuroscience Council regarding membership, and Mike would find out more details about this, and update BMS members in September.

AOB
None.

Minutes of 2011 meetings

Conference call, 9am, Friday 10th June 2011

Present:

David Hilton-Jones
Mike Hanna
Helen Roper
Mike Rose
Francesco Muntoni

Apologies:

Kate Bushby
Peter Baxter
Douglas Wilcox
Caroline Sewry
Janice Holton
Doug Turnbull

Minutes

Meeting programme for 2011

The following was agreed:

First session commissioning

Mike Hanna will contact Teresa Moss or an alternate national commissioning colleague to do an opening talk and update on national commissioning and specialised commissioning with particular relevance to neuromuscular disease

Mike Hanna will ask Robert Meadowcroft to do a short 15 minute update regarding commissioning work and MDC

Mike Hanna will give an update on what's being done with the commissioners across the four specialised commissioning regions regarding avoidable unplanned emergency admissions project

David Hilton-Jones will invite David Nicholl to do a 30 minute session on issues relating to orphan drugs and implications for neuromuscular disease

The second session will be on registries, databases and networks; it will include:

Mike Hanna will ask Professor Warren Lenney to talk on his work in relation to medicines in children network as well as cystic fibrosis network

Bruce Moreland agreed to talk about UKCSG paediatric cancer network

Adnan Manzur agreed to give an update on neuromuscular database including NorthStar, congenital myopathy and Smart-Net

Chris Turner, Hanns Lochmüller and David Hilton-Jones will coordinate a presentation on the recent Myotonic dystrophy workshop and new Myotonic dystrophy database –Mike will invite Chris and Hanns

Matt Parton agreed to present on the IBM-net workstream and database

Kate Bushby or Volker Straub agreed to present on the FKRP database registry and also give a brief update on TREAT-NMD

There will be an update regarding recent adult and paediatric physiotherapy workshops to be coordinated by Anna Mayhew, Elaine Scott and Gita Ramdharry. Mike Hanna will contact these individuals to arrange

Francesco Muntoni will contact the SMA charity and the Myotubular Trust charity to give them the opportunity to provide a short update regarding their activities and their registries they are developing. Francesco Muntoni will feedback regarding the precise format of this session which would be no more thatn30-40 minutes.

Mike Hanna will contact Janice and Caroline to assess whether there is any update on pathology services this year

Mike Hanna will ask if Celia Thomas would like to attend the meeting and if she would like to say a few words before or after dinner

Day two: Helen Roper has agreed to coordinate the Muscle Interest Group solved and unsolved cases in adults and paediatrics from 9-12.30.

Mike Hanna will invite Mary Reilly to give an update on the BPNS and potential synergy with the BMS

Mike Rose will as Chris Graham to give a 20 minute update on the muscle quality of life study

As suggested by Mike Rose Mike Hanna will send an email to all BMS members to ask if there are any new studies or new ideas they would like to float with the group that can take advantage of the BMS network. If there is a positive response to this, a session will be set aside for 30 minutes for this purpose.

David Hilton-Jones will liase with Margurete Hill to coordinate a myasthenia gravis session from 14.30-16.00 on day two. This will include potentially sessions on myasthenia in pregnancy, new potassium channel antibody (that is not directed against the potassium channel!), and other interesting topics in myasthenia

It was agreed that there should be a keynote speaker, Francesco suggested and the group agreed that a topical talk would be to get a national or international expert on next generation sequencing and to discuss how this is going to impact on diagnostic and neuromuscular disease in the near to medium-term future. It was agreed that Mike and Francesco would discuss potential speakers and feedback to the group.

Subscriptions

Mike indicated that requests for subscriptions for £25 a year had been issued and were starting to be received.

Charitable status

Mike is still in the process of finalising charitable status which is more complex than anticipated, but should be completed by September.

Council membership

It was agreed that a vote would take place with all registered members who had paid subscriptions having a single vote following the BMS meeting. The current council membership will be asked if they would like to continue for a further term of three years. The names of those that would like to remain on council will then be put to the society membership for a majority vote on if they are content for members of the Council to stay on for three years. For those members of Council who wish to come off the Council, expressions of interest will be requested for members who would like to go onto Council. This will also be part of the majority vote.

Date of next conference call to be confirmed.

AOB

None

AGM minutes

Minutes from 2009 AGM
7.45pm, 2nd July, St Anne's College Oxford

Present:

Council:

Peter Baxter	Northern General Hospital, Sheffield
Kate Bushby	University of Newcastle
Michael Hanna	Institute of Neurology, UCL
David Hilton-Jones	University of Oxford
Janice Holton	Institute of Neurology, UCL
Francesco Muntoni	Institute of Child Health, UCL
Helen Roper	Birmingham Heartlands Hospital
Michael Rose	King's College Hospital
Caroline Sewry	Institute of Child Health, UCL & RJAH, Oswestry
Doug Turnbull	University of Newcastle
Douglas Wilcox	University of Glasgow

Members:

Rita Barresi	University of Newcastle
Charlotte Brierley	University of Cambridge
Richard Charlton	Newcastle University Teaching Hospitals
Gabriel Chow	University Hospital, Nottingham
Angus Clarke	Cardiff University
Elizabeth Curtis	University Hospitals Birmingham NHS Trust
Max Damian	University Hospitals of Leicester
Nicholas Davies	University Hospitals Birmingham
Yvette Easthope-Mowatt	RJAH, Oswestry
Michael Farrell	Beaumont Hospital, Dublin
Maria Farrugia	Ninewells Hospital, Dundee
Jane Fenton-May	University Hospital Wales
Robert Griggs	University of Rochester
Nick Gutowski	Peninsula Medical School
Simon Hammans	Wessex Neurological Centre, Southampton University
Louise Hartley	University Hospital of Wales, Cardiff
David Hilton	Derriford Hospital, Plymouth
Thomas Jacques	Institute of Child Health, UCL
Jacob Joseph	Royal Preston Hospital
Heinz Jungbluth	Evelina Children's Hospital
Russell Lane	Imperial College
Anirban Majumdar	North Bristol NHS Trust

Roger Malcolmson	Birmingham Children's Hospital
Emma Matthews	Institute of Neurology, UCL
Adnan Manzur	Great Ormond Street Hospital
Andria Merrison	University of Bristol
Rhiannon Morris	University of Cambridge
Fiona Norwood	King's College Hospital
Richard Orrell	Institute of Neurology, UCL
Matt Parton	National Hospital for and Neurosurgery
Richard Petty	Southern General Hospital, Glasgow
Margaret Phillips	Derby City Hospital, University of Nottingham
Simona Portaro	Institute of Neurology
Kelvin Poulton	Queen Elizabeth Hospital, Birmingham
Ros Quinlivan	Robert Jones and Agnes Hunt Hospital, Oswestry
Aleks Radunovic	Royal London Hospital
Wojtek Rakowicz	Imperial College Healthcare NHS Trust
Mark Roberts	University of Manchester
Mark Rogers	Cardiff and Vale NHS Trust
Chris Turner	National Hospital for Neurology
Rod Walsh	Bristol PCT
Jon Walters	Morriston, Swansea and Cardiff
Cathy White	Swansea NHS Trust
John Winer	University of Birmingham
Elizabeth Wraige	Guy's & St Thomas' Hospital

The following items were discussed and agreed.

1. Mike Hanna and Francesco Muntoni welcomed everyone to the first AGM meeting

2. The BMS rules were noted and no changes suggested at this time.

3. The format of the Annual BMS meeting was discussed and it was agreed that while the BMS was being established it was reasonable that for the next two years (2010 and 2011) there would be an annual meeting broadly adopting the format and timings of this first meeting and including a session of case presentations organised by the muscle interest group.

4. The possibility of linking with the Oxford summer muscle meeting was discussed and it was agreed that MH would contact Dr Chris Fursden Davis to explore this possibility.

5. It was agreed by a show of hands that MH would continue as chairman and would organise the next two BMS annual meetings 2010 and 2011 in collaboration with council. MH agreed to continue to provide the secretariat during this period.

6. It was agreed that after the 2010 meeting and before the 2011 meeting there would be an e-vote regarding chairmanship and members of council in accordance with the rules of the BMS.

7. It was agreed that there would not be a membership fee at present and this will be reviewed at the next annual meeting.

8. It was agreed that charity registration would be pursued.

9. Accounts- the only accounts were related to the income and expenditure from this first annual meeting and will be presented at the second annual meeting.

10. AOB – none

Minutes from 2010 AGM

8pm, 2nd September, St Anne's College Oxford

Apologies:
Doug Turnbull, Peter Baxter

Present:
Mike Hanna, Caroline Sewry, David Hilton-Jones, Douglas Wilcox, Helen Roper, Janice Holton, Kate Bushby, Michael Rose, Francesco Muntoni, Robert Meadowcroft, Rita Barresi , Jackie Palace, Bobby McFarland, Mark Roberts, Chris Turner, Adnan Manzur, Stephanie Robb, Heinz Jungbluth, Marianne de Visser, Alexandra Crampton, Nic Bungay, Edmund Jessop, Russell Lane, Matt Parton, Ingrid Mazanti , Andria Merrison, Imelda Hughes, Richard Charlton, Bryan Lecky, Richard Petty, Ros Quinlivan, Richard Orrell, Margaret Phillips, Gabriel Chow, Cathy White, James Miller, Stefan Spinty, Alison Wilcox, Charlotte Dougan, Lucy Feng, Aditya Shivane, Elizabeth Wraige, Marita Pohlschmidt, Simon Hammans, Georgina Burke, Fiona Norwood, Jacob Joseph, Kelvin Poulton, Nick Gutowski, Lyn Inman, Reghan Foley, Hector Chinoy, Peter Lunt, Petra Kolditz, Ann Mathew, Yvonne Robb, Elizabeth Curtis, Zoë Scott, Stefen Brady, Sarah Finlayson, Marcio Neves Cardoso, Sebahattin Cirak, Wojtek Rakowicz, Valeria Ricotti.

Minutes of the 2009 AGM:
These were accepted as a correct record of the meeting.

BMS organising group

It was agreed that the current organising group will continue to run the BMS. The Chair will ask members for an expression of interest for Council membership, which will be conducted by an internet vote.

Accounts

The publication of accounts is a requirement for charities. The BMS made a loss of around £800 from the first annual meeting, which was covered by the UCL MRC

Centre for Neuromuscular Diseases. Mike Hanna is keen to keep the BMS financially sustainable, and Genyzme agreed to sponsor this year's annual meeting. However it was proposed that it would be reasonable to consider charging a small membership fee. Douglas Wilcox stated that other professional organisations have a subscription, and this would help the society lessen its dependence on external sponsorship. The Chair proposed a vote of an annual membership fee of £25 – all present were in favour.

Oxford Summer Muscle Meeting

Mike Hanna stated that he has discussed the opportunity to link the BMS annual meeting with the Oxford Muscle Symposium held each July. It has become clear that the two meetings have different aims. The Muscle Symposium Oxford has an international focus and presents interesting cases, whereas the BMS is more UK-focussed, bringing British clinicians together to discuss UK commissioning. It was agreed that trying to merge these meetings would be impractical.

AOB

None.

2011 AGM Agenda

1. Minutes of the previous meeting
2. Registered charity status
3. Accounts
4. Rules of the Society
5. Council membership
6. AOB

MRC BMS workshops and other meetings 2010 - 2011

2010 MRC Myotonic Dystrophy Workshop

1st December 2010
Queen Square, London
Organised by Dr Chris Turner. Contact chris.turner@uclh.nhs.uk for further details.

2011 Myotonic Dystrophy Registry and Standards of Care Workshop

8th July 2011
Centre for Life, Newcastle
Organised by Dr Chris Turner. Contact chris.turner@uclh.nhs.uk for further details.

2011 Respiratory Study Day

12th October 2011
Queen Square, London
Organised by Dr Ros Quinlivan. Contact ros.quinlivan@uclh.nhs.uk for further details.

Regular Meetings

Muscle Interest Group
Occurs every 6 months
Contact: Helen Roper helen.roper@heartofengland.nhs.uk

Myasthenia Interest Group
Contact: Marguerite Hill marguerite.hill@swansea-tr.wales.nhs.uk

British Peripheral Nerve Society
Meets twice a year
Contact: Mary Reilly m.reilly@ucl.ac.uk

UK Databases/Registries

North Star
Contact: Adnan Manzur ManzuA@gosh.nhs.uk

SmartNet
Contact: Adnan Manzur ManzuA@gosh.nhs.uk

IBM-NET
Contact: Matt Parton matt.parton@uclh.nhs.uk

Current UK Neuromuscular Clinical Trials

MRC Centre CTIMPs Set-up Phase Trials

TAPP: THERAPEUTIC TRIAL OF POTASSIUM AND ACETAZOLAMIDE IN ANDERSEN-TAWIL SYNDROME

Status: Set-up Phase
Sponsor: University College London (UCL)
Funder: National Institutes of Health (NIH – USA)
PI: Prof Hanna
Recruitment target: 12

Andersen-Tawil Syndrome (ATS) is a rare form of periodic paralysis that is associated with serious heart-rhythm abnormalities. ATS is characterized by a triad of episodic muscle weakness, long-QT syndrome with potentially fatal cardiac dysrhythmias and skeletal developmental anomalies. The underlying cause of this potentially fatal condition is only partly understood and there are no established treatments. Mutations in the KCNJ2 gene encoding Kir2.1, an inward-rectifying potassium channel account for approximately 60% of ATS cases (termed ATS1), the remaining 40% are presumed to have an as yet undetermined gene lesion and are designated ATS2. ATS1 and ATS2 are phenotypically indistinguishable. The treatment of ATS has been largely anecdotal and empirical.

This proposal involves a multi-centre, placebo-controlled 'n of 1' study design of total duration 45 weeks. The expected total enrolment for this multi-centre study is 16 participants. The aim of this study is to determine whether potassium supplements and/or acetazolamide alter the duration of muscle weakness and potentially life-threatening heart rhythm abnormalities in patients with ATS.

For information on the status of recruitment please contact Dr. James Burge at James.burge@uclh.nhs.uk or Gisela Barreto, Trials Coordinator at Gisela.barreto@uclh.nhs.uk.

DMD HEART PROTECTION TRIAL

Full-Title: A double-blind randomised multi-centre, placebo-controlled trial of combined ACE-inhibitor and beta-blocker therapy in preventing the development of cardiomyopathy in genetically characterised males with DMD without echo-detectable left ventricular dysfunction.

Status: Set-up phase
Sponsor: Newcastle NHS Foundation
Planned start date: 2011
Funder: British Heart Foundation
PI: Prof. Muntoni
Recruitment target: 140

Duchenne muscular dystrophy [DMD] is an X-linked recessively inherited neuromuscular disorder due to a deficiency in the expression of the protein dystrophin on the inner aspect of cell sarcolemma. Its clinical course has traditionally been characterised by progressive weakness of proximal limb-girdle muscles and calf muscle hypertrophy. Duchenne-affected individuals typically lose ambulation and become wheelchair-dependent before the age of 13 and die from cardio-respiratory failure at around the age of 20 years. From the cardiology perspective, some 90% of males with DMD develop a severe, progressive form of cardiomyopathy. Twenty to 30% have evidence of left ventricular impairment on echocardiography by age 10 years. Abnormalities in left ventricular function are evident in an even larger proportion of patients at all ages when more sensitive imaging techniques, such as tissue Doppler, magnetic resonance or metabolic imaging, are deployed. Despite the severity of cardiac involvement in

DMD, cardiologists have largely ignored this particular inherited form of cardiomyopathy. This is due to the fact that, because of their inability to exercise, cardiac symptoms only occur terminally in DMD patients when all cardiac reserve has been eroded. Even today in most hospitals, cardio-active drug therapy is only started in patients with DMD when overt heart failure is evident and, even then, is typically deployed tentatively for symptom control, without any expectation that it can prolong life. The objective of this trial is to determine whether the introduction of ACE inhibitor combined with beta-blocker therapy, before the onset of echo-detectable left ventricular dysfunction, can delay the age of onset and/or slow the rate of progression of cardiomyopathy compared to placebo in males with DMD.This is a double-blind randomised, placebo-controlled Phase III trial of combined ACEinhibitor and beta-blocker therapy (perindopril and bisoprolol) over a minimum of three years and a maximum of five years. 140 participants (70 per arm) are to be enrolled and randomised. For more information about the study please contact the trial coordinator on 020 7905 2639.

A PILOT STUDY OF VALPROATE SODIUM FOR MCARDLE DISEASE
Status: Set-up phase
Sponsor: UCL
Planned start date: 2011
Funder: Muscular Dystrophy campaign
PI: Prof. Ros QuinlivanRecruitment target: 15

McArdle disease (Glycogen storage disease type V, GSDV) is an inherited metabolic disorder of skeletal muscle. Affected patients are unable to produce lactate during ischaemic exercise [McArdle 1951] because they have a congenital absence of the enzyme muscle glycogen phosphorylase, which is essential for glycogen metabolism [Mommaerts 1959, Schmidt and Mahler 1959]. The condition is caused by homozygous or compound heterozygous mutations in the muscle glycogen phosphorylase gene (PYGM) located at chromosome 11q13 [Beynon 2002]. This enzyme deficiency results in the inability to mobilise muscle glycogen stores that are normally required for energy during anaerobic metabolism. In affected people, symptoms of fatigue and cramp occur within minutes of initiating any activity and during strenuous activity such as lifting heavy weights or walking uphill, if the activity is continued despite severe cramping, a contracture occurs which leads to muscle damage (rhabdomyolysis), myoglobinuria and, when severe, acute renal failure.

Currently, there is no satisfactory treatment that can be recommended for the condition [Quinlivan 2008]. Taking glucose prior to exercise may alleviate muscle symptoms by inducing a second ‘second wind’, but this is not a good strategy for daily living as it may result in significant weight gain [Vissing 2003]. There is limited evidence for subjective benefit from creatine supplementation in five out of nine subjects from a randomised controlled trial [Vorgerd 2002], although this has not been confirmed in the clinic setting.

Although most people with McArdle disease have complete absence of skeletal muscle phosphorylase, there are a small minority of patients who possess splice site mutations that enable production of very small amounts (1-2%)of functional enzyme [Vissing]. These people have a milder phenotype with less severe symptoms, and functional exercise assessments have shown better exercise capacity than typical patients with the condition. Findings from these atypical individuals suggest potential therapeutic agents might only need to produce very small amounts of enzyme for significant functional improvement. Furthermore, finding a therapeutic agent to ‘switch on’ expression of the foetal isoenzyme may be a potential therapeutic strategy.

Sodium Valproate (Valproic acid) is one of a group of drugs known as histone deacetylase inhibitors (HDACIs) that can affect gene expression by acetylating lysine residues, which in turn has a direct effect on chromatin [Thiagalingam 2003]. There is some evidence from animal studies to suggest that sodium valproate can ‘switch on’ the foetal phosphorylase isoenzyme.

MRC Centre CTIMPs Open Trials

PHASE II, MULTICENTER, RANDOMIZED, ADAPTIVE, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY TO ASSESS SAFETY AND EFFICACY OF OLESOXIME (TRO19622) IN 3-25 YEAR OLD SPINAL MUSCULAR ATROPHY (SMA) PATIENTS
Status: Open
Sponsor: TROPHOS
Funder: Association Francaise contre les Myopathies
PIs: Francesco Muntoni, Hanns Lochmuller, Helen Roper
Recruitment target (UK): 30; due for completion by 31st September 2013
The UCL Institute of Child Health and Great Ormond Street Hospital for Children (London), Birmingham Heartlands Hospital, and Newcastle upon Tyne Hospitals Royal Victoria Infirmary have been invited to collaborate in this phase II clinical trial in non-ambulant patients with SMA II and III with a documented homozygous absence of SMN1 exon 7 and/or deletion and mutation on the other allele. This is a multicentre, double-blind, randomized, placebo-controlled study in patients with SMA type 2 or non-ambulant type 3. The study will be conducted in multiple centres across Europe and will be sponsored by Trophos (a biopharmaceutical company based in France) and funded by AFM (Association francaise contre les myopathies). The aim is to assess efficacy, futility, safety and tolerability of a new drug called olesoxime. This is a neuroprotective drug that acts by interacting with protein components of the
mitochondrial permeability transition pore (mPTP), preventing the release of apoptotic factors and in turn neuronic death. Olesoxime has displayed an excellent safety profile and has been well tolerated in phase I clinical trials in healthy subjects. For each participant, this phase II study will involve a 4 week screening period followed by a 24 month (104 week) treatment period. Following screening procedures and confirmation of eligibility, subjects will be randomised to receive either olesoxime or placebo in a 2:1 ratio. Olesoxime (or matched placebo) will be taken daily with evening meal as a liquid
formulation at a dose of 10mg/kg. 150 subjects in total will be recruited, with a target of 30 patients in the UK. Recruitment is planned to be completed in 6 months. It is possible a dose adjustment may be made once 45 patients across Europe have been received study drug for 3 months based on a
review by a designated independent Data Monitoring Committee. The patients to be recruited should be at least 3 years of age but younger than 26 years at the time of enrolment, with the age of onset of symptomsto be at 3 years of age or younger. They should not be taking any medication intended for the treatment of SMA within 30 days prior to being enrolled on the study. Eligible patients can be taking oral salbutamol as long as this has been commenced at least six months prior to enrolment on the study and remains at a stable dose during the study period. Participation in another investigational drug or therapy study within 3 months of enrolment is an exclusion criterion, as well as a hypersensitivity to sesame oil and use of medications that could interfere with olesoxime absorption (including cholesteramine, fibrates, fish-oils, niacin, phytosterols and ezetimibe). Further information about this study can be obtained from the Clinical Trials Coordinator on 020 7905 2639.

HYP HOP: DICHLORPHENAMIDE vs. PLACEBO FOR PERIODIC PARALYSIS
Full Title: Double-blind, placebo-controlled, parallel group, phase III study comparing dichlorphenamide vs. placebo for the treatment of periodic paralysis
Status: Open to Recruitment
Sponsor: University Rochester
Funder: National Institutes of Health (NIH - USA)
PI: Prof. Hanna
Patients recruited:13; target 40
This is a phase III trial into Periodic Paralysis. This proposal involves a multi-centre, double-blind, placebo-controlled parallel group, nine-week studies comparing the effects of

dichlorphenamide(DCP) vs placebo in patients with period paralysis (Hyper, Hypokalemic periodic paralysis). The 9-week studies will investigate the prevention of attacks of weakness and it will be followed by 1-year extensions without placebo to compare the long term effects of DCP on the course of the diseases and on inter-attack weakness. Approximately 40 participants will be recruited from the United Kingdom. For information on the status of recruitment please contact Dr. James Burge at James.burge@uclh.nhs.uk or Gisela Barreto, Trials Coordinator at Gisela.barreto@uclh.nhs.uk.

ARIMOCLOMOL FOR SPORADIC INCLUSION BODY MYOSITIS (IBM)

Full Title: A Randomised, Double-blinded, Placebo-controlled Pilot Study Assessing the Safety and Tolerability of Arimoclomol in Adult Patients with Sporadic Inclusion Body Myositis

Status: Closed to Recruitment
Sponsor: University College London (UCL)
Funder: Arthritis Research UK and Myositis Support Group
PI: Prof. Hanna
Patients recruited: 12; target 12

Sporadic Inclusion Body Myositis (IBM) is the commonest acquired disease of muscle affecting people aged 50 years and over. This is a progressive and debilitating disease with both muscle weakness and wasting, characteristically of the quadriceps and finger flexors. Over time the condition can lead to severe disability, falls and swallowing impairment. Affected muscle tissue demonstrates inflammation and degeneration.

Arimoclomol is a new compound which acts by enhancing a normal, inbuilt protective cell reaction to stresses. The products of this response are 'Heat Shock Proteins (HSPs) which counteract processes that end up leading to abnormal protein deposition and to damage mediated by inflammation. This proposal involves a multi-centre, double-blind, placebo-controlled parallel study of total duration twelve weeks. This study proposal aims to assess the safety and tolerability of Arimoclomol (100 mg TDS) as compared with placebo over 4 months of treatment in patients with IBM. Recruitment will take place at the National Hospital for Neurology and Neurosurgery and twelve patients will be enrolled.

For information on the status of recruitment please contact Dr. Pedro Machado at p.machado@ion.ucl.ac.uk or Gisela Barreto, Trials Coordinator at Gisela.barreto@uclh.nhs.uk.

GSK/PROSENSA CLINICAL TRIAL IN DMD BOYS WITH STUDY DRUG GSK2402968 (PRO051)

Full Title: A phase II, double-blind, exploratory, parallel-group, placebo-controlled clinical study to assess two dosing regimens of GSK2402968 for efficacy, safety, tolerability and pharmacokinetics in ambulant subjects with Duchenne muscular dystrophy

Status: Ongoing
Sponsor: GlaxoSmithKline
Funder: GlaxoSmithKline
PIs: Volker Straub, Francesco Muntoni
Patients recruited: 8; target (UK) 8

A multicentre trial with this study drug is recruiting DMD boys in UK at the Great Ormond Street Hospital(GOSH), London and at the Royal Victoria Infirmary, Newcastle. It is a Phase lla, double blind, exploratory, parallel clinical trial to assess the optimal dose of GSK2402968 for safety, tolerability and efficacy, in ambulant patients with DMD. This study is designed to explore efficacy and safety of GSK2402968 given as a continuous regimen and an intermittent regimen over 24 and 48 weeks. Objective(s)

Primary objective:

• To assess the efficacy of 2 different dosing regimens of subcutaneous GSK2402968 administered over
24 weeks in ambulant subjects with DMD.
Secondary objectives:
• To assess the safety and tolerability of 2 different dosing regimens of subcutaneous GSK2402968 administered over 48 weeks in ambulant subjects with DMD.
• To assess the PK of 2 different dosing regimens of subcutaneous GSK2402968 administered over 48 weeks in ambulant subjects with DMD.
• To assess long term efficacy of 2 different dosing regimens of subcutaneous GSK2402968 administered over 48 weeks in ambulant subjects with DMD.
Study Design
The study aims to randomise 54 subjects. There will be 2 parallel cohorts. Each cohort will include 16 subjects on GSK2402968 and 8 subjects on matched placebo (2:1 ratio). Further information about this study can be obtained from the MRC Centre Clinical Trials Coordinator on 020 7905 2639.

INVESTIGATION OF THE ABILITY OF OTELIXIZUMAB TO INHIBIT IN VITRO ANTIGEN-SPECIFIC T CELL RESPONSES FROM MYASTHENIA GRAVIS PATIENTS
Status: Open to Recruitment
Sponsor/Funder: GlaxoSmithKline
PI: Prof Kullmann
Patients recruited: 26; target 40
Myasthenia Gravis (MG) is the best understood autoimnune disease (a disease in which the immune system attacks some part of the body). This attack is directed by various parts of the immune system.
There is a continued search for newer drugs that will be of benefit in the treatment of MG. There is a continued search for newer drugs that will be of benefit in the treatment of MG. Otelixizumab has been identified as a possible treatment for MG. However before clinical trials can be considered additional information is needed to determine how it interacts with the immune system of patients with MG.

In this study adult patients with MG will be invited to provide blood samples (50 ml) for research purposes. Blood collected from patients will be used for Tcell assay and autoantibody assay development. Patients may be asked to provide a repeat blood sample (additional 50ml) after 46 months following the initial collection to see if T cell activation changes over time. Up to 40 participants will be enrolled in the UK. The study is being sponsored by GlaxoSmithKline group of companies.

For information on recruitment contact Natalie James (natalie.James@uclh.nhs.uk).

THERAPEUTIC TRIAL OF LITHIUM CARBONATE IN MND/ALS (LICALS)
Full title: A double-blind, randomised, placebo controlled trial of lithium carbonate in patients with amyotrophic lateral sclerosis.

Status: Ongoing (closed to recruitment)
Sponsor: University College London Hospitals NHS Foundation Trust
Start date: June 2009
Funder: Motor Neurone Disease Association, and NIHR
UCL PI: Dr Richard Orrell

Patients recruited: 22, target: open-ended

Recent research suggested that lithium carbonate may be effective in lowing the progression of MND/ALS. Lithium may protect motor neurons through a range of mechanisms, including improving the transport of proteins along the motor neuron, improving the transport of

mitochondria, and activating cell survival factors. In one study, lithium prolonged survival in a mouse model of MND/ALS. This is a multi-centre UK study, involving 215 patients with MND/ALS, taking lithium or placebo, for 18 months. The trial is designed to assess the safety, efficacy and tolerability of lithium in combination with riluzole as a treatment for MND/ALS. Assessments include survival, symptoms, quality of life, and function. Participants are randomised to take lithium or placebo, the level of lithium in the blood is monitored, and the dose of lithium (and placebo) adjusted as needed.

LiCALS OPEN LABEL EXTENSION

Full title: LiCALS open label extension trial of lithium carbonate in amytrophic lateral sclerosis.

Status: Recruiting.
Sponsor: University College London Hospitals NHS Foundation Trust
Start date: March 2011
Funder: Motor Neurone Disease Association, and NIHR
UCL PI: Dr Richard Orrell
Patients recruited: 3 of 8 recruited

This is an open label extension study for those who have completed the randomised double blind trial of lithium carbonate in ALS. The objective is to obtain further evidence of the safety of lithium carbonate in doses achieving levels of 0.4-0.8 mmol/l.

GSK1223249 IN MND/ALS (THE NOGO-A STUDY)

Full title: A Phase I, multi-center, randomized, placebo-controlled, double-blind, single and repeat dose escalation of a drug to treat ALS.

Status: Recruiting
Sponsor: Royal Free Hampstead NHS Trust
Start date: September 2010
Funder: GlaxoSmithKline
UCL PI: Dr Richard Orrell
Patients recruited: 2, target: 2

GSK 1223249 is a new drug developed by GlaxoSmithKline, that targets a protein called Neurite Outgrowth Inhibitor (Nogo-A), which impairs neurone regeneration. There is evidence of increased Nogo-A, which impairs neuron regeneration, in muscle of people with MND/ALS. By blocking the effect of Nogo-A, GSK1223249 may be an effective treatment for the disease. GSK1223249 delays symptom onset and prolongs survival in a mouse model of MND/ALS. The trial will provide safety and tolerability information, together with biomarker and functional information. This may leader to further trials to assess effectiveness. The study includes an infusion of the drug (or placebo), with a muscle biopsy taken before and following the infusion, together with other monitoring assessments. For further information please contact Dr Richard Orrell (r.orrell@ucl.ac.uk)

BIOMARKER STUDIES IN MND/ALS

Full title: Characterisation of a panel of disease biomarkers in peripheral blood from individuals with motor neuron disease

Sponsor: University College London Hospitals NHS Foundation Trust
Start date: May 2009
Funder: Motor Neurone Disease Association
UCL PI: Dr Richard Orrell

Motor neuron disease (MND) is an adult-onset neurodegenerative diseases and one of the

commonest neuromuscular disorders. The speed of progression of MND varies among individuals and the condition can develop with different clinical manifestations. Currently, there are no blood tests that could help us to predict the speed of progression of the disease and the likely clinical manifestations (e.g. predominant

involvement of speech and swallowing or of the limb muscles). We are testing specific disease biomarkers in the blood. To assess change over time, a blood sample is taken every 3 months. The sample has to be carefully processed as soon as it is taken to preserve the quality of the blood contents. We are studying a range of blood constituents including proteins, DNA and RNA. From some participants we also collect samples of cerebrospinal fluid. If repeated samples are not possible, a single sample of blood for DNA studies is also helpful. We also examine samples from participants without MND/ALS, and individuals with similar but unrelated neuromuscular conditions. Parallel studies of biomarkers in an animal model of ALS are informing our choice of biomarkers. The study is in collaboration with Queen Mary University of London, and other participating centres.

MRC Centre CTIMPs Completed Trials

RANDOMISED DOUBLE-BLINDED PLACEBO CONTROLLED TRIAL OF LONG-ERM ASCORBIC ACID TREAMENT IN CHARCOT-MARIE-TOOTH DISEASE TYPE 1A
Status: Completed
Sponsor: University College London
Funder: Muscular Dystrophy Campaign (MDC)
PI: Prof. Reilly
Patients recruited: 50
Charcot-Marie-Tooth disease 1A (CMT1A) is associated with a duplication of the peripheral myelin protein 22 (PMP22) gene. To date there is no pharmacological treatment for CMT1A patients. Treatments and therapy for CMT is restricted to symptomatic treatments such as physiotherapy and surgery for skeletal deformities.
Recently, treatment with ascorbic acid (AA) has been shown to be effective for transgenic mice over-expressing PMP22, a model of the human disease. Treated animals had much less severe neuropathy as compared to untreated controls as shown by clinical and histological findings. Some clinical parameters even improved during treatment.
This is a phase III prospective, multi-centre, randomised, double-blind, placebo-controlled study aiming to evaluate the efficacy of AA treatment in CMT1A.
The study is now complete. Fifty participants were enrolled in the UK site at the MRC Centre for Neuromuscular Diseases. Paper in press.

THERAPEUTIC TRIAL OF MEXILETINE IN NON-DYSTROPHIC MYOTONIA
Full Title: A Phase II Randomised, Double-Blind, Placebo controlled, Cross-Over Study to Investigate the Efficacy of Mexiletine in Patients with Non-Dystrophic Myotonia
Status: Completed
Sponsor: University College London (UCL)
Funder: Food and Drug Administration (FDA – USA)
PI: Prof. Hanna
Patients recruited: 14; target 15
The non-dystrophic myotonia (NDM) is a group of rare neuromuscular disorders that causes episodes of muscle stiffness (known as myotonias) and paralysis. Predominantly the muscles of the face, hands and legs are affected. In addition to these episodes a permanent and debilitating muscle weakness can develop. The optimal treatment for these disorders is

unknown. Non-dystrophic myotonias are due to abnormalities of ion channels present in skeletal muscle membranes. There is experimental evidence that drugs like mexiletine which block the abnormal function of these ion channels allow the muscle to perform normally. The study aims to test the efficacy of mexiletine in the treatment of the non-dystrophic myotonias. This proposal involves a multi-centre, double-blind, placebo-controlled cross over trial of total duration nine weeks. Fifteen participants have been enrolled in the UK at the MRC Centre. For information on the status of recruitment please contact Dr. Dipa Raja Rayan at d.rajarayan@ion.ucl.ac.uk or Gisela Barreto, Trials Coordinator at Gisela.barreto@uclh.nhs.uk

A PHASE IIb EFFICACY AND SAFETY STUDY OF PTC124 IN SUBJECTS WITH NONSENSE MUTATION-MEDIATED DUCHENNE AND BECKER MUSCULAR DYSTROPHY

Status: Completed
Sponsor: PTC Therapeutics
Funder: PTC Therapeutics
PIs: Prof. Muntoni, Prof. Bushby
Patients recruited: 11

Duchenne muscular dystrophy (DMD) is an X-linked genetic disorder affecting young boys. The condition is disabling and life-threatening. A small subset of boys are classified as having Becker muscular dystrophy (BMD), a phenotypically milder form of the dystrophic muscle disease.

In approximately 10 to 15% of boys with DMD and BMD the causative defect is the presence of a nonsense mutation in the dystrophin gene that truncates dystrophin protein production by introducing a premature stop codon into the dystrophin messenger ribonucleic acid (mRNA).

PTC124 is a novel, orally bioavailable, small-molecule drug that promotes ribosomal read-through of mRNA containing a premature stop codon. Through this mechanism of action, PTC124 has the potential to overcome the genetic defect in boys for whom a nonsense mutation causes DMD/BMD.

In vitro studies in cell lines with dystrophin nonsense mutations have shown that PTC124 can restore production of the missing dystrophin gene.

This is an international, multi-centre, randomised, double-blind, placebo-controlled, dose-ranging, efficacy and safety study.

The study primary aim is to evaluate the effect of PTC124 on ambulation as assessed by the distance walked during a 6-minute walk test (6MWT).

The double-blind arm of the study randomised 174 participants worldwide which are to be followed for a period of 12 months. At the completion of the blinded treatment, all compliant participants were eligible to receive open-label PTC124 in a separate extension study.

(Ataluren is now the non-proprietary generic name for PTC124).

This work has been completed.

The preliminary findings from the Ataluren Study 007 did not show significant muscle improvement in the patients who participated in the study. The study was therefore discontinued. An update on this study was presented at the International Congress on Neuromuscular Diseases, Naples, Italy, 17-22 July 2010 by Professor Kate Bushby. Details of this presentation is available on www.ptcbio.com Briefly, analysis showed that, on average, patients treated with low-dose ataluren experienced better outcomes on measures of efficacy than patients treated with high-dose ataluren or placebo - this phenomenon is not unique for ataluren and has been observed with other drugs for other diseases. Further analysis of efficacy data is ongoing.

ANTISENSE OLIGONUCLEOTIDE INDUCED EXON SKIPPING IN DUCHENNE MUSCULAR DYSTROPHY

This initiative is led by the MDEX consortium (The MDEX consortium led by Professor Muntoni, is a multidisciplinary enterprise to promote translational research into muscular dystrophies, and is formed by the clinical groups of Professor Francesco Muntoni (UCL Institute of Child Health) and Professor Kate Bushby and Professor Volker Straub (Newcastle University), and scientists from Imperial College London (Professor Dominic Wells), UCL Institute of Child Health (Dr Jennifer Morgan), Royal Holloway University of London (Professor George Dickson and Dr Ian Graham), Oxford University (Dr Matthew Wood) and University of Western Australia (Prof Steve Wilton). In addition, the charities Muscular Dystrophy Campaign (MDC), Action Duchenne and Duchenne Family Support Group also participate in the Consortium, www.mdex.org.uk).
The current two trials led by the consortium are mentioned below.

RESTORING DYSTROPHIN EXPRESSION IN DUCHENNE MUSCULAR DYSTROPHY: A PHASE I/II CLINICAL TRIAL USING AVI-4658

Status: completed
Sponsor: Imperial College London
Funder: Department of Health (DoH)
PI: Prof. Muntoni
Patients recruited: 8

The primary scope of the trial is to assess efficacy (dystrophin production) and safety of intramuscular administered morpholino oligomer directed against exon 51 (AVI – 4658 PMO).

Antisense therapy with the use of antisense oligomers has the potential to restore effectively the production of dystrophin, the defective protein, in >70% of DMD. This could result in increased life expectancy through improved muscle survival and function. Recent scientific research has demonstrated the potential of this technique to skip mutated dystrophin exons, restore the reading frame and generate functional dystrophin protein. Having demonstrated proof-of-principle in human cell culture and animal model studies, we now intend to determine efficacy and safety of this approach to induce dystrophin exon skipping in children with DMD. This study is aimed at children with Duchenne muscular dystrophy above the age of 10 years with mutations than can be rescued by the skipping of exon 51 [45-50; 47-50; 48-50; 49-50; 50; 52; 52-63].

This work has been completed and outcome data published in the journal Lancet Neurology (Volume 8, Issue 10, Pages 918 - 928, October 2009)

DOSE-RANGING STUDY OF AVI-4658 TO INDUCE DYSTROPHIN EXPRESSION IN SELECTED DUCHENNE MUSCULAR DYSTROPHY (DMD) PATIENTS – (Systemic study)

Status: Completed
Sponsor: AVI Biopharma
Funder: Medical Research Council (MRC) and AVI Biopharma
PI: Prof. Muntoni
Patients recruited: 19

This is a safety study of AVI-4658 (a 30-base phosphorodiamidate Morpholino oligomer [PMO]), to skip exon 51 of the dystrophin gene in relevant subjects with DMD.

This is an open-label, two-centre, dose-ranging comparative clinical study of duration twelve weeks.
The objectives of the study are to assess safety and to select the optimum dose that elicits at least 10% de novo dystrophin-positive fibres and dystrophin in a sentinel muscle group after an intravenous AVI-4658 dosing regimen.

A total of up to 16 subjects (ambulatory paediatric males, aged ≥5 and ≤15 years of age) will be enrolled in this study, consisting of four treatment cohorts and four subjects per cohort. It is expected that there will be four treatment arms ranging from 0.5 mg/kg to 4 mg/kg. All subjects will receive 12 weekly intravenous infusions of AVI-4658.

Precedent studies have demonstrate that AVI-4658 might have therapeutic relevance in managing DMD for boys whose frame-shifted dystrophin gene lesion could be restored after excision of exon 51 if sufficient drug is translocated into the nucleus of the afflicted muscle cell.

This trial was conducted in London and Newcastle.

A total of 19 subject (12 at GOSH and 7 at RVI, Newcastle) were recruited and final data is being analysed for submission to regulatory authorities in Europe and the USA. Outcome data were presented at the World Muscle Society, 12-16 October 2010 in Japan and published.

www.thelancet.com Published online July 25, 2011 DOI:10.1016/SO140-60756-3.

ECULIZUMAB FOR MYASTHENIA GRAVIS

Full Title: A Randomised, Double-Blind, Placebo-controlled, Cross-over, Multicenter Study of Eculizumab in Patients with Generalised Myasthenia Gravis (GMG) who have Moderate to Severe Muscle Weakness Despite Treatment with Immunosupressants

Status: Closed
Sponsor/Funder: Alexion Pharmaceuticals, Inc.
PI: Prof. Dimitri Kullmann

This is a randomized, double-blind, placebo-controlled, cross-over, multicenter study to evaluate the safety and efficacy of eculizumab for the treatment of patients with myasthenia gravis. Myasthenia gravis (MG) is an acquired autoimmune syndrome caused by the failure of neuromuscular transmission, which results from the binding of autoantibodies to proteins involved in signalling at the neuromuscular junction (NMJ). These proteins include the nicotinic AChR or, less frequently, a muscle-specific tyrosine kinase (MuSK) involved in AChR clustering.

Current available treatments for myasthenia gravis aim to modulate neuromuscular transmission, to inhibit the production or effects of pathogenic antibodies, or to inhibit inflammatory cytokines. There is currently no specific treatment that corrects the autoimmune defect in MG.

Eculizumab is a humanized murine monoclonal antibody that blocks the activation of complement by selectively binding to C5 and preventing the enzymatic cleavage of C5 to C5a and C5b. The blockade of complement activation at this point in the cascade has been shown to prevent the proinflammatory effects of both C5a and C5b, especially the chemotaxis of inflammatory cells, and MAC (C5b-9)-mediated cell activation and lysis. Since eculizumab effectively inhibits complement, especially MAC formation, it is a potentially effective therapeutic approach for diseases such as MG in which the formation of the MAC and/or the release of C5a leads to localized destruction of the postsynaptic NMJ membrane and play a important role in the disease process.

atients will receive approximately 22 infusions including 11infusions of eculizumab and 11 infusions of placebo. The estimated duration of a patient's participation is approximately 41 weeks. For more information about the study please contact Dr. Jennifer Spillane at jspillane@ion.ucl.ac.uk or Natalie James at Natalie.James@uclh.nhs.uk.

Natural History – Longitudinal Studies

Set-up Phase

OUTCOME MEASURES IN SMA TYPE II AND II

Status: Recruitment to commence shortly

Funder: SMA Europe

PI: Prof Muntoni

This project provides an excellent opportunity as for the first time, ten leading neuromuscular centers in Europe which have been involved in the development and validation of functional scales for SMA will collaborate to validate and cross validate measures that have been suggested to be the most suitable for multicentric trials by a large international consensus, but have not been tested in large multicentric studies yet.

One hundred and thirty patients across Europe affected by type II and type III SMA will be enrolled and assessed at baseline and 6 and 12 months later. Non ambulant patients will be assessed using the modified version of the Hammersmith Motor Functional Scale while ambulant patients will be assessed using the extended module of the Hammersmith Motor Functional Scale and timed items, the 6 minute walk and a step activity monitor. All patients will also be assessed using the MFM,that covers the whole range of activities for both ambulant and non ambulant patients. All measures will undergo a process of validation including inter observer reliability. This information will be most valuable for any future trial and will make the groups involved ready to participate to future collaborative studies saving a lot of time on the preliminary aspects (validation, reliability, training) that will be fulfilled by the present study. The study will also provide natural history data for a 12 month period on patients with SMA II and III.

Further information can be obtained from the Trials Coordinator or Research Physiotherapist on 020 7905 2639.

Open Trials

ANDERSEN-TAWIL SYNDROME: GENOTYPE AND PHENOTYPE CORRELATION AND LONGITUDINAL STUDY

Status: Open to recruitment

Sponsor: University College London

Funder: National Institutes of Health (NIH – USA)

PI: Prof. Hanna

Patients recruited: 11

Andersen-Tawil syndrome is a neuromuscular disorder caused by a mutation in the KCNJ2 gene which codes for the inwardly rectifying potassium channel Kir2.1. A number of different mutations in this gene have already been identified in affected individuals. This disorder is characterised by the triad of periodic paralysis, developmental abnormalities and cardiac arrhythmias.

This project is a natural history trial into Andersen-Tawil Syndrome. The aim of the trial is to study the relationship between the genetic abnormalities underlying the disorder and the diverse clinical features.

Eleven patients have been enrolled so far at the National Hospital for Neurology and Neurosurgery.

For information on the status of recruitment please contact Dr. Dipa Raja Rayan at d.rajarayan@ion.ucl.ac.uk.

EPISODIC ATAXIA SYNDROME: GENOTYPE-PHENOTYPE CORRELATION AND LONGITUDINAL STUDY
Status: Recruiting
Sponsor: University College London
Funder: National Institutes of Health (NIH – USA)
PI: Prof. Hanna
Patients recruited: 36

Episodic Ataxia Syndrome is a rare, genetic disease that causes recurrent episodes of dizziness and incoordination. The majority of cases are likely caused by an inherent genetic mutation. However in some patients the mutation is unidentifiable. The purpose of this study is to collect prospective standardized data from subjects to better define the clinical phenotype of the EAs and to establish clinically relevant endpoints for use in therapeutic trials.

The study will also :

- Fully characterize the clinical spectra and the natural history of genetically defined EA.
- Systematically investigate phenotypic differences between EA subjects harboring KCNA1/CACNA1A mutations and those that do not.

This proposal involves a multi-center cross-sectional data collection analysis as well as a prospective longitudinal study. Since EA is a chronic disease whose course is measured in years rather than months, the subjects will be followed longitudinally at a yearly interval for a period of two years.

For information about the study please contact Tracey Graves at tracey.graves@btinternet.com.

CMT: A NATURAL HISTORY STUDY
Full Title: Charcot-Marie-Tooth Disease and related disorders: A Natural History Study
Status: Open to Recruitment
Sponsor: University College London Hospitals
Funder: National Institutes of Health (NIH – USA)
PI: Dr Reilly/Prof Muntoni
Patients recruited: 162; target (UK) >50

Charcot-Marie-Tooth Disease (CMT) and related disorders (distal hereditary motor neuropathy (dHMN) and hereditary sensory and autonomic neuropathy (HSAN)) are a clinically and genetically heterogenous group of disorders affecting approximately 1 in 2500 people.

People with this condition present with upper and lower limb weakness, wasting and sensory loss as a result of degeneration of the long peripheral nerves supplying the distal muscles. Despite the clinical similarities among patients with CMT the group is genetically heterogeneous. Advances have been made in identifying the genes that cause CMT and the molecular organisation of the peripheral nervous system (PNS) nevertheless the optimal management and treatment of the different variants of this disorder is not known and moreover natural history data is lacking for most forms of inherited neuropathies. This is a 5 year study that will be conducted by four centres in United States and two centres in the UK (National Hospital for Neurology and Neurosurgery and Great Ormond Street Hospital).

The aim of the project is to fully characterise the features of different types of CMT and the longitudinal progression of the disease. The data will also be used to establish clinical relevant endpoints for use in therapeutic trials. The identification and genetic characterisation of patients will facilitate the recruitment of participants for future therapeutic trials. Ultimately the information gained with this study will lead to the improvement in the treatment and management of CMT.
The study is also seeking to establish an appropriate paediatric impairment scoring method for CMT and establish a database for the inherited neuropathies. The study will include both adult and paediatric patients. Evaluations will consist of a neurological history and examination, nerve conduction velocity (NCV) study and in some selected cases skin biopsy. This is a NIH funded study. At least fifty patients will be enrolled at the National Hospital for Neurology and Great Ormond Street Hospital.
For more information about the study please contact Dr. Matilde Laura at m.laura@ucl.ac.uk.

MITOCHONDRIAL DISEASE COHORT
Status: Open to Recruitment
Sponsor: The University of Newcastle Upon Tyne
Funder: MRC
PI: Dr R McFarland
Patients recruited: 456; target 1500
The current project proposes to develop a cohort of UK patients with mitochondrial diseases. The details are to be stored in a database that will enable clinicians to gain adequate information for future clinical trials.

Mitochondrial diseases present a huge challenge to patients and doctors because no effective treatment is available. The extremely diverse phenotypic presentation of mitochondrial disease has previously limited cohort development.
The cohort will comprise symptomatic adults and children, in whom a mitochondrial disease phenotype and (where possible) genotype, have been confirmed. Asymptomatic individuals who have requested genotyping and proved positive will also be included. Genotyping is important because the same mitochondrial phenotype may be caused by several distinct mutations in either the mitochondrial or nuclear genomes. Phenotype will be characterized in all individuals (symptomatic and asymptomatic) on the basis of clinical history, clinical examination and detailed investigation.

Two centres will receive referrals (Newcastle University and University College London Hospitals). The database will physically be stored at Newcastle University and it will have a dedicated, electronic secure server.

The project anticipates collecting details on 1500 patients in total.

For information on the status of recruitment please contact Dr. Robert Pitceathly (London) r.pitceathly@ion.ucl.ac.uk or Geoff Bell (Newcastle) geoff.bell@nuth.nhs.uk.

THE NATURAL HISTORY OF INCLUSION BODY MYOSITIS (IBM-Net)
Status: Open to Recruitment

Sponsor: University College Hospitals

Funder: MDC

PI: Dr Matt Parton/Prof Mike Hanna
Inclusion body myositis (IBM) is probably the commonest muscle disease beginning in those aged over 50. It leads to progressive disability with, classically, a characteristic pattern of muscle involvement. However it is poorly understood: its cause is unknown, there is no conclusive diagnostic test and it has no treatment. Furthermore, information on the pattern

and prognosis of IBM is more based on anecdote from clinical experience, rather than firm fact. The largest published series of data on the natural history of the illness followed only eleven patients for six months.

The current project seeks to better characterise IBM by gathering clinical data from as many cases as possible.

Serial standardised assessment (annually for five years) will chart disease progression and so both expand and strengthen knowledge of the natural history of the illness. Furthermore, establishment of a cohort of reliably-defined cases will build a valuable resource that could potentially form the starting-point for future studies.

For information on the status of recruitment please contact Dr. Pedro Machado at p.machado@ion.ucl.ac.uk

PERIPHERAL NEUROPATHY OUTCOME MEASURES STANDARDISATION STUDY (PERINOMS)

Status: Open
Sponsor: Erasmus Medical Center
PI: Dr M Lunn
Patients recruited: 110 (NHNN 4); overall target 120

The current study aims to expand the clinimetric knowledge on outcome measures at various levels of outcome (pathology, impairment, activity & participation limitation, and quality of life) in autoimmune polyneuropathies, particularly in GBS, CIDP, MMN, MGUSP, and autoimmune small fibre neuropathies (AI-SFN). Also, the general applicability of an autonomic symptoms scale plus some selected activity limitation scales will be examined.

Outcome measures will be assessed in a cross-sectional and longitudinal group of patients at the level of:

-Pathology: Intraepidermal nerve fibre (IENF) density will be assessed in patients with GBS, CIDP, MGUSP, and AI-SFN (in sarcoidosis). IENF density will be examined regarding its correlation with other outcome measures (validity), its reliability (intra-observer and inter-observer), and its responsiveness to clinical changes over time.

- Impairment: comparison studies, evaluating the validity, reliability, and responsiveness will be performed between MRC sumscore versus NIS motor subset, INCAT sensory sumscore versus NIS sensory sumscore, and hand-held Vigorimeter versus Jamar dynamometer. Also, the correlation of electrophysiological studies with other impairment outcome measures will be evaluated. Finally, the scientific soundness of the modified Dutch composite autonomic symptoms scale (mdCompass) will be examined.

-Activity limitation: comparison studies, evaluating the validity, reliability, and responsiveness will be performed between the ODSS and an overall neuropathy limitations scale (ONLS). Also, a newly devised weighted (based on Rasch analyses) activity and participation scale will be constructed, aiming specifically on the limitations in patients with polyneuropathy.

- Quality of life: Disease-specific versus generic quality of life measures will be assessed, determining their clinimetric soundness and by comparison studies in the various polyneuropathy groups.

The ultimate goal of the current study will be the presentation of a *specific* minimum core set of outcome measures to be used in future clinical and follow-up studies in patients with polyneuropathy, mainly those patients with autoimmune mediated polyneuropathies. The study will be performed in collaboration with several local, European, and USA neurological centres with great experience in dealing with inflammatory neurological disorders

Closed Trials

NON-DYSTROPHIC MYOTONIAS: GENOTYPE AND PHENOTYPE CORRELATION AND LONGITUDINAL STUDIES

Status: Closed to recruitment
Sponsor: University College London
Funder: National Institutes of Health (NIH – USA)
PI: Prof. Hanna
Patients recruited: 20

This multi-centre project involves a prospective, cross-sectional and longitudinal natural history in non-dystrophic myotonias (NDM).

The aim is to collect standardized data from NDM patients, to include clinical symptoms, exam findings, as well as the results of strength, functional, and electrophysiological testing. Genetic testing will permit precise identification of individual NDM subtype. This information will allow for the identification and implementation of appropriate endpoints in studies of potential treatments.

This is a NIH funded study. Twenty patients were enrolled at the National Hospital for Neurology and Neurosurgery.

For more information about the study please contact Dr. Emma Matthews at d.rajarayan@ion.ucl.ac.uk.

Exercise Studies

Set-up Phase

AEROBIC TRAINING IN CHARCOT-MARIE-TOOTH DISEASE AND INCLUSION BODY MYOSITIS

Status: In set-up
Sponsor: University College Hospitals
Funder: TBC
PI: Dr Gita Ramdharry

The specific objective of the present study is to investigate the effect of aerobic training in two common neuromuscular diseases (NMD): Charcot-Marie-Tooth disease (CMT) and Inclusion Body Myositis (IBM). These diseases result in progressive muscle wasting and substantial morbidity and disability. The effect of aerobic training on fitness levels, muscle strength and function will be systematically examined. This study will also monitor the safety, feasibility and impact on quality of life of this type of exercise training in these groups.

Sixty subjects, (30 from each disease group, aged between 18 and 75), will be recruited from the neuromuscular clinics at Queen Square. Both disease groups will be investigated concurrently with the same methods but will be viewed and analysed as separate studies. A crossover design will be used with training and control periods. The trial will span three years with each subject participating for a 34 week period. For the training intervention, participants will train in select local gyms and train on a bicycle ergometer.

The primary outcome measure for this study is maximum aerobic capacity during exercise testing. There will also be measures of muscle strength, body composition, and activity levels. In addition the study will investigate non-motoric effects of exercise such as mood, motivation, sleep and fatigue.

Open Trials

EXERCISE TRAINING IN PATIENTS WITH MITOCHONDRIAL DISEASE: ASSESSING THE BENEFITS
Status: Recruiting
Sponsor: University Newcastle
Funder: Muscular Dystrophy Campaign (MDC)
PI: Prof Turnbull
Collaboration site MRC Centre London (Hanna)
Patients recruited: 6- 5 Newcaslte 1 London
Mitochondrial myopathies are a very important group of muscle diseases associated with weakness, pain and fatigue. At present, treatment options are very limited.
Exercise therapy has been found to have some benefit in this group of patients and we wish to explore this further in terms of both strength and endurance.
The aim of this study is to demonstrate that strength exercise training is an effective approach to therapy in certain patients with mitochondrial myopathy, specifically those with sporadic mutations in mitochondrial DNA. Based on our previous research studies, we believe that such training will improve muscle strength, mitochondrial function, exercise tolerance and overall quality of life.
The main objectives will be:
To confirm that endurance training in patients with mitochondrial abnormalities improves quality of life, exercise tolerance and oxidative capacity.
To determine the ability of resistance muscle strength training to improve skeletal muscle strength and oxidative capacity by incorporation of satellite cells into mature myofibres.
Participants are expected to commit to an exercise training and testing over a period of 4 to 8 months.
The study will include patients between the ages of 18 and 65 years who have had a previous muscle biopsy showing a defect in skeletal muscle mitochondrial DNA that is either in the form of a sporadic point mutation or single large-scale deletion. Patients who have this type of mutation and do not have any family members that are affected and have no major cardiac involvement, hypertension, pulmonary or peripheral vascular disease that may complicate findings.
For information about recruitment contact Geoff Bell at geoff.bell@nuth.nhs.uk or Dr Robert Pitceathly at r.pitceathly@ion.ucl.ac.uk.

CARDIAC ADAPTATIONS TO EXERCISE IN MITOCHONDRIAL DISEASE
Status: Recruiting
Sponsor: Newcastle upon Tyne Hospitals NHS Foundation Trust
Funder: MRC
PI: Prof D M Turnbull/Dr MI Trenell,
Patients recruited: 9; target 24
Twenty four people with mitochondrial disease will take part in the study. Participants will undergo cardiac, cognitive and movement examination and then they will be randomised into two groups. They will receive either; exercise counselling and support (n = 12) or continue standard care (n = 12) over a 16 week period. At the end of the 16 week period baseline measures will be repeated. Participants to be studied will have biopsy proven mitochondrial disease (age 18−60 years; BMI 20−35 kg/m2; and do not take part in regular exercise). Subjects with heart disease that would produce an adverse response to exercise will be excluded. Subjects with significant kidney disease or in vivo ferrous material will be excluded also as these are contra-indications to the use of gadolinium-based contrast agents and magnetic resonance imaging respectively. Magnetic resonance and echocardiographic evaluation of cardiac function as well as movement and cognitive function will be assessed a

at baseline and at 16 weeks. A progressive exercise test will be undertaken at baseline to establish maximal aerobic capacity and evaluate for an adverse response to exercise.
The patient exercise group will be matched with a control group of individuals without known mitochondrial disease who will undergo the same evaluation and training regime (n = 12). In total, the study will require each participant to attend the research facility for three visits for metabolic examination. The exercise groups will be requested to attend 48 exercise sessions over 16 weeks.
For information about recruitment contact Geoff Bell at geoff.bell@nuth.nhs.uk.

PHYSICAL ACTIVITY AND INCLUSION BODY MYOSITIS
Status: Recruiting
Sponsor: Newcastle upon Tyne Hospitals NHS Foundation Trust
Funder: MRC
PI: Dr M Trenell
Collaborating site MRC Centre London
Recruitment: 500 recruits expected, across 5 disease sites (all not open yet), stroke arm has 36 recruited, 100 expected
The aim of this study is to collect data on day to day physical activity levels and metabolic control in individuals with chronic disease.
DESIGN:
Participants will be identified from chronic disease clinics by the following lead clinicians: Stroke-Prof Gary Ford, Neuromuscular disorders-Prof Kate Bushby, Metabolic disorders-Prof Roy Taylor, fatigue-Prof Julia Newton and Ageing-Prof Julia Newton. An equal sample of male and female participants will be used in the study which will be up to 100 patients in each disease group.
METHODOLOGY:
Step 1: Relevant practitioners will highlight possible candidates for the study.
Step 2: Visit 1: At the start of the study participants will either be asked to attend Newcastle University's Campus for Ageing and Vitality (Newcastle General Hospital), or if they are an inpatient will be visited on the ward. Participants will be provided with an information sheet about the study. They will be given the opportunity to talk with the team and ask questions. Once fully informed, participants will provide signed informed consent.
Participants will be asked to fill in a disease screening questionnaire at the start of the process. The height and weight of the participants will be recorded and this information will be entered into the physical activity monitors. Instructions will be provided as to how to use the monitors. A resting blood sample may also be taken at this point. This will be analysed for glucose, insulin, lipid profile and liver function.
Step 3: Participants will wear the arm monitors for five days including one weekend day.
Step 4: Visit 2: At the end of the five day period participants will attend the research centre again or attend a pre-arranged session either at their home work place or on the ward to return the activity monitor. Here they will complete a brief physical activity questionnaire and two brief fatigue questionnaires. Data from the physical activity monitor will be fed into a computer. Each participant will be provided with a printout of their weekly activity levels and given the opportunity to discuss their results.
For information about recruitment contact Geoff Bell at geoff.bell@nuth.nhs.uk.

EXERCISE AND SARCOPENIA
Status: Recruiting
Sponsor: Newcastle upon Tyne Hospitals NHS Foundation Trust Funder: MRC
PI: Prof DM Turnbull
Collaborating site MRC Centre London
Patients recruited: 0; target: 36

Sarcopenia, which is a complex multifactor process, has significant implications on quality of life, performance of daily activities, maintenance of independence and on projected healthcare costs.

Studies show that low physical activity correlates with poor mitochondrial function. Conversely, exercise correlates with better mitochondrial function, clinical improvement and improved perceived quality of life. Endurance training has been proven to be safe and efficacious in mitochondrial disease which may provide a model for the aging process albeit in an accelerated form with biochemical, histological and genetic changes seen in aged muscle also found in various mitochondrial conditions.

Aims:

1.To assess the rate and extent of motor unit loss in the eighth decade of life- cross-sectional (time 0) and longitudinal analysis (end of study)2.To correlate the extent of motor unit loss with histological correlates and the development of sarcopenia3 To assess the impact of exercise on the rate and extent of motor neuron loss

4.To observe whether endurance training initiated in late middle age prevents loss of muscle strength and mass in senescence

5.To assess the impact of neuronal loss on the inability to retain gains made in muscle strength following training after the 7th decade of life

6.To characterise effects of exercise upon neural activity, muscle oxidative capacity and mitochondrial and satellite cell plasticity with age.

Method:

Thirty six (36) female participants, matched for body mass index who do not take regular exercise will be invited to participate: 40- 45 years (12), 60-65 years (12) and 80- 85 years (12). Inclusion criteria will be capacity to undertake cycling exercise and ability to give informed consent. Exclusion criteria will be co-existing active coronary artery disease or steroid therapy.

These patients will be recruited via the media and social support groups. All expenses (travel, accommodation and meals) will be paid for from the research grant.

The study will take place over 24 weeks. Participants will attend the study centre for 7 visits in total. The study will include 2 main visits at the beginning and end of the study. Each main visit will last 3 days. There will also be 5 one day visits.

For information about recruitment contact Geoff Bell at geoff.bell@nuth.nhs.uk.

Closed Trials

STRENGTHENING HIP MUSCLES TO IMPROVE WALKING DISTANCE IN PEOPLE WITH CHARCOT- MARIE-TOOTH DISEASE

Status: Completed

Sponsor: University College London Hospitals
Funder: Muscular Dystrophy Campaign (MDC)
PI: Dr. Reilly
Patients recruited: 32

Charcot-Marie-Tooth (CMT) disease is a form of hereditary peripheral neuropathy.

People with CMT present with weakness, wasting and sensory loss as a result of degeneration of the long peripheral nerves supplying the distal muscles. The aim of this study will be to investigate the efficacy of a 16 week home based programme of training to increase hip flexor muscle strength and walking endurance. Additional measures of gait speed, exertion, fatigue, disability and general activity will also be recorded. Baseline impairment measures will be obtained to ascertain predictors of strength gains.

This study will use a single blinded, randomised cross over design to investigate if training the hip flexor muscles will strengthen the hip flexor muscle and improve walking endurance in people with all types of CMT.

The trial will include people aged between 18 and 70 years, who have been diagnosed with CMT on the basis of genetic tests (where possible), family history and neurophysiology testing. Each subject will be involved with the study for a 40 week period.

Imaging Studies

Set-Up Phase

None

Open Trials

MRI IN IBM AND CMT

Full Title: A Study of Quantitative Magnetic Resonance Imaging and the Clinical Features of Inclusion Body Myositis and Charcot Marie Tooth Disease

Status: Open to recruitment

Sponsor: University College London Hospitals

Funder: MRC

PI: Prof T Yousry/Dr J Thornton

Patients recruited: 52; target 80

Magnetic resonance imaging (MRI) is a key tool in the diagnosis and management of a number of diseases. Despite the wide use of MRI in several clinical settings, so far its role in neuromuscular disease has not been well established. The current standard for the diagnosis of neuromuscular disorders includes clinical examination, electrophysiological investigations, biopsy and genetic testing. Due to the nature of the involvement of prominent muscles and peripheral nerves in these disorders it is proposed that MRI could play a prominent role in understanding of neuromuscular disease.

This study aims to investigate the use of MRI as a tool in the study of nerve and muscle diseases by focusing on two particular neuromuscular diseases, one primarily neuropathic and one principally myopathic. Two separate patient cohorts with neuromuscular disease will be recruited. Forty patients with Sporadic Inclusion Body Myositis (IBM) and 40 patients with genetically confirmed Charcot Marie Tooth Disease (CMT). In addition to the two patient cohorts, two groups of healthy volunteers each of size 40 will act as comparators for the disease groups. Each of the patients enrolled in the study will undergo an MRI scanning session in which the quantitative MR techniques developed in Phase 1 with the health volunteers will be applied. In addition to the MRI scanning sessions, each patient will undergo a clinical examination to record the main clinical features of their disease status including an electrophysiological nerve conduction assessment. In the final phase of the study, a sub-group of the patients will then be followed-up at 6 month intervals for 5 years in a longitudinal natural history study of IBM and CMT that focuses on the MR methods and clinical findings that were shown to be most illuminating.

Changes over time in the MRI parameters in the diseased groups and Healthy volunteers will be compared.

Objectives:

To detect, using quantitative magnetic resonance imaging (qMRI), the changes in the nerves and muscles of patients with inclusion body myositis or Charcot Marie Tooth disease, and to relate these changes to the measurable clinical and neurophysiological features in these

diseases. This will allow the value of various qMRI techniques as markers of disease activity and progression to be tested.

Secondary objectives of the study include:

The development of novel quantitative MR techniques for targeted assessment of the human neuromuscular system.

To more fully characterise both the magnetic resonance imaging and clinical features of inclusion body myositis or Charcot Marie Tooth disease as compared with healthy individuals and to study the progression of these characteristics with time over a period of 5 years.

For more information about the study please contact Dr Jasper Morrow at j.morrow@ucl.ac.uk.

MRI IN FKRP-RELATED LGMD2I

Full-Title: A study using Magnetic Resonance Imaging (MRI) and Magnetic Resonance Spectroscopy (MRS) in Patients with Limb Girdle Muscular Dystrophy 2I; an assessment of muscle damage.

Status: Open to recruitment

Sponsor: Newcastle NHS Trust

Funder: MRC

PI - Prof V Straub

Re-defined in 1995, the LGMDs are face-sparing, proximally predominant, progressive muscular dystrophies with elevated creatine kinase levels and dystrophic features on muscle biopsy. In the current classification system, LGMDs are divided into autosomal dominant (LGMD1) and autosomal recessive (LGMD2) disorders with a superimposed lettering system denoting the chronological order of the chromosomal linkage.

Limb Girdle Muscular Dystrophy 2I (LGMD2I) is caused by a mutation in the fukutin related protein gene (FKRP)1 and manifests temporal variability. Clinically the age of onset, rate of progression and severity varies greatly between cases and even within the same family. They range from asymptomatic patients with mildly raised creatine kinase levels to those severely affected and non ambulant. The respiratory and cardiac complications, well known to occur in this type of muscular dystrophy, in 30% and 60% of patients respectively, occur independently of the general muscle weakness and also cardiac complications occur independently from respiratory compromise.

Magnetic Resonance imaging (MRI) has been increasingly used in imaging in patients with neuromuscular disorders over the past 5 years.

•Studies have shown that whilst there is considerable overlap in muscle involvement there is also striking differences that can be of diagnostic value. In both patients with LGMD2A and LGMD2I there is a prominent pattern of involvement of the posterior thigh muscles, however in LGMD2A there is also selective involvement of the medial gastrocnemius and soleus muscles in the lower leg, which was not seen in LGMD2I. Although it is clearly demonstrated that MRI findings mirror those obtained from clinical examination, it has been reported recently that in fact MRI abnormalities can be detected in patients with neuromuscular disorders when clinical examination of particular muscle groups have been normal. MRI can therefore be useful to show early manifestations of a disease and to monitor the effect of early therapeutic interventions.

•Beside MRI another non-invasive technique to consider is phosphorus magnetic resonance spectroscopy (P-MRS). P-MRS studies have demonstrated several metabolic abnormalities in the skeletal muscle of patients with Duchenne Muscular Dystrophy (DMD)/ Becker Muscular Dystrophy (BMD) and in the group of autosomal recessive LGMDs, associated with sarcoglycan deficiency (LGMD2C-F) . These changes are thought to be specific for

dystrophies secondary to deficits in the dystrophin-glycoprotein complex. In these patients there appears to be an increased cytosolic pH in both groups, however there is also abnormal concentrations of phosphorylated compounds (in particular, decreased phosphocreatine and increased inorganic phosphate concentrations). The study overall aim is to develop and evaluate non-invasive techniques to quantify muscle pathology and the rate of change over time in LGMD2I, which is potentially a useful tool for monitoring response to treatment and therapies. This shall be achieved by measuring static MRI over a 2 year period and comparing this to age matched adult controls including the quantitative 3-point Dixon technique for measuring fat. At the same time we will also be measuring the Pi and cytosolic pH, ATP and ADP via MRS to see whether a specific pattern of metabolic abnormality is detected in these patients.
For further information about the study please contact Dr. Jasper Morrow at j.morrow@ucl.ac.uk.

Future Meetings

MRC Centre for Neuromuscular Diseases / Muscular Dystrophy Campaign UK Translational Research conference 2012

Thursday 22nd & Friday 23rd March 2012

International Centre for Life, Newcastle

Contact Zoë Scott on z.scott@ucl.ac.uk for further details

Date of BMS Annual Meeting 2012:

tbc

Industry Sponsor:
Genzyme

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http://www.cnmd.ac.uk/British_Myology_Society
http://www.myology.org.uk/

RCP CPD approval has been applied for
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BMS 2011 Conference brochure prepared by
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