Contents

Welcome from the British Myology Society Council

Dear Member,

We are delighted to welcome you to this sixth meeting of the British Myology Society at Wolfson College in Oxford.

This year the council have again devised a programme which continues to build on the themes covered in the first five meetings. We are delighted that Professor Doug Turnbull will be our after-dinner speaker.

In addition to the BMS Annual meeting, this year the BMS is proud to introduce its first 'UK Clinicians Muscle Teaching Day', taking place on 11th September.

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

The 2014 organising committee:

Kate Bushby
Michael Hanna
David Hilton-Jones
Janice Holton
Francesco Muntoni
Richard Petty
Ros Quinlivan
Helen Roper
Michael Rose
Caroline Sewry
Simon Hammans

The History of the British Myology Society

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 holds registered charitable status (number 1142966). The Society's rules can be found later on within this brochure.

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

Our Fifth Annual Meeting took place on 18th and 19th September 2013 at Worcester College, Oxford.

The key themes that were covered included:

- Commissioning neuromuscular services in the UK
- Myotonic Dystrophy
- Congenital Myopathy
- Muscle Interest Group difficult cases

Invited speakers included Professor Charles Thornton, University of Rochester, USA

Our Fourth Annual Meeting took place on 4th & 5th of September 2012 at St Anne's College, Oxford.

The key themes that were covered included:

- Commissioning neuromuscular services in the UK
- Duchenne
- Pathology services
- Rhabdomyolosis
- Muscle Interest Group difficult cases

Our Third Annual Meeting took place on Tuesday 6th & Wednesday 7th of September 2011 at St Anne's College, Woodstock Road, Oxford.

The key themes that were covered included:

- Commissioning neuromuscular services in the UK
- Registries and Databases
- Patient Organisations
- Myasthenia
- Muscle Interest group difficult cases

Invited speakers were Dr Mike Hubank –UCL genetics and Professor Alan Emery.

The Second Annual Meeting of the BMS was held on Thursday 2nd & Friday 3rd September 2010 at St. Anne's College, Oxford.

Key themes 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

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

The first annual meeting of the BMS took place on 2nd & 3rd July 2009 at St Anne's College, Oxford.

Key themes covered in the interactive sessions included:

- Commissioning neuromuscular services in Great Britain and Ireland
- Planning muscle pathology services for the UK and Ireland
- Update on current neuromuscular NCG services including NCG support to diagnose difficult cases
- Update from UK neuromuscular workshops (including IBM, MG) 2008
- Developing clinical networks/clinical trials

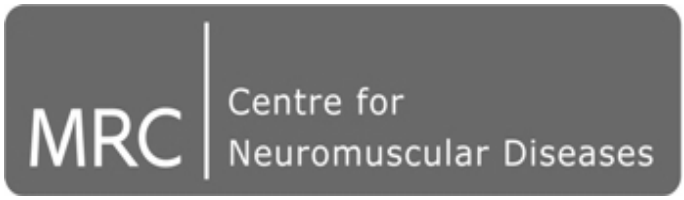
We were delighted that Professor Robert C Griggs, President of the American Academy of Neurology appeared as our guest speaker, and provided insights into his long experience of running the North American Muscle Study Group.

Running the BMS

At present the secretariat for the BMS is located at and sponsored by the MRC Centre for Neuromuscular Diseases in London as per an agreement made at the 2010 AGM.

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 MRC Centre was established in 2008 and has been successfully renewed by the MRC until 2018- its aims remain 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, MRC Biobank to increase availability of patient tissues and cells for preclinical science, assessing animal models, applying MRI to humans and animals and dedicated clinical and non-clinical PhD programmes to developing a cadre of highly trained scientists and clinician scientists for future nm disease research.

Professional and Patient Organisation Partners

2014 MEETING PROGRAMME

Location:
Wolfson College, Linton Road, Oxford OX2 6UD

Thursday 11th September

16:30-17:00 **Registration and Tea**

Session 1
Chair: Michael Hanna

17:00-17:10 **Welcome and introduction**
Professor Michael Hanna, Director, UCL Institute of Neurology and MRC Centre for Neuromuscular Diseases

17:10-17:20 **Muscular Dystrophy Campaign & service developments**
Robert Meadowcroft, Chief Executive, Muscular Dystrophy Campaign

17:20-17:50 **Enabling independence in the profoundly disabled**
Dr David Henderson-Slater, Nuffield Orthopaedic Centre

17:50-18:20 **The role of the rehabilitation team in NMD patient care**
Dr Margaret Phillips, University Hospital, Derby

18:20-18:50 **'Bridging the gap' an NHS England funded project**
Nic Bungay and Bobby Ancil, Muscular Dystrophy Campaign

18:50-20:00 **AGM**
Feedback from the BMS council (10 mins each)
BMS rules and Aims/ attracting new membership: Professor Mike Hanna
Training day for trainees: Dr Simon Hammans/ Dr David Hilton-Jones
Workforce planning: Dr Richard Petty
Neuromuscular curriculum: Dr Helen Roper
Standards of Care: Dr Michael Rose
Muscle pathology services: Professor Caroline Sewry/ Dr Janice Holton
North Star forms: late non-ambulant: Dr Ros Quinlivan

20:00 **Dinner at Wolfson College**

21:00 **After-dinner talk**
Professor Doug Turnbull

2014 Meeting programme contd…

Friday 12th September

Session 2
Chair: Simon Hammans

08:30-09:00 **Muscle Channelopathies; diagnosis and management**
Professor Mike Hanna, Institute of Neurology

09:00-09:30 **Diagnosis and management of DM2: Experience from Germany**
Professor Benedikt Schoser, Ludwig-Maximilians University of Munich

09:30-10:00 **An update on the Congenital Myasthenic Syndromes**
Professor David Beeson, University of Oxford

10:00-10:30 **Coffee**

Session 3
Chair: Ros Quinlivan

10:30-11:00 **Myofibrillar Myopathies: from patients to cell and animal models and back again**
Professor Rolf Schroeder, University of Erlangen

11:00-11:30 **An update on Mitochondrial Disease**
Professor Doug Turnbull, University of Newcastle

11:30-12:00 **Oculopharyngeal Muscular Dystrophy**
Dr Simon Hammans, Southampton General Hospital

12:00-12:30 **Adult DMD and North Star Network**
Professor Katie Bushby and Dr Ros Quinlivan

12:30-13:30 **Lunch**

Muscle Interest Group Session
Chair: Helen Roper

13:30-15:30 **MIG case discussions**

15:30-16:00 **Tea / Close**

16:00 OXFORD MUSCLE MEETING (pls contact D Hilton-Jones or Monica Hofer)

BMS Council

Kate Bushby	University of Newcastle	kate.bushby@newcastle.ac.uk
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Michael Hanna	Institute of Neurology, UCL	m.hanna@ucl.ac.uk
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Francesco Muntoni	Institute of Child Health, UCL	f.muntoni@ich.ucl.ac.uk
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Helen Roper	Heartlands Hospital	helen.roper@heartofengland.nhs.uk
Michael Rose	King's College Hospital	m.r.rose@kcl.ac.uk
Caroline Sewry	Institute of Child Health, UCL & RJAH, Oswestry	c.sewry@nhs.net

BMS Delegates 2014

Bobby Ancil	Muscular Dystrophy Campaign	b.ancil@muscular-dystrophy.org
Rita Barresi	Newcastle NHS Trust	rita.barresi@newcastle.ac.uk
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Marianne de Visser	University of Amsterdam	m.devisser@amc.uva.nl
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Simon Hammans	University Hospital Southampton	Simon.Hammans@uhs.nhs.uk

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David Hilton-Jones	John Radcliffe Hospital	david.hilton-jones@ndcn.ox.ac.uk
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Stefan Spinty	Alder Hey Children's Hospital	stefan.spinty@alderhey.nhs.uk
Antonia Torgersen	Western General	antonia.torgersen@nhs.net
Doug Turnbull	Newcastle University	doug.turnbull@newcastle.ac.uk
Chris Turner	NHNN / UCLH	chris.turner@uclh.nhs.uk
Stuart Viegas	Imperial College Healthcare Trust	stuart.viegas@nhs.net
Tracey Willis	The Robert Jones and Agnes Hunt Orthopaedic Hospital	tracey.willis1@nhs.net

Rules of the British Myology Society

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 organizations

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 one member of the Association in writing to the Honorary Secretary (including email) by the time of the last Council Meeting prior to the Annual General Meeting.

10. The Council shall approve candidates from those nominated as Ordinary or Honorary Members.

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 seven 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 and working groups.

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 five years following which there will be re-election or renewal for a second term. 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 organization.

Previous 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 of the 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 Genzyme 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

Minutes of the 2011 AGM:

8.15pm, 7th September, St Anne's College Oxford

Apologies
Doug Turnbull, Doug Wilcox, Kate Bushby, Francesco Muntoni

Present
Mike Hanna, David Hilton-Jones, Helen Roper, Janice Holton, Peter Baxter, Caroline Sewry, Nick Gutowski, Paul Maddison, Cheryl Longman, Matt Parton, Fiona Norwood, Richard Petty, Margaret Phillips, Heinz Jungbluth, Rita Barresi, Richard Orrell, Elizabeth Wraige, Lucy Feng, Stefan Spinty, Georgina Burke, James miller, Adnan Manzur, Aleksandar Radunovic, Chris Turner, Rahul Phadke, Ros Quinlivan, Max Damian, Charlotte Dougan, Jennifer Dunne, Waney Squier, Yvonne Robb, Mark Rogers, Simon Hammans, Stephanie Robb.

Minutes of the 2010 AGM:
These were accepted as a correct record of the meeting.

Charitable status confirmed
The BMS has been successfully registered as a charity with the Charity Commission. The Charity Commission require that the BMS holds an AGM. The main advantage of charity registration is the VAT exemption which will reduce the cost of annual meeting registration for delegates, and gives the BMS status as a legal entity.

Accounts
At the 2010 AGM it was agreed that a small membership fee of £25 would be introduced, which has now been implemented. In previous years the annual meeting ran at a loss which was absorbed by the MRC Centre for Neuromuscular Diseases, but the BMS is now in balance, as costs have been covered by the membership fee, registration fees and Genzyme sponsorship.

Joint Neuroscience Council & links to other professional organisations
Links have been formed with the ABN (David Hilton-Jones is Chair of a sub-committee), and the BMS is now a member of the Joint Neuroscience Council, an umbrella organisation of neuroscience organisations which has now been running for five years. It was reported that Francesco Muntoni has made links with the British Paediatric Neurology Association. Caroline Sewry and Janice Holton have made links with the British Neuropathology Society which will be strengthened as Janice will soon be more involved with training-related matters.

Re-elections
A Doodle vote was undertaken after last year's annual meeting as to whether we should continue to hold the meeting in Oxford, and it was agreed that this should be the case until at least 2012. It was agreed that in future years the annual meeting could rotate around the country. It was agreed that Council membership would be discussed separately, and that Mike Hanna would write to the eleven members to see if they wished to remain on the Council after

their first three-year term. Mike Hanna will inform members of any changes in personnel. Caroline Sewry suggested Federico Roncaroli as he is strongly involved with neuropathology training.

Date of next year's meeting
The 2012 annual meeting will be held around this time of year. Mike Hanna agreed to take on board the fact that the 2011 annual meeting had an intense programme on the first day. The meeting will start at around 3pm and finish at 6.30pm with more time prior to dinner.

CPD Approval

The 2011 meeting has been recognised by the RCP for CPD approval, and Zoë Scott will email certificates of attendance after the meeting.

AOB
None

Minutes of the 2012 AGM:

Wednesday, September 5th 1.40pm

Agenda

1. Minutes of previous AGM

2. Accounts

3. Rules of the Society

4. Council Membership

5. AOB

Minutes of AGM

1. Minutes of Previous AGM

   - The minutes of the previous AGM were agreed

2. Accounts

   - Prof Mike Hanna reported that in the first few years the BMS ran at a loss and was underwritten by the MRC Centre. Members then later agreed a £25 membership fee and a meeting fee which together cover the cost of running the meeting.
   - Prof Hanna asked if the £25 membership fee was okay to continue for 2013. This was agreed by the AGM.

3. Rules of the Society

   - There were no changes to the rules for 2012-13

4. Council Membership

- Those council members standing down were thanked for their efforts in support of the BMS.
- Mike Hanna formally welcomed new council members Simon Hammans and Ros Quinlivan.

5. AOB

- Mike Hanna added that the BMS Council's main responsibility is the planning of the annual meeting. The aim for the meeting continues to be that it remains useful to clinicians and scientists working in neuromuscular diseases, and to update and inform them on commissioning and clinical practice.

- David Hilton-Jones agreed to continue as the BMS's sponsor in Oxford.
- Mike Hanna invited all members to suggest a new meeting location.
- Ros Quinlivan asked if the BMS has a strategy for inviting new members.
- Mike Hanna responded that it would be very helpful if all members let any colleagues who weren't current members know about the Society
- Mike Hanna added that the society has a public website.

Minutes of the 2013 AGM

Wednesday, September 18th 8pm

Agenda

1. Minutes of previous AGM

2. Accounts

3. Secretariat

4. Rules of the Society

5. Council Membership

6. BMS Annual Meeting 2014

Minutes of AGM

1. Minutes of Previous AGM

- The minutes of the previous AGM were agreed

2. Accounts

- Prof Mike Hanna reported that the BMS was running close to break even and that the AGM this year was part-funded by sponsorship of £2000 from Genzyme
- Prof Hanna asked if the £25 membership fee was agreed to continue for 2014. This was agreed by the AGM.

3. Secretariat

- Christine Oldfield was introduced as administrator of the BMS

4. Rules of the Society

- MH reported that following the 4th Sept Council Meeting, which all Council members attended, rules changes were to be put forward as follows:

  1) Rules will be changed to reflect that there will be council members with responsibility in each of the following areas:

  Trainee day 2014
  Algorhythm and App development
  Workforce mapping
  Standards of care
  Pathology

  2) Rules will be changed to reflect the importance of PPI to be co-opted onto subgroups
  3) Council members will be able to sit for 5 years rather than 3 and that 2 consecutive term may be served.

- All rule changes above were agreed.

5. Council Membership

- There were no changes in Council membership this year

6. BMS Annual Meeting 2014

- Mike Hanna invited all members to suggest a new meeting location
- Mike Hanna invited all members to offer to take on organization and hosting of the meeting, nothing that the organizing parties would need to provide secretarial support for the meeting organization.
- Provisional dates for next year's meeting were given as 11/12th September, with the possibility of running the meeting back to back (with some overlap) with the University of Oxford muscle meeting. It was agreed this would be the broad plan if no alternative proposed in next three weeks.
- MH reported that the Council had discussed adding a training day to the BMS annual meeting.

6. AOB

- In addition to the above, MH reported the following items as points of discussion from the BMS Council meeting of Sept 4th
    - There was interest in recruiting more junior members to the BMS
    - David Hilton-Jones mentioned looking further into developing an algorhythm for managing myasthenia, to be made into an app for trainee / junior neurologists. FM suggested liaison with the Jane foundation as they had something similar for congenital myopathies.
    - MH reported that Michael Rose had raised the issue of developing Standards of care.
    - Neuromuscular training curriculum
    - Ros Quinlivan mentioned investigation of Manpower in terms of trainees and neuromuscular services – Katie Bushby reported that some work had already been done by TreatNMD using existing European and US work and that it would be interesting to look at getting this work used more widely by Universities and Colleges
    - MH reported that the council would meet again in 4 or 5 months.

Agenda for 2014 AGM:

1. Minutes of previous AGM
2. Accounts
3. Secretariat
4. Rules of the Society
5. Council Membership
6. BMS Annual Meeting 2015

Current UK Neuromuscular Clinical Trials

MRC Centre CTIMPs Set-up Phase trials

1. A Phase 3, Randomized, Double-blind, Sham-Procedure Controlled Study to Assess the Clinical Efficacy and Safety of ISIS 396443 Administered Intrathecally in Patients with Infantile-onset Spinal Muscular Atrophy
Sponsor: ISIS PHARMACEUTICALS, INC.
PI: Francesco Muntoni
Target patient number; 2-3 recruited to date 0
This randomized, double-blind, sham-procedure controlled study will test the clinical efficacy, safety, tolerability, and pharmacokinetics of intrathecal ISIS 396443 over 13 months. Approximately 111 subjects will be randomized in a 2:1 ratio (74 ISIS 396443: 37 control) to receive ISIS 396443 by intrathecal lumbar puncture (LP) injection or to a sham-procedure control. A scaled equivalent dose of 12 mg ISIS 396443 will be given at each of 6 times (i.e., on Study Days 1, 15, 29, 64, 183, and 302).

2. A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Multiple-Dose Study To Investigate The Safety, Tolerability, Pharmacokinetics, And Pharmacodynamics Of Ro6885247 Following 12 Weeks Of Treatment In Adult And Pediatric Patients With Spinal Muscular Atrophy (Moonfish)
Sponsor: ROCHE
PI: Francesco Muntoni
Target patient number; 5-8, recruited to date 0
This is a multicenter, randomized, double-blind, 12-week, placebo-controlled multiple dose Phase Ib study to investigate the safety, tolerability, pharmacokinetics, and pharmacodynamics of RO6885247 in adult and pediatric patients with SMA.

3. A multicenter, randomized, double-blind, placebo controlled efficacy and safety trial of intravenous zoledronic acid twice yearly compared to placebo in osteoporotic children treated with glucocorticoids
Sponsor: Novartis
PI: Francesco Muntoni
Target patient number; (unknown to me) recruited to date 0
Evaluate the efficacy and safety of zoledronic acid plus vitamin D and calcium compared to placebo plus vitamin D and calcium in osteoporotic children treated with glucocorticoids. The primary efficacy objective of the study is to demonstrate that zoledronic acid administered every 6 months 0.05 mg/kg (max 5 mg) is superior to placebo for the change in lumbar spine (LS) areal bone mineral density (BMD) Z-score at Month 12 relative to baseline.

4. A Phase 3 Extension Study Of Ataluren (Ptc124) In Patients With Nonsense Mutation Dystrophinopathy (PTC20e –PTC 20 is being extended)
Sponsor PTC therapeutics
PI: Francesco Muntoni
Target patient number 6-9; 0 recruited to date
Primary Objective To evaluate the long-term safety of ataluren in boys with nonsense mutation dystrophinopathy, as determined by adverse events and laboratory abnormalities. All previously enrolled in PTC20 will be eligible to enter the extension.

5. A 2-Part, Randomized, Double-Blind, Placebo-Controlled, Dose-Titration, Safety, Tolerability, and Pharmacokinetics Study (Part 1) Followed by an Open-Label Efficacy and Safety Evaluation (Part 2) of SRP-4053 in Patients with Duchenne Muscular Dystrophy Amenable to Exon 53 Skipping
Sponsor: Sarepta Therapeutics, Inc, EU Grant
PI: Francesco Muntoni
Target patient number; 12 patients (GOSH) 48 total: recruited to date 0
This is a first-in-human, multi-center, multiple-dose study to assess the safety, tolerability, efficacy, and pharmacokinetics of once weekly IV infusions of SRP-4053 in patients with genotypically-confirmed DMD with an eligible deletion(s) amenable to exon 53 skipping (e.g. 42-52, 45–52, 47–52, 48–52, 49–52, 50–52; 52; 54-58).

6. SMT C11003 - A placebo-controlled, multi-centre, randomized, double-blind, 3-period dose escalation study to evaluate the PK and safety of SMT C1100 in paediatric patients with Duchenne muscular dystrophy (DMD) who follow a balanced diet.
Sponsor:Summit Corporation plc
PI: Francesco Muntoni
Target patient number; 12 patients, 4 (GOSH) recruited to date 0
This is a 3-period 3-group 3-treatment study. Up to 15 boys with DMD (with a view to obtaining data on 12) will be enrolled onto this placebo controlled study of single and multiple oral doses of SMT C1100.
Primary Objective: To determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD who follow a balanced diet.

7. 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 Gisela Barreto, Trials Coordinator at Gisela.barreto@uclh.nhs.uk.

8. A Pilot Study of Valproate Sodium for McArdle Disease
Status: Set-up phase awaiting R&D
Sponsor: UCL

Planned start date: 2014
Funder: Muscular Dystrophy campaign
PI: Prof. Ros Quinlivan
Recruitment 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.

A recent clinical trial of the drug in McArdle sheep that were given sodium valproate for three months showed the presence of phosphorylase positive muscle fibres, in the absence of muscle necrosis and/or regeneration [Howell 2010].

The current proposes an open label uncontrolled pilot study to evaluate safety and efficacy of Sodium valproate (slow release) 20mg /kg once daily for six months. 15 subjects, adult male and post-menopausal women attending specialist centres for McArdle disease will be recruited across three sites: London, Copenhagen and Dallas.

9. Eplerenone versus triamterene in CAI non-responsive periodic paralysis (HOP Study)
Status: Set-up phase
Sponsor: UCL
Funder: MDA
Planned start date: TBC
PI: Michael Hanna
Recruitment target: 11

There have been no previous systematic investigations of patients with hypokalemic periodic paralysis who fail to respond or are worsened by carbonic anhydrase inhibitors. The initial impression that only 10-15% of patients fall into this category now appears erroneous (Matthews, Portaro et al. 2011, Neurology). Approximately 50% of genetically-confirmed patients with periodic paralysis do not derive sufficient benefit to remain on treatment. By pursuing a pilot study of alternative treatments for this subgroup of patients we hope to start addressing what is arguably the greatest need of the community of patients with the periodic paralyses.

Specific Aims

1) To obtain preliminary efficacy data of triamterene and eplerenone in HOP patients unresponsive to or unable to tolerate carbonic anhydrase inhibitors. To achieve these aims, we will perform an 18 week, 2 centres, randomized, double-blind, placebo controlled crossover pilot trial with eplerenone and triamterene versus placebo in CAI non-responsive HOP patients. Patients with clinically well documented HOP who have defined mutations in the Na or Ca channels and who have worsened with, not responded to or not been able to tolerate CAI, will be studied. Following a 4 weeks run in period (phase 1) 22 patients will receive 4 weeks placebo, 4 weeks eplerenone and 4 weeks triamterene in a randomized fashion. Each 4 weeks period will be separated by a 1 week washout period. Improvement in attack rate, severity weighted attack rate, and quality of life will be measured.
2) To select the drug, triamterene or eplerenone, with the optimal efficacy and adverse effect profile for a future larger trial.

10. Bumetanide in HypoPP
A randomised, double-blind, placebo-controlled, phase II clinical trial with a cross-over design assessing efficacy of a single dose of bumetanide in reducing focal attack severity in hypokalaemic periodic paralysis assessed using the McManis protocol
Status: Set-up phase/ REC/MHRA approved
Sponsor: UCL
Funder: TBC
Planned start date: September 2014
PI: Doreen Fialho
Recruitment target: 12

This is a planned phase II clinical trial, double-blind, randomised, placebo-controlled cross-over, single-site study to investigate the efficacy of bumetanide in patients with hypokalemic periodic paralysis (HypoPP). The objective is to assess the efficacy of bumetanide in reducing severity and duration of acute attacks of weakness in HypoPP patients. Hypokalaemic periodic paralysis is an autosomal dominant muscle channelopathy with onset in the first or second decade, characterized by attacks of reversible flaccid paralysis lasting from several hours to days. These patients may have frequent attacks of weakness interfering with daily activities and work, and are often hospitalized for intravenous potassium treatment causing a significant economic burden. They may also progress to a chronic myopathy especially because there are no optimal treatments available nowadays.
Experimental evidence of the use of bumetanide in a mouse model of HypoPP has provided convincing evidence that it can abort paralytic attacks.

We would expect bumetanide to abort acute attacks of weakness faster and reduce their severity, reducing the likelihood of patients being hospitalized during severe attacks. Bumetanide will add as an adjuvant therapy to potassium intake during an attack.

11. A phase IIb/III of Arimoclomol in IBM
Status: Set-up phase
Sponsor: UCL
Funder: FDA/Orphazyme (TBC)
Planned start date: TBC
PI: Doreen Fialho
Recruitment target: 150
(This is a follow-up of the phase IIa RCT study concluded in 2012)
We are proposing a one year randomized, placebo-controlled Phase IIb/III study of arimoclomol in 150 IBM subject. The primary aim is to assess the efficacy and safety of arimoclomol (200 mg TID). The primary efficacy endpoint is the IBMFRS. Secondary efficacy outcomes will include different measures of strength and function: manual muscle testing (MMT), maximum voluntary isometric contraction (MVICT), timed up and go (TUG), timed 10 meter walk test, 6 minute walk test, Purdue pegboard test, grip and pinch test; a general physical function measure: Health Assessment Questionnaire (HAQ- DI); a HRQoL measure using SF36 and MRI acute thigh pathology (oedema), chronic pathology (fat fraction) and muscle volume. Safety laboratory and adverse events will be collected. Our long-term goal is to find an effective treatment for people with IBM.
For further information please contact Dr Pedro Machado at p.machado@ucl.ac.uk

12. Multicenter, open-label extension study to investigate the long-term safety and efficacy of IgPro20 in maintenance treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) in subjects completing study IgPro20_3003 (PATH extension Study)
Status: Set-up / awaiting R&D
Sponsor: CSL Behring
PI: Dr Michael Lunn
Patient target: 5
The current study is an extension study to the pivotal study IgPro20_3003. Clinical studies have demonstrated the clinical efficacy and safety of using IVIGs to treat CIDP (Kieser et al., 2008; Eftimov et al., 2009: Hughes at al., 2008). Study IgPr20_3003 is being conducted to provide evidence of subcutaneous immunoglobulin (SCIG) as an alternative treatment option for CIDP in demonstrating safety and efficacy of IgPro20 as maintenance therapy in subjects treated with IVIG and switched to SCIG.

Methodology:

This is an open-label prospective, multicenter extension study for subjects who have participated in the subcutaneous (SC) Treatment Period of the preceding pivotal CIDP study IgPro20_3003. Subjects may either transition directly from study Igpro20-3003 to IgPr20-3004 or with an interval (1 - For subjects who had the completion visit in study IgPro20_3003 before IgPro20_3004 study was open for enrolment at the subject's site, enrolment is not later than 8 weeks after study IgPro203004 is open for enrolment at the subject's site; 2- For subjects who completed study IgPro20_3003 after IgPro20_3004 study was open for

enrolment at the subject's study site, enrolment is not later than 8 weeks after completion visit of study IgPro20_3003 for this subject).

Subjects who receive IgG between studies IgPro20_3003 and IgPro20_3004 should be enrolled within 1 week after the last administration of IgG.

MRC Centre CTIMPs Open Trials

13. GSK/Prosensa clinical trial in DMD boys with study drug GSK2402968 (GSK Extension Study)

Full Title: An open-label extension study of the long-term safety, tolerability and efficacy of GSK2402968 in subjects with Duchenne Muscular Dystrophy.
Status: Closed to recruitment/ Dosing suspended
Sponsor: GlaxoSmithKline
Funder: GlaxoSmithKline
PIs: Volker Straub, Francesco Muntoni
Patients recruited: 8; target (UK) 8

Description: A Phase III, multicenter, open-label extension, study in male outpatients with Duchenne Muscular Dystrophy (DMD) who have participated in eitherDMD114117 or DMD114044. All subjects will receive 6mg/kg GSK2402968 weekly for a minimum period of two years or an intermittent dosing frequency of 6mg/kgGSK2402968 for a minimum period of two years.

Objective(s)

Primary objective:

• To evaluate the long term safety, tolerability and efficacy of subcutaneous 6mg/kg/weekGSK2402968 in subjects with DMD who have participated in either DMD114117 orDMD114044.

Secondary objectives:

• To evaluate the long-term PK of subcutaneous 6 mg/kg/week GSK2402968 in subjects with DMD who have participated in either DMD114117 or DMD114044.

• To evaluate the long-term impact on health-related quality of life (HRQoL) and functional outcomes of continued treatment with GSK2402968 in subjects with DMD who have participated in either DMD114117 or DMD114044.

• To evaluate DMD disease progression and outcomes (clinical, HRQoL and functional) in subjects who discontinue active treatment during the conduct of study (natural history component).

• To evaluate the long-term safety, efficacy and PK of an intermittent dosing option in those subjects unable to tolerate GSK2402968 6mg/kg/week dosing.

This study aims to enrol approximately 200 subjects. In the primary dosing arm, subjects will receive GSK2402968 6 mg/kg as subcutaneous injections once a week for a period of 104 weeks. Further information about this study can be obtained from the MRC Centre Clinical Trials Coordinator on 020 7905 2639.

14. The PATH Study

Full title: Randomized, multicenter, double-blind, placebo-controlled, parallel-group phase III study to investigate the efficacy, safety and tolerability of 2 different

doses of Igpro20 (subcutaneous immunoglobulin) for the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) – the Path Study
Status: Open
Sponsor: CSL Behring
PI: Dr Michael Lunn
Patient target: 5; recruited 6

CIDP is an acquired neurological, demyelinating neuropathy with an assumed autoimmune-mediated pathogenesis. Due to its heterogeneous presentation and the limitations in the individual diagnosis procedures (clinical, serologic, and electrophysiological), the diagnosis relies on findings from multiple modalities. The probable autoimmune nature of the condition is most strongly suggested by response to immunotherapies such as intravenous immunoglobulins (IVIGs), plasmapheresis (PE), and corticosteroids.

In addition, despite less definitive published evidence of efficacy, corticosteroids are also considered as first-line therapy because of their long history of use.

Apart from IVIGs, there are currently no other medications approved for the treatment of CIDP; however experimental use of azathioprine, mycophenolate mofetil, methotrexate and cyclosporine are common and whilst there are also emerging reports of the use of B Lymphocyte antigen CD20 and anti-complement monoclonal antibody therapies, efficacy has not been established for any of these agents.

This is a prospective, multicenter, randomised, double-blind, placebo-controlled, parallel-group 3-arm study to investigate 2 different doses of SCIG IgPro20 compared to SC (subcutaneous) placebo for maintenance treatment of subjects with CIDP. Subjects on IVIG maintenance therapy experiencing CIDP relapse during an IVIG Withdrawal period will be administered the IVIG IgPro10 (1 loading dose and 3 or 4 maintenance doses every 3 weeks) during an IVIG Re-stabilization Period. Subjects with improved and maintained INCAT score at the last 2 assessments in the IVIG Re-stabilization Period will be randomised to 1 of 2 Igpro20 doses (0.2 or 0.4 g/kg body weight) or placebo during the SC Treatment Period.

IgPro20 is a ready-to-use formulation of human IgG with ≥98% purity for subcutaneous (SC) administration. Igpro20 is approved in the United States of America (US), in the EU, in Switzerland and Canada under the brand name Hizentra® for SC application in primary immune deficiency syndromes and is also under review by other regulatory agencies for use in primary and secondary immunodeficiencies.

IgPro10 is a ready-to-use liquid formulation of polyvalent IgG for intravenous (IV) application approved and marketed in several countries including the European Union (EU) and the US for use in primary immunodeficiency (PID) syndromes and for immune thrombocytopenic purpura (ITP). In the EU, IgPro10 is further approved for other conditions associated with immunodeficiencies resulting in the need for replacement therapy and in Guillian-Barre Syndrome (GBS) where IVIG is thought to have immunomodulatory effects on the peripheral nervous system. For the treatment of GBS and CIDP, a similar mode of action is assumed.

IgPro10 is currently under investigation in a confirmatory phase III study in subjects with CIDP.

Several randomised clinical studies have demonstrated the clinical efficacy and safety of using IVIGs to treat CIDP.

IVIGs requires subjects to visit a clinic or hospital for 1 to 5 days on a regular basis, usually every 2 to 6 weeks. This study is being conducted to provide SCIG as an alternative treatment option for CIDP that allows subject (or their caregiver) to self-administer the product in the home setting.

15. 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: Open to recruitment
Sponsor: Newcastle NHS Foundation
Funder: British Heart Foundation
PI: Prof. Muntoni
Recruitment target: 50-60 (GOSH) 20-30 (Newcastle)
Patients recruited: 45 (GOSH) 16 (Newcastle) (recruitment ends December 2014)
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 ACE inhibitor 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.

16. FOR-DMD
Full Title: Duchenne muscular dystrophy: double-blind randomized trial to find optimum steroid regimen (FOR-DMD)
Status: Open to recruitment
Sponsor: University of Rochester
Funder: NIH
PI: Prof Francesco Muntoni, Prof Volker Straub
Patients recruited: 5 (GOSH) 5 (Newcastle)
Target: 8
This is a multi-centre, double-blind, parallel group, 36-60 month study, comparing three corticosteroid regimens in wide use in DMD:

- daily prednisone (0.75 mg/kg/day)

- intermittent prednisone (0.75 mg/kg/day, 10 days on, 10 days off)
- daily deflazacort (0.9 mg/kg/day)

Primary study objective: The proposed randomized controlled trial will compare 3 corticosteroid regimens to address the pragmatic hypothesis that daily corticosteroids (prednisone or deflazacort) will be of greater benefit in terms of function and subject/parent satisfaction than intermittent corticosteroids (prednisone).

Secondary study objectives: A second hypothesis is that daily deflazacort will be associated with a better side effect profile than daily prednisone. The study protocol includes standardized regimens for prevention/ treatment of predictable side effects of corticosteroid medication, as well as standards of care for the general management of DMD. The trial directly addresses the current chaos in prescribed treatment schedules; its results will have direct impact on the current and future management of boys with DMD throughout the world by providing the evidence base for rational clinical practice.

The results of the trial will allow the generation of clear and specific evidence-based guidelines for patient treatment.

17. PTC124-GD-019 Open label
Full-Title: An open-label study for previously treated Ataluren (PTC124®) patients with nonsense mutation dystrophinopathy
Status: **Closed to recruitment**
Sponsor& Funder: PTC
Patients recruited: 8 (GOSH), 11 (Newcastle)

This study comprises a phase III, open-label study of ataluren in patients with nmDBMD who previously received ataluren at an investigator site in a prior PTC-sponsored clinical study. Subjects will receive ataluren 3 times per day (TID) at respective morning, midday, and evening
doses of 10 mg/kg, 10 mg/kg, and 20 mg/kg, for approximately 96 weeks. Study assessments will be performed at clinic visits during screening, on the first day of ataluren dosing, and then
every 12 weeks during the ataluren treatment period.

Primary Objective:

The primary objective of this study is to assess the long-term safety and tolerability of 10, 10, 20 mg/kg ataluren in patients with nmDBMD who had prior exposure to ataluren in a PTC-sponsored clinical trial.

Secondary objectives include the following:

- Ambulatory patients (able to run/walk 10 meters in ≤30 seconds) - To determine the effect of

ataluren on ambulation and other aspects of physical function

- Nonambulatory patients (unable to run/walk 10 meters in ≤30 seconds) - To assess the effect

of ataluren on activities of daily living, upper limb function, and pulmonary function

- All patients – To assess patient and/or parent/caregiver reports of changes in disease status:

Retrospectively during and after participation in previous studies (Studies 007 and 007e) and prospectively during the current study.

18. Full Title: A phase III efficacy & safety study of Ataluren (PTC124) in patients with nonsense mutation dystrophinopathy (PTC Phase III) PTC124-GD-020-DMD
Status: Open to recruitment
Sponsor: PTC

Funder: PTC
PI: Prof Francesco Muntoni, Dr Michela Guglieri
Patients recruited: 6 (GOSH) 3 (Newcastle)
Target: 3-5

A phase 3 efficacy and safety study of ataluren (ptc124) in patients with nonsense mutation dystrophinopathy

The primary objective of this study is to determine the ability of ataluren to slow disease progression as assessed by ambulatory decline (decrease in 6MWD) in patients with nonsense mutation dystrophinopathy.
Secondary endpoints have been chosen to evaluate changes in skeletal muscle function through assessment of proximal muscle function, as assessed by the time to run/walk 10 meters, time to ascend 4 stairs and time to descend 4 stairs and patient or parent/caregiver perception of physical functioning. Additional secondary endpoints have been selected to enhance understanding of the primary and secondary treatment effects. For example, a beneficial effect in physical function relative to placebo, as assessed by the North Star Ambulatory Assessment (NSAA), would compliment positive changes in ambulation proximal muscle function. Collection of patient and/or parent reported changes in disease status provides an opportunity to expand the implications of a drug effect on the patient's disease symptoms and activities of daily living.

19. Full Title: A phase IIb, open-label study to assess the efficacy, safety, pharmacodynamics and pharmacokinetics of multiple doses of PRO045 in subjects with Duchenne muscular dystrophy (PRO045)
Status: Open to recruitment
Sponsor: Prosensa
Funder: Prosensa
PI: Prof Francesco Muntoni, Prof Volker Straub
Patients recruited: 1 (GOSH) 1 (Newcastle)
Target: 4-5 (GOSH)
Primary objective: To assess the efficacy of PRO045 after 48 weeks treatment in ambulant subjects with Duchenne muscular dystrophy.
Secondary objectives: To assess the safety and tolerability of PRO045 after 48 weeks of treatment in all study subjects with Duchenne muscular dystrophy including subjects from the dose-escalation phase of the study. To determine the pharmacokinetics of PRO045 at different dose levels after subcutaneous administration in subjects with Duchenne muscular dystrophy.
To assess the pharmacokinetics, bioavailability and safety of PRO045 following single intravenous dose administration at different dose levels.
To assess the pharmacodynamics of PRO045 at different dose levels after subcutaneous administration in subjects with Duchenne muscular dystrophy.
To assess trend in efficacy in all subjects with Duchenne Muscular Dystrophy not included in the primary objective after 48 weeks of treatment.

20. An Open-label, multicenter, multinational, ascending dose study of the safety, tolerability, pharmacokinetics, pharmacodynamics, and exploratory efficacy of repeated biweekly infusions of neoGAA in naïve and alglucosidasealfa treated late-onset Pompe disease patients.
Status: Open to recruitment

Sponsor: Genzyme
Funder: Genzyme
PI: Volker Straub
Patient recruited: 0
Target: 1
Phase I, multicenter, multinational, open-label, ascending dose, repeated bi-weekly intravenous infusion study of neoGAA in:
• Group 1 – Late-onset Pompe disease patients naïve to treatment, 3 dose levels
• Group 2 – Late-onset Pompe disease patients previously treated with alglucosidasealfa, 3 dose levels

Objectives:
Group 1
To determine in treatment naïve patients with late-onset Pompe disease patients:
• The safety and tolerability of neoGAA
• The pharmacokinetic parameters of neoGAA
• The pharmacodynamic effects of neoGAA on skeletal muscle and other exploratory biomarkers
• The effect of neoGAA on exploratory efficacy endpoints
Group 2
To determine in alglucosidasealfa treated late-onset Pompe disease patients:
• The safety and tolerability of neoGAA
• The pharmacokinetic parameters of neoGAA
• The pharmacodynamic effects of neoGAA on skeletal muscle and other exploratory biomarkers
• The effect of neoGAA on exploratory efficacy endpoints

21. A randomized, double-blind, placebo-controlled, multicenter, parallel group, dose-finding, pivotal, phase IIb/III study to evaluate the efficacy, safety and tolerability of intravenous BYM338 at 52 weeks on physical function, muscle strength, and mobility and additional long-term safety up to 2 years in patients with sporadic inclusion body myositis
Sponsor: Novartis
Status: Recruiting
PI: Michael Hanna
Recruitment target: 10
The purpose of this dose-finding study is to demonstrate that at least one dose regimen of BYM338 in sporadic inclusion body myositis (sIBM) patients improves physical function and mobility when compared to placebo after 52 weeks of treatment. The study will assess efficacy, safety, tolerability and pharmacodynamic effect of i.v. administration of BYM338 compared to placebo on lean body mass, muscle strength, physical function and mobility in sIBM patients.
The results will support marketing authorization applications for BYM338 as treatment for sIBM patients.
This is a multi-center, pivotal, randomized, double-blind, placebo-controlled, 4 arm dose-finding, phase IIb/III trial.
For more information contact Dr Pedro Machado: p.machado@ucl.ac.uk

22. A Phase 2/3 Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of ISIS 420915 in Patients with Familial Amyloid Polyneuropathy

Sponsor: ISIS Pharmaceutical
Status: Recruiting
PI: Prof Reilly
Gobal Recruitment target: 195
Multicentre, randomized, double-blind, placebo-controlled study. Approximately 195 patients will be randomized in a 2:1 ratio (130 ISIS 420915 and 65 PBO) to receive 300 mg ISIS 420915 or placebo. Study Drug (ISIS 420915 or placebo) will be administered three times on alternate days during Week 1 (Days 1, 3 and 5), and then once weekly during Weeks 2-65 (for a total of 67 doses). Patients will also receive daily supplemental doses of the recommended daily allowance of vitamin A. The end of treatment (EOT) efficacy assessment is conducted at Week 66. Following treatment and the EOT efficacy assessment, eligible patients (including patients that received placebo), may elect to enrol in an open-label extension (OLE) study pending study approval by the IRB/IEC and the appropriate regulatory authority. All participating patients in the OLE study will receive 300 mg ISIS 420915 once weekly. Otherwise, patients will enter the 6 month post-treatment evaluation portion of the study.

MRC Centre CTIMPs Completed Trials

23. RANDOMISED DOUBLE-BLIND PLACEBO CONTROLLED TRIAL OF LONG-TERM ASCORBIC ACID TREATMENT IN CHARCOT-MARIE-TOOTH DISEASE TYPE 1A Status: Completed.

Sponsor: University College London
Funder: Muscular Dystrophy Campaign (MDC)
PI: Prof. Reilly
Patients recruited: 50 target 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 published in *Lancet Neurology 2010*.

24. 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.

This work has been completed and outcome data published in *JAMA (Volume 308, No.13, pages 1357 - 1365, October 2012).*

25. 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.

26. 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)*

27. 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.*

28. 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.

Patients 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.

Wiley Periodicals, Inc. Published online March 2013, (wileyonlinelibrary.com) DOI 10.1002/mus.23839

29. 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: Completed
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.

Manuscript in preparation for publication

30. Investigation of the ability of Otelixizumab to inhibit in vitro antigen-specific T cell responses from Myasthenia Gravis patients
Status: Completed
Sponsor/Funder: GlaxoSmithKline
PI: Prof Kullmann
Patients recruited: 39; target 40

Myasthenia Gravis (MG) is the best understood autoimmune 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. 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 T-cell 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).

31. 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: Completed
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.
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.
In the process of being published

32. 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: Completed
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 lowering 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. *Results in Press*

33. LiCALS Open Label Extension
Full title: LiCALS open label extension trial of lithium carbonate in amytrophic lateral sclerosis
Status: Completed
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. *Results in Press*

34. GSK1223249 in MND/ALS (the Nogo-A study)
Full title: A Phase I, multi-centres, randomized, placebo-controlled, double-blind, single and repeat dose escalation of a drug to treat ALS
Status: Completed
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). *Results in Press*

35. 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: Completed

Sponsor: University Rochester
Funder: National Institutes of Health (NIH - USA)
PI: Prof. Hanna
Patients recruited:14; target 40
This is a phase III trial into Periodic Paralysis. This proposal involves a multi-center, 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.
Manuscript in preparation

36. Pro053: Title: A Phase I/II, open-label, dose escalating with 48-week treatment study to assess the safety and tolerability, pharmacokinetics, pharmacodynamics and efficacy of PRO053 in subjects with Duchenne muscular dystrophy
Status: Closed to Recruitment
Sponsor & Funder: Prosensa
PI: FM
Patients Recruited: 1 (GOSH)
Recruitment target: 1-2
A Phase I/II, open-label study. The study consists of two phases; a single dose-escalation phase and a 48-week treatment phase. All subjects will have a screening period prior to their first dose of PRO053.
Efficacy, safety, pharmacokinetics (PK) and pharmacodynamic (PD) assessments will be conducted at regular intervals throughout the study.

Primary Objective is to assess the efficacy of PRO053 after 48 weeks treatment in ambulant subjects with Duchenne muscular dystrophy. Secondary objectives are to assess the safety and tolerability of PRO053 after single intravenous (IV) and subcutaneous (SC) doses and after 48 weeks of treatment in subjects with Duchenne muscular dystrophy; to investigate the pharmacokinetics PRO053 at different dose levels in subjects with Duchenne muscular dystrophy; to assess the pharmacodynamics of PRO053 at different dose levels in subjects with Duchenne muscular dystrophy; to assess efficacy trends of PRO053 in subjects with Duchenne Muscular Dystrophy not included in the primary analysis after 48 weeks of treatment.

37. 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: Completed
Sponsor: TROPHOS
Funder: Association Francaise contre les Myopathies
PIs: Francesco Muntoni, Hanns Lochmuller, Helen Roper
Recruitment target (UK): 30; GOSH: 10, Newcastle: 3
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 symptoms to 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.
Data in analysis

38. SMT C1100 – A Phase 1, Open-label, Single and Multiple Oral Dose, Safety, Tolerability and Pharmacokinetic Study in Paediatric Patients with Duchenne Muscular Dystrophy
Status: Closed
Sponsor & Funder: Summit
PI: F. Muntoni
Patients Recruited: 4 consented (GOSH)
Recruitment target 4 (GOSH), UK target 12
This will be an open-label, single and multiple oral dose study. Up to 12 patients with DMD will be enrolled onto the study. Primary Objective is to determine the safety and tolerability of single and multiple oral doses of SMT C1100 in patients with Duchenne Muscular Dystrophy (DMD). Secondary Objectives are to determine the single and multiple oral dose pharmacokinetics of SMT C1100 and its metabolites in patients with DMD.

SMT C1100 is the first in a new pharmacological class of orally available small molecules that act to modulate transcriptional control of utrophin. SMT C1100 is being developed with the potential to treat DMD independent of the dystrophin mutation, by maintaining production of utrophin to compensate, at least in part, for the loss of the dystrophin protein. Outcomes from non-clinical pharmacodynamic studies indicate that SMT C1100 increases utrophin mRNA and protein levels and improves muscle structure and function.

Natural History – Longitudinal Studies

Set-up Phase

39. LEMS Disease Registry – UK Proposal
Status: set-up
Sponsor: BioMarin Europe Ltd
PI: Hanna
Patients target: 10 from the NHNN

The LEMS registry is a voluntary multi-centre, multinational, observational program for patients with LEMS disease and is intended to track the routine clinical outcomes of patients with LEMS over time.

The purpose of the LEMS registry is to collect additional data on the long term safety and efficacy of Firdapse for patients who have been prescribed Firdapse by their treating physician. The registry will also track the use of treatment for LEMS including drugs other than Firdapse. The data collected by the registry are intended to enable better characterisation of the natural history of LEMS.

As this is an observational (non-interventional) programme no experimental treatments or assessments are involved, it is up to the treating physician to determine the actual frequency of assessments according to the patients' individual need for medical care and routine follow-up.

All patients with a confirmed diagnosis of LEMS is eligible to participate in this programme, confirmation can be by abnormal Electromyogram (EMG) or positive result for Voltage Gated Calcium Channel (VGCC) antibodies, however patients cannot be participating in any other study with Firdapse.

40. Charcot Marie Tooth disease (CMT) Translational Research in Europe for the Assessment and Treatment of Neuromuscular Diseases (TREAT-NMD) International Database (ID)
Status: Set-up
Sponsor: University College London
Funder: National Institutes of Health (NIH – USA)
PI: Dr Reilly
Patients to be recruited: unlimited

Charcot Marie Tooth Translational Research in Europe for the Assessment and Treatment of Neuromuscular Diseases International Database (CMT-TREAT-NMD-ID) is an observational/registry study. The system will have an international set-up composed of national registries from interested countries around the world. Currently 8 international centers are participating. Its objective is to capture every case of CMT in each participating country, with sufficiently detailed data to identify patients likely to be eligible for a variety of studies.

Inherited peripheral neuropathies are often collectively referred to as Charcot Marie Tooth disease (CMT). These are heterogeneous group of peripheral neuropathies caused by mutations in over 40 different genes. Typically cases of CMT are separable into autosomal dominantly inherited demyelinating (CMT1) or axonal (CMT2), X-linked (CMTX) and autosomal recessive (CMT4) forms. Although most cases of CMT are sensorimotor, predominantly sensory (Hereditary Sensory Neuropathies; HSN) and motor forms (distal Hereditary Motor Neuropathies; dHMN) also exist.

Participants will need to have a diagnosis of Charcot Marie Tooth disease, Hereditary Neuropathy with liability to Pressure Palsies (HNPP), Hereditary Motor Neuropathy (HMN) or Hereditary Sensory Neuropathy (HSN) and also the ability to provide consent.
Data such as diagnosis including genetic testing, family/developmental history, mobility, sensation, optic nerve atrophy and hearing loss will be collected. Patients may also undergo a neurophysiological test.

41. Prospective. Longitudinal Study of the Natural History and functional status of patients with MyoTubular Myopathy (NatHis-MTM)
Status: set-up
Sponsor: Institute of Myology
PI: Prof Francesco Muntoni
Patients target: 6-8
Centronuclear myopathy (CNM) is an inherited neuromuscular disorder. It is a group of rare congenital myopathies characterized by the presence of hypotrophic myofibers with centrally placed nuclei on muscle biopsies. CNM exists in 3 forms: i) X-linked recessive (OMIM 310400), ii) autosomal dominant (OMIM 160150) and iii) autosomal recessive form (OMIM 255200). This study will be a multicentre international study in Europe and USA. Presently, there is no effective therapy to treat the muscle weakness in XLMTM patients. Current treatments include mainly respiratory, feeding and orthopedic management. These treatments improve muscular function, quality of life and longevity but do not directly target the disease mechanism. Primary objective of this study is to characterize the disease course in MTM patients using standardized evaluations. Secondary objectives are to identify prognostic variables of the disease; to identify the best outcome measure(s) for future treatment studies; to assess the immune response against AAV.

42. FSHD NH Study
A multicentre collaborative study on the clinical features, expression profiling, and quality of life of infantile onset facioscapulohumeral muscular dystrophy
This multicenter study will be conducted at participating US and International CINRG sites. Fifty individuals with infantile onset (diagnosed at <11 years of age) and genetically confirmed FSHD will be recruited for a cross-sectional study of pediatric FSHD. This will include children and youth (less than 18 years old) with FSHD who are currently followed in pediatric neuromuscular centers, as well as adults (18 years or older) with FSHD who are identified as having infantile onset of disease by chart review, clinical exam, and genetic confirmation. Our goal is to have close to 25 individuals with early infantile onset (<5 years) and 25 with late infantile onset (5 to 10 years) of FSHD in order to compare their clinical phenotypes and health-related outcomes.

<u>Open Studies</u>

43. FSHD registry
Status: Ongoing
The UK FSHD Patient Registry is a national registry for all people affected by facioscapulohumeral dystrophy living in England, Scotland, Wales and Northern Ireland. It is a patient driven online registry launched in May 2013. The main purpose of the registry is to facilitate and accelerate the recruitment into clinical research while also providing a resource to help plan and design clinical trials. In addition to collecting an internationally agreed

dataset the registry is a platform for additional research questionnaires collecting information about pain, quality of life and scapular fixation. The registry is funded by the Muscular Dystrophy Campaign and supported by the TREAT-NMD Alliance.

44. 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: NHNN 606; GOSH 57; target (UK) 650

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@ion.ucl.ac.uk.

45. Natural History study of Hereditary Sensory Neuropathy type 1 secondary to SPTLC1 and SPTLC2 mutations
Status: Open to Recruitment
Sponsor: University College London Hospitals
PI: Prof Reilly
Patients recruited: 32

Hereditary Sensory Neuropathy Type I secondary to SPTLC1 and 2 mutations is the commonest of the Hereditary Sensory Neuropathies. It is a slowly progressive neuropathy leading to profound loss of sensation especially pain and temperature sensation with variable but often

severe motor involvement. Most patients have sensory complications such as recurrent ulcers; osteomyelitis and amputations are common. Over time, there is considerable disability requiring extensive carer support.

There is emerging evidence for the use of serine as a potential treatment option. This rapid progress has led to the possibility of a clinical therapeutic trial of serine in our UK HSN1 population.

A longitudinal study is now underway to determine the best way of measuring diseases progression in this condition which can be used in a clinical trial. We have a unique population within the United Kingdom where all the SPTCL1 patients (56) have a common mutation (C133W). Despite this, there is significant heterogeneity in the phenotype. A variety of assessment methods to cover the spectrum of deficits noted in this condition will be performed and repeated after a year. These include: CMT Neuropathy Score, comprehensive neurophysiological assessment, Quantitative Sensory Testing (DFNS protocol), muscle MRI studies of the thighs and calves, machine myometry, analysis of plasma DSB levels, upper thigh skin biopsy (epidermal nerve fibre density measurements) and patient questionnaires (SF36 and NPSI).

For more information contact: Dr Maiya Kugathasan, u.kugathasan@ucl.ac.uk

46. MITOCHONDRIAL DISEASE COHORT New Title MRC Centre Mitochondrial Disease Patient Cohort: A Natural History Study and Patient Registry
Status: Ongoing
Sponsor: Newcastle Upon Tyne Hospitals NHS Foundation
Funder: MRC
PIs: Dr R McFarland, MG Hanna, DM Turnbull
patients recruited >1000; target > 1000
Total target 1500
Recruitment to date 1111
Newcastle: 518
UCL: 340
Oxford: 111
GOSH: 37
Satellites: 105

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 symptomaticadults 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.

Multiple centers receive referrals and are registered directly as Newcastle, London, Oxford and GOSH sites, satellite sites contact trial management team to register patients and send details via case report forms.). The database will physically stored and centrally managed at Newcastle University and it will have a dedicated, electronic secure server.
The project anticipated collecting details on 1000 patients in total between 2009-2013, renewed target of 1500 individual by 2018.
For information on the status of recruitment please contact Dr. Robert Pitceathly (London) r.pitceathly@ion.ucl.ac.uk or Julia.Maddison@newcastle.ac.uk and Dr Yi Ng (Newcastle) yi.ng@ncl.ac.uk

47. THE NATURAL HISTORY OF INCLUSION BODY MYOSITIS (IBM Net)
Status: Open to Recruitment
Sponsor: University College Hospitals
Funder: MDC
PIs: Dr Matt Parton/Mike Hanna
Target 120-150; recruited 67
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@ucl.ac.uk
Neuromuscul Disord. 2013 May;23(5):404-12. doi:10.1016/j.nmd.2013.02.010. Epub 2013 Mar 11. PubMed PMID: 23489664

48. Kennedy's Disease – Study and Register
Status: Open
Sponsor: UCLH
PI: Hanna
Patients recruited: 56
The primary purpose of this study is to create a national register of patients with Kennedy's Disease (spinal and bulbar muscular atrophy) with a view to facilitating research into the disorder. In particular, we aim to systematically characterise diagnostic features of the disorder and their natural history and attempt to estimate the incidence and prevalence of Kennedy's disease in the United Kingdom. Furthermore we intend to assess the experience of patients with regard to specialist neurological, endocrinological and clinical genetic care and, by so doing, to establish best practice guidelines for the diagnosis and management of this disorder.

Kennedy's disease was first described as a separate entity in a series of 9 males in 2 families (Kennedy et al., 1968) and prior to this was not distinguished from adult-onset forms of spinal muscular atrophy. Kennedy described the disorder as being X-linked on the basis of his pedigrees, and the causative mutation in the X-chromosome was tracked in 1991 to the Androgen Receptor. The disease is caused by the expansion of an intragenic CAG triplet repeat in exon 1 of the gene which is translated into a polyglutamine segment in the AR protein. As such Kennedy's disease became the first in a series of 9 disorders now known to be caused by such expanded polyglutamine repeats (the others being Huntington's disease, dentato-rubral pallido-luysian atrophy and spino cerebellar ataxias).
The earliest clinical features are androgen insensitivity, postural hand tremor and muscle pains with subsequent development of motor neuropathy, bulbar signs and symptoms and a distal sensory neuropathy which is usually subclinical.
As the prognoses of these two conditions are very different it is clearly important that these patients are correctly identified and managed. Furthermore, patients with Kennedy's disease have an additional set of endocrine and metabolic problems over and above the more well-defined neurological deficits. The endocrine and metabolic aspects of the disorder in particular are poorly characterised and their relationship to the genotype is controversial. Their implications for patients in terms of morbidity has also not been investigated.
The study proposes to, if possible, interview and examine patients directly and attempt to gain a time course of the development of individual symptoms and signs. Wherever molecular genetic confirmation of the diagnosis has not already been performed by the referring hospital this will be performed by standard PCR methods with the prior explicit consent of the patient and the referring neurologist. Creatine kinase, and endocrine function (testosterone, luteinising hormone and sex-hormone binding globulin levels) will be assessed from blood samples by standard techniques. Pedigrees for the patient's families will be obtained from the hospital notes, or from direct interview where this has been possible.
By creating a register of the United Kingdom's Kennedy's population we hope to obtain clear evidence of phenotype-genotype correlation and, over time, establish relationships with disease severity and prognosis.
For further information contact: Dr Pietro.Fratta, p.fratta@prion.ucl.ac.uk

49. Investigation of Human Neurological Ion Channel Disorders
Status: ongoing
Sponsor: University College London Hospitals
PI: Prof. Hanna
Recruited: 56
Ion channels are membrane bound proteins that allow the flux of charged ions across cell membrane in excitable tissue including muscle and nerve. These ion channels are usually specific for a particular ion e.g. potassium or calcium. An increasing number of inherited and acquired neurological diseases are attributed to disorders of ion channels. The 'channelopathies' include non-dystrophic myotonia, periodic paralysis, episodic ataxias types 1 and 2 (EA1 and EA2), familial hemiplegic migraine types 1 and 3 (FHM1 and 3) and some forms of epilepsy. The mechanisms by which ion channel dysfunction causes disease are incompletely understood, but the genetic channelopathies have provided unique insights into because the properties of mutant channels can be studied with great precision with biophysical methods.
Although each of the known channelopathies is rare, there is considerable circumstantial evidence that genetic variability in ion channels plays a major role in idiopathic epilepsy and migraine. These disorders, which are characterised by normal brain development and function punctuated by episodes of abnormal excitability, show strong heritability although typically do not respect Mendelian patterns of inheritance. They represent an important disease burden to society. It remains to be determined whether such disorders are caused by many, individually rare genetic variants or by a few common polymorphisms affecting ion channel splicing, assembly, trafficking or function.

Several intense programmes of research are underway to identify genetic susceptibility factors in epilepsy and other paroxysmal neurological diseases. The purpose of this proposal however, is to take a complementary approach to gain an insight into the consequences of genetic variability, focusing primarily on KCNA1, mutations of which cause EA1(5) and CACNA1A mutations which cause EA2(6), and to document these at all levels from molecular biophysics to cellular excitability studied in individuals harbouring the mutations. Only by understanding the degree to which variability of ion channel properties can be tolerated by the organism, or conversely affect neuronal excitability in a detectable manner, will we be able to interpret the functional impact of coding polymorphisms that are staring to be reported in population studies.

This research project aims to consolidate and expand on previous work by collating clinical data and continuing to sequence candidate genes in patients suspected to have ion channel disorders, particularly in Episodic Ataxia Type 1 (KCNA1 gene) and Episodic Ataxia type 2 (CACNA1A gene). As the project progresses it is possible that further candidate genes will be identified and we will sequence these also. In vitro expression of new mutations will be performed in order to further study how these genetic mutations result in channel dysfunction.

50. AFM Natural History Study
Full Title: Outcome measures in Duchenne Muscular Dystrophy: A Natural History Study
Status: Ongoing
Sponsor: UCL Institute of Child Health
Funder: AFM
PIs: Francesco Muntoni, Kate Bushby
Patients recruited: 20 (GOSH) 18 (Newcastle)
Description: To document with quantified measurements the natural history of Duchenne Muscular Dystrophy. Several validated tools will be used to describe motor, orthopaedic and respiratory functions, quality of life and blood parameters along a 4 years follow-up study in ambulant and non-ambulant patients.

Primary objective is to document with quantified measurements the natural history of Duchenne Muscular Dystrophy. Several validated tools will be used to describe motor, orthopaedic and respiratory functions, quality of life and blood parameters along a 4 years follow-up study in ambulant and non-ambulant patients.
Secondary objectives are specific tests to ambulant and non-ambulant patients will be performed. All these tests should determine the most sensitive outcome measures to use in the assessment of efficacy of future therapies. This prospective longitudinal natural history study will be performed in two cohorts of patients with DMD according to their level of functional motor ability (ambulant/non-ambulant). Inclusion criteria and methods will be different in the two cohorts and will be described separately.

51. Using Next Generation Sequencing to Unravel the Pathogenesis of Sporadic Inclusion Body Myositis (IBM) – The International IBM Consortium Genetic Study
Status: Ongoing
Sponsor:
Funder: MRC
PI: Prof Hanna
Patients target: 400
Recruited: 73
The primary pathogenesis of IBM is not determined, although in IBM the aggregated proteins are in muscle tissue, many such as tau, alpha synuclein, TDP-43, beta amyloid and the prion

protein are implicated in neurodegeneration. It is possible that the defective processes that lead to the formation of these abnormal protein deposits are likely to have important implications for many neurological disorders.
The vast majority of IBM is sporadic but there is significant evidence to suggest that genetic factors are important in IBM; these include the compact age at onset, insidious progression, clinical and pathological features, infrequent occurrence in twins, siblings and families. There have been several Mendelian genes identified in families with IBM phenotypes but these are rare. To investigate the pathogenesis of IBM further requires a genomic approach on large numbers of defined cases.
We will establish an international collaboration to collect IBM patient DNA and detailed clinical information to facilitate IBM research - The International IBM Consortium Genetic Study (IIBMCGS).
The number of IBM cases worldwide is not large enough for an effective genome wide association study (GWAS) but using next generation exome sequencing we can identify rare coding variants and high-risk genome wide variants in IBM. This technique has been used effectively in the identification of mutations that cause Mendelian disorders and more recently found significant rare coding variants in type I diabetes and autism.
In this proposal we wish to employ exome sequencing to analyse 200 IBM cases and 200 normal muscle controls. We expect to identify a number of IBM rare variants that cluster in disease associated genes. We plan to replicate these findings in a further 700 IBM and 2200 controls. These data will be made publicly available (anonymously) to allow comparison with other muscle disorders and neurodegenerative conditions.
Orphanet J Rare Dis. 2014 Jun 19;9:88. doi:10.1186/1750-1172-9-88. PubMed PMID: 24948216; PMC4071018.

52. Hereditary Inclusion Body Myopathy-Patient Monitoring Program (HIBM-PMP): A Registry and Prospective Natural History Study to Assess HIBM Disease
Status: Recruiting
Sponsor: Ultragenyx
Funder: Ultragenyx
PI: Prof Hanns Lochmuller
Patients recruited: 12
Target: 15-20
HIBM is a severe progressive myopathy that typically presents in early adulthood as weakness in the distal muscles of the lower extremities and progresses proximally, leading to a loss of muscle strength and function, and ultimately a wheelchair-bound state. The rate of progression is gradual and variable over the course of 10-20 years or longer. There is a need to better understand the disease-specific features of HIBM to heighten disease awareness; facilitate early diagnosis; identify patients; expand knowledge of the clinical presentation, progression and variation of the disease; identify and validate biomarkers and other efficacy measures; inform on the design and interpretation of clinical studies of investigational products; and eventually to optimize patient management.

Up to 10 centers in North America, the European Union (EU), and the Middle East will participate in the HIBM prospective observational study (hereto referred to as the HIBM Natural History Study).
HIBM Disease Registry subjects may or may not be associated with a Study Site. Some disease registry subjects may enter only self-reported data and will not be associated with a clinical site. Other disease registry subjects who are in the same country as a natural history site may choose to have their data confirmed by one of those centers or opt-in to the HIBM Natural History Study.

The main objective of this program is to better understand HIBM.
The specific HIBM Disease Registry's objectives are to:
• Identify HIBM patients worldwide.
• Promote awareness and facilitate diagnosis of HIBM disease in the neuromuscular field.
• Obtain an assessment of the medical history, clinical presentation and progression of disease in HIBM patients and provide a connection for subjects to the broader HIBM community and associated programs.
• Provide customized information to subjects and their physicians that desire information on their disease status and progression.

The specific HIBM Natural History Study's objectives are to:
• Characterize HIBM disease presentation and progression over time using relevant clinical assessments of muscle strength and function.
• Obtain information to better characterize quality of life and understand the timing of significant life changing events in HIBM patients using patient-reported outcomes.

53. Full title: Prospective evaluation of gastrostomy in MND (PROGAS). Prospective evaluation of gastrostomy in MND (PROGAS).
Status: Ongoing
Sponsor: Royal Free London NHS Foundation Trust
Start date: 2011
Funder: Motor Neurone Disease Association / South Yorkshire CLRN
UCL PI: Dr Richard Orrell
Patients recruited: 6, target: open-ended
Difficulty in swallowing is a common problem in patients with MND. Patients with severe swallowing difficulty experience malnutrition, dehydration, choking and an increased risk of chest infections. Long-term nutritional support of patients with severe swallowing difficulty can be achieved by placing a feeding tube, known as a gastrostomy, directly into the stomach. However, the current practice of gastrostomy feeding is largely based on consensus and expert opinion rather than the outcomes of appropriately designed trials. Currently gastrostomy technique and timing of insertion within the disease course vary throughout the UK. There is a lack of evidence to suggest what the optimal timing for gastrostomy is, or which method is most appropriate. In addition, although gastrostomy is routinely performed, the benefits, such as improved survival and quality of life following gastrostomy, have not been proven. The main aim of this study is to develop evidence-based guidelines for gastrostomy use in patients with MND. Patients and carers will be recruited at the participating MND Centres around the UK. Questionnaires will be used to assess the safety, complications and benefits of the differing timings and methods of gastrostomy insertion. The results of this work will translate into the development of guidelines, which will optimise the benefit, and the patient and carer experience of gastrostomy. The principles will be readily applicable to patients with severe swallowing problems who are eligible for gastrostomy insertion due to other neurological diseases

54. THERAPEUTIC TRIAL OF diaphragmatic pacing IN MND/ALS (DiPALS)
Full title: A randomised controlled trial in patients with respiratory muscle weakness due to motor neurone disease of the NeuRx RA/4 Diaphragm Pacing System
Status: Ongoing
Sponsor: Royal Free London NHS Foundation Trust
Start date: March 2013
Funder: NIHR Health Technology Assessment Programme / Motor Neurone Disease Association / Department of Health subvention funding
UCL PI: Dr Richard Orrell

Patients target: 4 plus

Non Invasive Ventilation (NIV) therapy is the current standard treatment to help allow patients with MND/ALS to breathe. Patients wear a face mask over their nose or mouth or both and as they breathe in, the machine gives an extra push of air to support the patient's weak breathing muscles, enabling a bigger deeper breath. Some MND patients do not tolerate NIV due to the type of mask they have. During the day problems with using NIV include issues like claustrophobia, feeding and communication. Eventually respiratory muscle weakness will progress to a point at which intermittent/overnight NIV is ineffective. Diaphragm pacing (DP) is a means of increasing the strength of the main breathing muscle. The NeuRx RA/4 Diaphragm Pacing System has been developed for patients who are unable to control their diaphragms because of stable high spinal cord injuries or because they have a neuromuscular disease such as MND. The pacing wires are inserted into the diaphragm muscle during a small operation and are connected to a small portable box that the patient can easily carry about. The proposed study will assess if treatment with DP prolongs life and maintains quality of life when given in addition to current standard care with NIV. 108 patients will be recruited to the study in up to 10 NHS hospitals in the UK. Patients will be randomised to either have NIV or receive DP in addition to NIV. Study participants will be required to complete outcome measures at 5 follow up time points (2, 3, 6, 9 and 12 months). Patients in the DP group will have additional visits for surgery and a 1 week post operative follow up. 12 patients (and their carers) from the DP group will also be asked to complete 2 qualitative interviews.

55. 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.

56. International Guillain-Barre' Syndrome (GBS) Outcome Study - IGOS

Status: Open

Sponsor: Glasgow University

Funder: Wellcome Trust/GBS Support group

PI: Dr Lunn

Patients target: 10 from the NHNN

Despite partially effective forms of treatment, outcome in patients with Guillain-Barre' syndrome (GBS) has not improved in the last two decades. At present about 10 to 20% of patients remain severely disabled and about 5% die. One explanation for this stagnation is the highly variable clinical course of GBS. Determinants of disease progression and recovery in GBS are still poorly understood. GBS may consist of distinct pathogenic subgroups, in which disease onset and progression is influenced by different types of preceding infections, anti-neural antibodies and genetic polymorphisms. Optimal treatment of individual patients may depend on the pathogenesis and clinical severity.
The international GBS Outcome Study (IGOS) aims to identify clinical and biological determinants of disease progression and recovery in GBS. This information will be used to understand the diversity in clinical presentation and response to treatment of GBS and to develop new prognostic models to predict the clinical course and outcome in individual patients.
IGOS is a prospective observational international multi-centre study including at least 1000 patients with GBS or variants of GBS, including the Miller Fisher syndrome (MFS) and overlap syndromes. The study has a follow-up of one year.
The aim is to obtain a detailed and standardised database on clinic features, treatment, and diagnostic electrophysiology, and collect a biobank with serum samples and DNA at specific visits.
There is an option to collect cerebrospinal fluid (CSF) during routine diagnostic work-up for proteomic studies, and to conduct an extended follow-up of two and three years. Additional studies may be added in the future.
For further details please contact Dr Lunn, Michael.lunn@uclh.nhs.uk

57. Identification of disease susceptibility genes associated with development and clinical characteristics of primary inflammatory muscle diseases, PM, DM and IBM
Status: Ongoing
Sponsor: University of Manchester
Funder: ARC
PI: Isenberg
PM, DM and IBM are a subset of inflammatory muscle disorders of unknown cause, currently classified under the umbrella term of idiopathic inflammatory myopathies (IIM). PM, DM and IBM are characterised by skeletal muscle inflammation and progressive muscle weakness, which can be debilitating and chronic in nature (occasionally fatal). Steroid and immuno-suppressive treatments are often only partially effective at reducing symptoms, and toxic side effects also limit their usefulness.
The cause of muscle inflammation in PM, DM and IBM is unknown. There is, however, increasing evidence that genetic factors, such as the polymorphisms around the complex HLA molecules, as well as certain inflammatory cytokines, are intimately involved in both the development and expression (in terms of disease severity and organs targeted for damage) of these conditions. Many of the inflammatory mechanisms responsible for the pathological changes of PM, DM and IBM are similar to those mediating damage in other inflammatory diseases, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), so it seems likely that genetic factors will similarly be involved in the development and expression of PM, DM and IBM.

Establishing the extent of involvement of these genetic mechanisms in PM, DM and IBM is of great importance, since understanding the aetiological mechanisms of any disease may eventually permit the development of specific and therefore more effective therapies.

Primary Objectives:
To identify and characterise the disease susceptibility genes associated with the development and clinical characteristics of the primary inflammatory muscle diseases, PM, DM and IBM.
Secondary:
To gain further insights into the aetiological mechanisms responsible for the development of the primary muscle diseases PM, DM and IBM and ultimately identify new therapeutic targets for treatment.

58. Full Title: Study of clinical and radiological changes in teenagers with Duchenne muscular dystrophy theoretically treatable with exon 53 skipping (Pre-U7)
Status: Open to Recruitment
Sponsor: Genethon
Funder: Genethon
PI: Volker Straub/Prof Francesco Muntoni
Patients recruited 5 Target 5

PreU7-53 is a natural history study. The objective is to monitor the clinical and radiological course of upper limb muscle impairment in patients with DMD, potentially treatable with AAV-mediated exon 53 skipping (i.e.: deletions exons 10-52, 45-52, 46-52, 47-52, 48-52, 49-52, 50-52, 52 of the dystrophin gene), and to assess serum and urine biomarkers to monitor non-invasively disease progression, and finally to assess the prevalence of immunity against adenoviral vectors in this relevant DMD population.

59. SMA registry
PI: Prof Lochmuller
Status: Ongoing
The UK SMA (Spinal Muscular Atrophy) registry is for all patients living the UK and Ireland who are affected by all types of Spinal Muscular Atrophy. The aim of the registry is to encourage genetically diagnosed SMA patients to register so that they may be considered for relevant clinical trials, receive the most up to date information regarding standards of care for their disease and help provide the research community with an understanding of disease prevalence. People with SMA, or the parents/guardians of children with SMA, can register themselves online. The UK SMA registry was set up in 2008 as a collaboration between TREAT-NMD and the Jennifer Trust for Spinal Muscular Atrophy, and is part of the TREAT-NMD Global SMA Registry. Since 2012, the registry is supported by the Jennifer Trust.

60. UK Myotonic Dystrophy patient registry
PI: Prof Lochmuller
Status: Ongoing
The UK Myotonic Dystrophy Patient Registry is an online patient driven resource launched in May 2012. The primary aim of the registry is to facilitate and accelerate the planning, design and recruitment of clinical research while also providing a snapshot of the myotonic dystrophy population in the UK. The registry collects an internationally agreed dataset with the majority of information provided by the patient themselves, additional clinical and genetic details are provided by their neuromuscular specialist. The registry is funded by the Myotonic Dystrophy Support Group and Muscular Dystrophy Campaign with support from the TREAT-NMD Alliance.

61. Global FKRP registry
PI: Prof Straub
Status: Ongoing
The Global FKRP Registry is an international registry for all persons affected by conditions caused by a mutation in the *Fukutin-Related Protein* (*FKRP*) gene, namely Limb Girdle Muscular Dystrophy type 2I (LGMD2I), and also the rarer conditions Congenital Muscular Dystrophy type 1C (MDC1C), Muscle Eye Brain Disease and Walker-Warburg Syndrome. The Registry aims to facilitate recruitment into clinical trials by identifying patients more readily, accelerate research, and provide more detailed knowledge about the natural history and prevalence of FKRP-related muscular dystrophies, whilst keeping patients informed. The Registry was set-up in 2011 as an online patient driven registry and is currently supported by the LGMD2I Research Fund.

62. GNE myopathy-Disease Monitoring Programme (GNE-DMP): A registry and prospective observational natural history study to assess HIBM disease
PI: Prof Straub
Status: Ongoing
The Disease Monitoring Program is a public-private partnership between Ultragenyx Pharmaceutical Inc. (USA) and Newcastle University (UK). The program was designed to collect data on clinical presentation and progression of GNE myopathy to improve knowledge and support treatment development. The unique structure of the program allows a combination of longitudinal data collected through an online global patient registry and a hospital based natural history study in a single platform. The Natural History study is performed by selected centres in Europe, Middle East and North America. Anonymous data gathered through the registry will be accessible to the medical and research community, patients, families and patient organisations upon approval from the Steering Committee and Ethical Committee in the hope that this information will provide insight into the disease, and help drive clinical trials and research that could lead to better treatment strategies.

63. SMA REACH UK
Spinal Muscular Atrophy Research and Clinical Hub UK
Status: Open to recruitment
Funder: UK SMA charity: SMA TRUST
Sponsor: Great Ormond Street Hospital
Chief Investigator: Francesco Muntoni
Newcastle PI: Prof Katie Bushby
Target: ~70 Recruitment: 36
The primary aim of this project is to establish the first national clinical and research network named SMA REACH UK (SMA Research And Clinical Hub UK) to establish a national agreement on clinical and physiotherapy assessment and standards of care. We propose designing, piloting and expanding an electronic database created to streamline the collection of data for patients with SMA. This UK SMA database would be a unique infrastructure started at GOSH and Newcastle which would soon be built up and accessible to specialist centres across the UK who treat patients with SMA.

64. OPTIMISTIC
Observational Prolonged Trial in Myotonic Dystrophy type 1 to Improve Quality of Life Standards, a Target Identification Collaboration
Status: Open

Funder: EU Seventh Framework Programme
Sponsor: The Newcastle upon Tyne Hospitals NHS Foundation Trust
PI: Dr Grainne Gorman
End of July recruitment 23
UK Target 72
OPTIMISTIC is a two-arm, multi-centre, randomised controlled trial designed to compare a tailored behavioural change intervention against standard patient management regimes. It is expected that the trial and outcome work will lead to new clinical guidelines for DM1 management. The intervention comprises cognitive behavioural therapy (CBT) and graded physical activity, both of which aim to achieve a more active lifestyle. The effectiveness of this intervention, together with any adverse events associated with it, will be compared to standard patient management. Outcome measures will be measured at baseline, 5 months, 10 months (the end of the intervention period) and at 6-months post intervention (i.e. 16 months from baseline).

Closed Studies

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

Status: Closed
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.
Brain. 2013 Jul; 136 (Pt 7):2189-200. DOI: 10.1093/brain/awt133. Epub 2013 Jun
PMID: 23771340
[PubMed - in process]

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

Status: Closed
Sponsor: University College London
Funder: National Institutes of Health (NIH – USA)
PI: Prof. Hanna
Patients recruited: 11 target >10
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.

67. EPISODIC ATAXIA SYNDROME: GENOTYPE-PHENOTYPE CORRELATION AND LONGITUDINAL STUDY
Status: Closed
Sponsor: University College London
Funder: National Institutes of Health (NIH – USA)
PI: Prof. Hanna
Patients recruited: 36 target >20
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. *Brain 2014: 137;1009-1018*

68. OUTCOME MEASURES IN SMA TYPE II AND III
Status: Complete
Sponsor: UCL Institute of Child Health
Funder: SMA Europe
PIs: Prof Muntoni; Kate Bushby
Patients recruited: 26; target (UK) 23
Description: The primary aim of this project is to establish, for the first time, a clinical network involving most of the leading neuromuscular centres in Europe and to enable them to have common outcome measures in order to be ready for forthcoming multi-centre trials on SMA type II and III
Objective(s)
Primary objective:
• To establish a clinical network involving most of the leading neuromuscular centres in Europe enabling them to have common outcome measures on SMA type II and III.
Secondary objectives:
• To ensure the functional scales used are suitable and clinically relevant for future trials, that we understand how the different measures relate to one another and how they may change over a 12 month period
This prospective longitudinal natural history study will be performed in two cohorts of patients with SMA type II and III identified according to their level of functional motor ability

(ambulant/non ambulant). Inclusion criteria and methods will be different in the two cohorts and will be described separately. We have considerable retrospective data on SMA but very little planned data and none using the range of outcome measures proposed.
Further information can be obtained from the Trials Coordinator or Research Physiotherapist on 020 7905 2639.

69. PERIPHERAL NEUROPATHY OUTCOME MEASURES STANDARDISATION STUDY (PERINOMS)

Status: Complete
Sponsor: Erasmus Medical Center
PI: Dr M Lunn
Patients recruited: 110; 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.

70. Jain Foundation natural history and clinical outcomes study of dysferlinopathy (limb-girdle muscular dystrophy type 2B)
Status: closed to recruitment
Sponsor: The Newcastle upon Tyne Hospitals NHS Foundation Trust
Funder: Jain Foundation
PI: Prof Katie Bushby
Recruitment: 37 (Newcastle)
Target: 20
A clinical outcome study for Dysferlinopathy. To define the natural history of dysferlinopathy in a large unselected patient group with respect to age and nature of onset, progression and presence of complications via existing and expanded registries and databases. Study a selection of possible outcome measures for dysferlinopathy trials over a three year period in a multicentre evaluation of 150 patients based in centres of excellence for muscular dystrophy diagnosis and management. Extend the existing registry activities co-ordinated by the Jain Foundation to ensure a comprehensive

71. A Study of Biological Prognostic Factors for IGM Paraproteinemic Anti-Mag Associated Peripheral Neuropathy
Sponsor: UCL
Status: Closed
PI: M. Lunn
Recruitment target: 45 patients
Anti-MAG neuropathies have a variable severity and some have a non-significant response to immunotherapies, but all have significant risks of potentially severe adverse effects from treatment. It seems important to find predictive factors in order to determine which patients have a high risk of evolution to severe disability so treatment would be targeted to appropriate patients. We suggest studying factors which could influence the disease evolution including molecules that regulate the monoclonal IgN secreting B-cells (BAFF, APRIL, inflammatory cytokines), molecules that may modulate the alteration of the blood-nerve barrier (inflammatory cytokines, VEGFs, angiopoietins).

This is a retrospective cohort study, including patients from the National Hospital for Neurology, London, UK, and from the University Hospital of Rennes, France.

The objective is to determine biological factors in blood and CSF that could be predictive of severity of neuropathies associated with IgM anti-MAG antibodies.

Exercise Studies

Open Trials

72. Aerobic training in Charcot-Marie-Tooth disease and Inclusion Body Myositis.

Status: Recruiting
Sponsor: University College Hospitals
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.

For further information please contact Dr Amanda Wallace, Amanda.wallace@uclh.nhs.uk

73. Full Title: Exploring the causes of falls and balance impairments in people with neuromuscular diseases

Status: Recruiting
Sponsor: University College Hospitals
Funder: NIHR
PI: Dr Gita Ramdharry

Falls are commonly reported by people with neuromuscular disorders but to date there has been little formal investigation of this problem. Frequent falling increases the risk of injury and reduces mobility due to avoidance of activities perceived to increase the threat of falls. The aim of this study is to ascertain falls risk from measurement of falls incidents, balance impairment and clinical presentation in people with different types of Charcot-Marie-Tooth (CMT), Distal Myopathy (DM) and Sensory Neuropathy (SN) with healthy controls. Measurements of static, anticipatory and reactive balance impairment

and prospective falls events will be used to ascertain relationships with clinical presentation in people with different types of CMT, DM and SN. The three pathologies have been chosen for comparison as this will allow some discernment between the sensory and motor contributions to falls. *Physiotherapy. 2014 mar; 100(1):61-5. doi:10.16/j.physio.2013.06.002. Epub 2013 Aug 15. PubMed PMID: 23954023*

74. 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
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 Julia.maddsion@newcastle.ac.uk.

75. EXERCISE AND SARCOPENIA
Status: Recruiting
Sponsor: Newcastle upon Tyne Hospitals NHS Foundation Trust
Funder: MRC
PI: Prof DM Turnbull
Collaborating site MRC Centre London (Recruitment at Newcastle only)
Target: 36
Recruitment as of July: 22

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 sarcopenia
3. 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: years 30-40, 50-60 and 70+ . 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 16 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 Julia.maddison@newcastle.ac.uk

76. A Randomised controlled trial of tailored home exercise versus advice and usual care for disability in people with immune mediated neuropathy
Status: Open
Sponsor: King's College London
Funder: GBS/CIDP
PI: Dr Lunn
Collaborating site KCL
Patients recruited: 0
Study design: A prospective parallel observer blind randomised controlled trial of a tailored home exercise programme (tHEP) versus information about exercise and usual care (UC) that included a 12 month follow-up with economic evaluation of cost-effectiveness and cost-utility and a nested qualitative process evaluation.
Sample: People with stable motor neuropathy, with or without sensory neuropathy as a result of GBS, CIDP or PDN will be recruited. The sample seize is based on a 80% power calculation to detect a difference between mean change in overall disability sum score (ODSS) of 1 point using a 2-sided test at the 5% significance level based on a SD of 1.27 from pilot study data. Fifty four people (27 per group) will be needed; therefore 70 people will be recruited to allow for a 25% attrition rate at 12 months.

Closed Trials

77. 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 target: 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.
Results published Journal of the Peripheral Nervous System, 2011; 16(S3):S115

78. EXERCISE TRAINING IN PATIENTS WITH MITOCHONDRIAL DISEASE: ASSESSING THE BENEFITS
Status: Closed
Sponsor: University Newcastle
Funder: Muscular Dystrophy Campaign (MDC)
PI: Prof Turnbull
Collaboration site MRC Centre London (Hanna)
Patients recruited: 9Newcastle; 0 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 are:
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.

79. CARDIAC ADAPTATIONS TO EXERCISE IN MITOCHONDRIAL DISEASE
Status: Closed
Sponsor: Newcastle upon Tyne Hospitals NHS Foundation Trust
Funder: MRC
PI: Prof D M Turnbull/Dr MI Trenell,
Patients recruited: 39

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 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 Julia.maddison@newcastle.ac.uk.

Imaging Studies

Set-up Phase

80. A study of Qualitative Magnetic Resonance Imaging in Channelopathies
Status: Set-up
Sponsor: UCL
PI: Prof M Hanna
The skeletal muscle channelopathies are a heterogenous group of diseases caused by mutations in voltage-gated skeletal muscle ion channels. Broadly speaking, they can be divided into the non-dystrophic myotonias (NDM) and the periodic paralyses (PP).

The objective of this retrospective study is to define the presence, frequency and pattern of MRI abnormalities in the lower limbs of patients with genetically proven PP compared with healthy volunteers. Furthermore, we will describe differences in MRI abnormalities in the subsets of PP.

It will involve approximately 40 patients with genetically confirmed periodic paralysis. To allow blinded analysis, in addition to the MRI scans available from 12 healthy volunteers involved in a previous research study, 12 healthy volunteers will undergo standard clinical lower limb MRI.
For more information about the study please contact Dr Matthew Evans at matthew.evans@ucl.ac.uk

Open Trials

81. Magnetic Resonance Imaging Characteristics of Inflammatory Neuropathies – a pilot study
Status: Open to recruitment
Sponsor: University College London Hospitals
PI: Dr Lunn
Patients recruited: 20: 10 patient; 10 controls
The assessment of patients with peripheral nervous system (PNS) disease is currently mainly dependent on clinical examination, neurophysiological tests and occasionally nerve biopsy. Clarification of nerve imaging characteristics in chronic inflammatory demyelinating polyneuropathy (CIDP) could alleviate the need for invasive procedures such as nerve biopsy in cases where there is uncertainty in the clinical diagnosis.
Magnetic resonance imaging (MRI) has been widely applied to neurological diseases of the central nervous system, but to a much lesser extent diseases of the PNS. Research in inflammatory neuropathies has included traditional T1 and T2-weighted sequences; some more recent work in mainly focal entrapment neuropathies has looked at novel MRI sequences such as diffusion tensor imaging.
CIDP is an immune mediated condition characterised by progressive or relapsing motor and sensory deficits in all four limbs. It is a treatable condition and often responds to immunomodulatory treatment. Currently the diagnosis is based on a combination of clinical, neurophysiological and supportive criteria. Diagnosis can be difficult as the

causative pathology is often proximally sited in the nerves, and their proximal portions are less anatomically accessible to neurophysiological examination.

Recent work in our unit has demonstrated that the sciatic nerve area in CIDP patients is significantly enlarged compared with controls, but with substantial overlap between the ranges of values obtained for disease and control groups. Since much of the pathology in CIDP is located at the nerve roots it is important to assess whether enlargement of the roots is able to differentiate between CIDP and controls.

There is no published research documenting the use of novel MRI techniques in patients with CIDP. Diffusion sequences and assessment of the magnetisation transfer ratio (MTR) of nerves may reveal diagnostic characteristics in diseased tissue, as is seen in the brain. **Aims:**

We aim to clarify the use of MRI for the diagnosis of patients with chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMNCB). Using 3T MRI, we will use both conventional and novel quantitative MRI sequences to examine the nerve roots, plexuses, sciatic nerves and forearm nerves of 10 patients each with CIDP, MMNCB and 20 healthy volunteers. We will quantify nerve root cross sectional area in cervical and lumbar regions in patients with CIDP, MMN and healthy controls. We will explore imaging characteristics of the sciatic nerve in patients with CIDP versus healthy controls. We will define imaging characteristics at sites of conduction block in nerves of patients with MMNCB. In a separate group of patients with suspected inflammatory neuropathy we will compare MRI to pathological findings on nerve biopsy. MRI may be shown to be a useful non-invasive diagnostic tool.

For further information, contact Dr Jasper Morrow, j.morrow@ucl.ac.uk

82. 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: Closed to Recruitment
Sponsor: University College London Hospitals
Funder: MRC
PI: Prof T Yousry/Dr J Thornton
Patients recruited: 72: 40 patients; 32 controls

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@ion.ucl.ac.uk.
Submitted to European Radiology

83. Magnetic Resonance Imaging as an outcome measure in Motor Neuropathies: a pilot study
Sponsor: UCL
PI: Hanna
The development of novel therapies for motor neuropathies necessitates the search for a reproducible outcome measure which can sensitively monitor disease progression. Muscle magnetic resonance imaging (MRI) is an excellent candidate due to its reproducibility and observer independence. We plan to investigate various parameters obtained through muscular MRI as longitudinal biomarkers in diseases of the motor neuron with different speeds of disease progression: amyotrophic lateral sclerosis (ALS), Kennedy's disease (KD) and distal hereditary motor neuropathy (dHMN). Using 3T MRI the research team will perform lower limb imaging with quantitative 3-point Dixon, magnetisation transfer and IDEAL-CPMG sequences in addition to standard qualitative T1 and STIR sequences in 12 patients each with ALS, KD and dHMN as well as 12 healthy volunteers. Detailed clinical data will be collected, including isokinetic and isometric lower limb strength. These assessments will be repeated at a 3 and 12 month interval in ALS patients and at a 6 and 12 month interval in dHMN and KD patients. We will analyse the value of quantitative MRI as an outcome measure in these conditions by analysing both correlation with clinical measures and sensitivity to

change over time. Data from this study will be able to be used to establish sample size in clinical trials to evaluate novel therapeutic strategies in these diseases.
MRI has been widely applied to neurological diseases of the central nervous system, but to a much lesser extent diseases of the peripheral nervous system (PNS), and even less frequently to the diseases in this study.
The hypothesis is that MRI can detect changes in the muscles in patients with ALS, KD and dHMN.
The proposed project will take place in two phases, an initial cross-sectional case control study of all patients and volunteers followed by a longitudinal natural history study.
MRI imaging will be performed of thigh and calf muscles at 3 Tesla in a scanning session lasting approximately an hour. All participants will undergo standard MRI imaging with T1-weighted and STIR sequences. The following quantitative MRI techniques will be used: magnetization transfer imaging, T2 relaxometry with IDEAL-CPMG and 3-point Dixon fat quantification. We will not be using gadolinium contrast in this pilot study.
For further information contact Dr Jasper Morrow, j.morrow@ucl.ac.uk

Closed Studies

84. 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: Closed
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@ion.ucl.ac.u.k.

LGMD2I Longitudinal paper accepted by PLOS ONE

85. A Study of Quantitative Magnetic Resonance Imaging to Monitor Disease Activity in Hypokalaemic Periodic Paralysis.

Status: Completed

Sponsor: UCL

Funder: MRC

PI: Hanna

Recruitment: 24: 12 patients; 12 controls

The commonest muscle channelopathy is hypokalaemic periodic paralysis caused by mutations in the voltage sensor regions of either the muscle sodium channel SCN4A or the muscle calcium channel CACN1AS. From childhood, patients experience disabling episodes of complete muscle paralysis lasting hours to days. In the early years patients recover in between attacks but over time they develop a permanent fixed muscle weakness (myopathy) and often become wheelchair bound. Although there are established treatment strategies which we and other centres in USA and Europe employ and which can reduce attack frequency, we do not have sensitive methods to monitor disease activity or to determine if the treatment regime is fully effective.

Recent data indicate that muscle water content may be a key determinant of muscle function in patients with higher abnormal water content (oedema) correlating with more weakness. Preliminary published data indicates patients with less oedema may have a better prognosis. Furthermore, we currently make decisions to adjust standard treatments based on attack frequency only and this may not be the most reliable way to monitor actual disease activity in affected muscles. In this study we wish to

evaluate abnormal muscle water content using MRI applied in the context of the normal current clinical practice and management in this patient group.
In this study we aim to show that patients with hypokalaemic periodic paralysis have abnormal muscle water on MRI which is inversely correlated with muscle strength and sensitive to changes over time. In a wider context than this study, similar techniques may be applied to other muscle diseases, where MRI could guide treatment in clinical practice and act as an outcome measure in clinical trials.
This study has two phases. The first phase is a period of MRI technique refinement in up to 10 healthy volunteers lasting up to two months. The main study phase is a longitudinal case control study and will study a minimum of twelve patients with hypokalaemic periodic paralysis and twelve healthy volunteers who will act as a comparison group for the patients. Assessments will be repeated at a four week interval to see if any changes in clinical parameters are reflected in changes on MRI parameters. One of the inclusion criteria for patient enrolment will be evidence of active disease in order to maximise differences between the two time points.
For further information contact Dr Jasper Morrow: j.morrow@ucl.ac.uk
Data in analysis

86. Full Title: Evaluation and Optimisation of Muscle Imaging Biomarkers in Support of Non-ambulant Duchenne Muscular Dystrophy Studies
Status: Closed to recruitment
Sponsor: UCL Institute of Child Health
Funder: GSK
PI: Prof Francesco Muntoni
Patient target: 15 (UK) Recruited 15 patients, 10 controls
The primary objective of this study is to characterise the differential involvement of muscle
groups occurring with disease progression (i.e. as a function of age) using skeletal muscle
MRI so as to more precisely define which muscle groups could provide the best markers for
therapeutic response in the non-ambulant boys.
The secondary objectives of this study are to

- Measure quantitative imaging changes in DMD muscle over the course of one year

using skeletal muscle and dynamic breathing MRI.

- Measure quantitative imaging changes in diaphragm movement occurring with

disease progression (i.e. as a function of age) using dynamic diaphragmMRI.
For more information about the study please contact Dr Valeria Ricotti at v.ricotti@ucl.ac.uk.

Future Meetings 2014 - 2015

DM Patient information day
8th November 2014
Basingstoke
Contact Dr Chris Turner. chris.turner@uclh.nhs.uk for further details

MRC Centre for Neuromuscular Diseases/Muscular Dystrophy Campaign UK Translational Research conference 2015
19-20th March 2015
Centre for Life, Newcastle
Organised by Christine Oldfield.

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

Appendix 1:

Minutes from previous council meetings 2008 – 2013

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
An annual meeting of the BMS over two days with an overnight stay for socialising and networking was agreed as the preferred format. Possible date: 23rd and 24th April 2009

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 i.e. 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.

1st October 2008, WMS meeting of BMS council, Newcastle

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.

Minutes of 2009 meetings

11th March 2009, BMS council telephone conference
All council members called in and programme agreed.

30th September 2009, conference call

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 i.e. 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

14th April 2010, conference call

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

Minutes of the BMS meeting debrief 30th September 2009 were accepted as a correct record.

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.

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:

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.

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.

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

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.

Minutes of 2011 meetings

10th June 2011, conference call

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

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 liaise with Marguerite 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

Minutes of 2012 meetings

MRC Centre for Neuromuscular Diseases

British Myology Society Conference Call
22nd May, 2012

Present:	**Apologies:**
Michael Hanna (Chair) David Hilton-Jones Francesco Muntoni Richard Petty Helen Roper Caroline Sewry Michael Wright (minutes)	Kate Bushby Janice Holton

1. Dates Confirmed
The dates for the 2012 BMS Annual meeting were confirmed as Tuesday 4th & Wednesday 5th September.

2. Agreed programme
The following sessions were agreed:

- A short session on Commissioning

Action point: Mike Hanna to contact Teresa Moss & Robert Meadowcroft

- Avoiding Emergency Admissions
- Registry Databases and Networks Update e.g. Northstar, IBM net, mito database, Neuromuscular database (to explore and make the link into commission process and service specification)

Action point: Mike to check status of current specifications

- Duchenne in Adults (to include transition, cardiac care, quality of life, ventilation and end of life issues)
- MRI
- Genetics Sequencing

Action point: Mike to contact Henry Holden as possible speaker

- CPC

Action point: Mike to invite someone to comment

- Rhabdomyolysis
- Statin & Muscle Diseases
- Exercise & Muscle Diseases
- Pathology and how to improve the situation in the UK

Action point: Caroline Sewry to talk with Janice Holton on potential speakers
Action point: Mike to invite Mary Reilly to give an update from BPNS (British Peripheral Nerve Society)

General comments:

- David Hilton-Jones noted that a greater clinical bias would help in attracting an audience.
- Francesco Muntoni suggested that the registry-commission-tariff link remains very important and that a report on progress from last year would be useful.
- Francesco suggested we invite a palliative care consultant to discuss the Duchenne topics.
- David suggested including a debate in the schedule and suggested possible issues of the arguments for neo-natal screening for Duchenne disease or CPC. If the former Francesco would be unable to act as advocate but Juliet Ellis & Stuart Mott might be suitable alternatives.

3. Myasthenia study group session

Mike asked if David thought the Myasthenia trust group would be interested in participating this year. David reported that Marjorie Hill would not be coming to the Annual Meeting.

4. MIG Session

(Not discussed)

5. Guest speaker

Mike asked for suggestions for an after dinner speaker
Action point: all council members to send suggestions to Mike Hanna

6. Date of next meeting

A second conference call will be held in approximately two weeks. Date TBD.

7. AOB

None

British Myology Society
26th June 2012, Conference Call

Present:	**Apologies:**
Michael Hanna (Chair) David Hilton-Jones Francesco Muntoni Richard Petty Helen Roper Caroline Sewry Michael Wright (minutes)	Kate Bushby Janice Holton Michael Rose

1. Minutes of the last meeting

The minutes of the last meeting were agreed. No matters arising.

2. Draft Programme for Annual Meeting, St Anne's College, Oxford

A draft meeting programme was distributed to Council prior to the meeting.

Day 1
Commissioning
The session on commissioning will include a short presentation from the NHS Specialised Services team on the service specification document currently being prepared.
Action Point: Mike Hanna to invite Teresa Moss

Managing Duchenne in Adults
It was agreed that a focused session on Duchenne and transition into adulthood should be included. The council were asked for suggestions as to speakers. It was suggested that John Bourke of Newcastle University would be good person to speak on cardiac issues, and on respiratory issues Anita Simonds from Royal Brompton and Harefield. As regards to palliative care Francesco Muntoni will provide the names of two colleagues from GOSH who might be interesting speakers.
Mike Hanna suggested that Ros Quinlivan be approached in regards to chairing a session. This was agreed.
Action Point: Francesco Muntoni to send Mike Hanna the two names from GOSH.
Action point: Mike Hanna to contact Ros Quinlivan to discuss.

Debate Session - Neonatal screening in Duchenne
The council was asked for suggestions as to possible speakers, for and against. Nick Catlin (CEO Action Duchenne) was suggested as a possible advocate, and Juliet Ellis

(King's College) as a potential opponent. David Hilton-Jones suggested that two polls be taken at the meeting, one before the session and again one afterwards.
Action point: Mike Hanna to contact Nick Catlin and Juliet Ellis.

National network databases/service specification
It was agreed that a session on databases would be of interest to members providing the presentation was kept to a summary of such databases as are in use now, and the steps in linking these to tariffs.
Action point: Mike Hanna to contact Adnan Manzur (GOSH), Matt Parton (MRC Centre for Neuromuscular Diseases) & Chris Turner (MRC Centre for Neuromuscular Diseases)

Update on pathology services
A session on pathology was agreed by the Council to be led by Caroline Sewry. Possible speakers to include Seth Love (Bristol University) and John Xureb (Cambridge University).
Action point: Caroline Sewry to contact Seth and John.

After Dinner Speaker
Action Point: ALL, to send Mike Hanna suggestions as to after dinner speakers.

Day 2
Exercise in Muscle Disease
Mike Hanna proposed an Exercise in Muscle Disease session to be hosted jointly between Mike Trenell (Newcastle University, MoveLab) and Gita Ramdharry (MRC Centre for Neuromuscular Diseases). In addition David Hilton-Jones suggested Helen Dawes (Oxford Brookes University) as a third co-host.
Action point: Mike Hanna to contact Helen Dawes

MRI in Muscle Practice Now
It was agreed that Jasper Morrow (MRC Centre for Neuromuscular Diseases) would be invited to present a session on MRI.
Action point: Mike Hanna to contact Jasper Morrow

Muscle Interest Group
Helen Roper agreed to take the lead on presenting a Muscle Interest Group session.

Training
Helen Roper proposed an additional session on Training. It was agreed this could be presented in combination with the Pathology session.

High Risk Audit Project
It was agreed that an update session on the high risk audit project being led by Tracey Willis (RJAH Orthopaedic Hospital) could be included if Tracey is available to present it.
Action point: Mike Hanna to discuss with Tracey Willis.

3. AOB: None

MRC Centre for Neuromuscular Diseases

Minutes of 2013 meetings

17 May 2013, Conference Call

Present:	**Apologies:**
Michael Hanna (Chair) David Hilton-Jones Janice Holton Francesco Muntoni Michael Rose Helen Roper Caroline Sewry Ros Quinlivan Simon Hammans	Kate Bushby Richard Petty

Minutes of the last meeting

The minutes of the last meeting were agreed. No matters arising.

The annual BMS meeting programme was discussed. The combination of the MSG, the MIG and the BMS all in Oxford during the same week was outlined.

The following format was agreed:

Day 1 5pm - 6pm
Commissioning session to include data on commissioning from Simon Hammons, MDC commissioning related research project.
Action: Mike to invite Robert Meadowcroft and Carolyn Young

6pm NIHR Translational Research Collaboration
Action: Mike to invite Patrick Chinnery

7-8pm NCG services, 3 short talks.

Latest developments in the mitochondrial service, the rare neuromuscular disease service, and the McArdle service.
To include full details of the latest referral forms and pathways for all NCG services in the brochure
Action: Mike to contact Tracey Willis regarding national diagnostic algorhythm and invite Katie, Bobbie and Ros

There will be an AGM just before dinner

After dinner speaker Victor Dubowitz
Action: Mike to invite Victor Dubowitz to give after dinner speech

Day 2: 8.30 to 10.30 is the Muscle Interest Group to be organised by Helen Roper.
Action: Christine to send Helen Roper Donna la Donna's email address and Birch Griggs email address so that they can invite USA colleagues if they want to contribute to the interest group session.

11 - 12.30 Session on Myotonic Dystrophy to include talk from Charles Thornton, Chris Turner, Mark Roberts and Perry Elliot (cardio)
Action: Mike to invite Charles Thornton and speakers.

Review of the management of Myotonic Dystrophy to include cardiac respiratory GI and somnolence
Chris Turner and Mark Roberts and Perry Elliot to talk about cardiology aspect
Action: Mike to invite all

The after lunch session will be a review of latest developments in congenital myopathy diagnosis and management, and is to include Francesco Muntoni, Heinz Jungbluth, and Ros Quinlivan. Include presentations of interesting cases
Action: Mike to invite all

Other items to note:
Meeting closes at 4pm
Please note meeting is in Worcester College
Noted that this meeting overlaps with the Myasthenia Interest Group meeting and also earlier in the week with the Muscle Study Group meeting.

Action: Christine to let Donna la Donna know that MSG Members are invited to the BMS meeting but they need to register in advance.

Agreed that a doodle poll will be set up to arrange a face to face meeting in London for BMS Council probably in early September to discuss the strategy of the BMS going forward.
Action: Christine to set up Doodle Poll

As Michael Wright, the acting secretary has left, it was agreed that secretarial duties would be taken over by Christine Oldfield

MINUTES FOR THE MEETING OF THE BMS COUNCIL
Wednesday 4th September 2013

Present: Mike Hanna (Chair), Michael Rose, Janice Holton, Caroline Sewry, Ros Quinlivan, Francesco Muntoni, Simon Hammans, Helen Roper, David Hilton-Jones Kate Bushby(by phone), Richard Petty.
In attendance: Christine Oldfield (minutes). Christine Oldfield was introduced as the new BMS administrator.

Apologies: none (all council present)

1) Welcome
MH welcomed all and explained that the aim of the meeting was to review with Council that the BMS is still meeting its aims, and/or whether any changes are needed to the aims, or processes in place to achieve them.

2) BMS rules and Aims
MH reported that the original aims of the BMS had stemmed from an idea to make NMD better served than by the existing professional associations and for the BMS to be less focused on neurologists. It aimed to develop a multi-disciplinary approach with membership that includes the full range of colleagues involved in the management and care of NM patient. Over the past 5 years meetings had been well attended and the BMS had established itself as an entity on the UK NM landscape that complemented existing mainly research focussed meetings. The BMS had achieved full registered charity status.

<u>MH asked for suggestions re: how the current aims were being met or could be changed</u>

MH explained that over the past 5 years while the BMS was being established the main focus had been on organising the annual meeting and working with Council to produce a programme that addressed the aims of the BMS and was of interest to the UK NM community.

There was now an opportunity for BMS to develop specific streams of activity that might take place between meetings to enhance delivery against its aims. This would require specific council members being allocated more specific roles and responsibilities. There was agreement by all council members this was a logical evolution for the BMS.

Discussion points
RQ proposed trying to encourage other therapists and trainees to attend the meeting (to **broaden the membership**)- this was agreed by the council

HR mentioned that progress has been made in **standards of care** in DMD which should be endorsed by the BMS and further work on standards of care might be linked to/lead by BMS.

FM mentioned that BMS could have an important role in **supporting best clinical practice** e.g. an algorhythm for muscular dystrophies could be an example of a deliverable for the BMS (and that there is some existing work on such an algorhythm). This was agreed by SH. DHJ proposed that this could be developed as a downloadable app for students. An app for myasthenia was also suggested.

DHJ proposed providing **training day for juniors linked to the BMS meeting** – the example of the BPN training day was given.

The following was agreed:

Training Day for trainees
It was agreed that in 2014 we would establish a training day, likely to be on the morning of the 1st day of the meeting. It would be further considered how to focus the teaching e.g. adult / paediatric topics. HR proposed that the training day could be opened also to those not currently in neuromuscular posts.
Responsible Council members DHJ SH

Neuromuscular Curriculum and attracting trainees
HR proposed to expand on current standard for neuromuscular training. KB mentioned that there was some discussion in the original BMS meeting about this. KB suggested targeting existing groups / other meetings to try to target good trainees and attract them into muscle work. An example was to have a BMS session at other meetings such as the ABN.
RQ proposed future workforce mapping to ensure that it is clear to potential trainees that there are
positions available later in their careers.
Action: KB to provide previous literature from European discussions about adult / paediatric training
Responsible Council member- HR

Planning the BMS programme each year
MR proposed linking each item of the BMS annual meeting to a BMS objective, with a post-review
meeting to check aims being met. It was also proposed that this could be an audit project.
Responsible Council member- MH plus all council

RP suggested putting in place a rating / scoring system to classify nurses / physios as neuromuscular specialists, as possibility to lose this to generic NHS positions. KB mentioned there is already a structure through North Star which could be linked with or built on. It was suggested that a member(s) from such a group may wish to collaborate with the BMS

Standards of Care in NMD

Standard of care: it was discussed that this has already been taken on by other organisations / that this work may require funding and a larger commitment than BMS council members are currently able to give. It was agreed that aims needed to be realistic although as existing BMS is made up of UK experts he felt that BMS activities would carry some weight. KB mentioned that a charity such as the MDC could be asked for funding help with this, and that there is existing guidance on how to develop these standards which could be used. It was noted MR had considerable experience in this area and was actively involved in developing standards of care. It was agreed that BMS endorsed guidelines could be a useful role of BMS given the major clinical nm expertise that exists amongst BMS members. It was agreed BMS should have a strategy around guidelines.

Responsible Council member MR

Muscle Pathology Services

CS and JH suggested development of initiatives to help pathologists to interact more with clinicians. It was suggested that the BMS meeting could be made more attractive to neuropathologists. It was suggested that the proposed BMS training day could be beneficial to neuropathologists if they could be engaged. A muscle pathology course under the auspices of the BMS should be considered e.g. at Queen Square lead by CS and JH.

Responsible Council Members JH and CS

Public and patient involvement and the BMS

MR mentioned that PPI is becoming very important and the possibility of recruiting a council member who was a patient / patient representative / layperson was discussed. RQ raised whether this fell within the BMS remit. It was agreed that patient representatives would be co-opted to subgroups as required, but that one would not at this time be recruited to council. It was agreed that the rules would be changed to reflect this.

Actions relating to above:

- **Responsible council members will take responsibility for allocated area and develop a brief strategy to report to council at next council meeting.**

- **Subject to approval at AGM BMS rules will be changed to reflect that there will be council members with responsibility in each of these areas.**
- **Rules will also be changed to reflect the importance of PPI to be co-opted onto subgroups**

Council agreed with all the above and it was suggested that subcommittees could be formed as appropriate.

Summary -It was agreed that the following council members would take responsibilities for aims as follows:

- **Trainee day 2014 – DHJ and SH**
- **Algorithm and App development FM and DHJ**
- **Workforce mapping – RQ and RP**
- **Standards of care – MR**
- **Pathology – CS JH**

Term of Office of Council members

It was discussed if terms of office of council members should be longer to avoid too much disruption to streams of work while ensuring that BMS members could have the opportunity to stand for council election.

JH suggested that 4-5 years (rather than 3) might be a reasonable term and this was generally agreed and will be put to AGM.

It was suggested by HR that two consecutive terms could be served and this was agreed.

Action: rule change as above to be proposed at AGM

MH proposed that elections should take place after the next BMS- this should include the chairman and any members of council who wished to stand down. It was discussed and agreed that the next chairman could come from BMS membership or from BMS council. It was agreed that as per the rules the chairman must provide a dedicated secretariat for the BMS which averages about 1 day a week over the year. The chairman's responsibilities include maintaining charitable status/accounts and generating funds for the secretariat.

3) BMS programme 2013

Copies were provided and a quick summary was given.

4) BMS 2014 proposal

Annual meeting location

The location of the annual meeting was raised. Previous requests for another venue and BMS member to take on the meeting and the organisation had not met with any volunteers.

Action: question of venue to be raised again in the AGM

DHJ reported that in 2014 the Oxford summer meeting week clashes with a major international NM meeting meeting it was proposed that for 2014 that the two meetings merge, running consecutively, possibly with an overlap.
Action: CO to check 2014 MSG date for possible clash.
FM and SH felt that this was a good, practical idea on the face of info give. MR mentioned that there might be a clash of cultures between the two meetings.
It was generally agreed this was a sensible idea and it should be proposed at AGM that there is a combined meeting in Oxford in 2014

5) Commissioning

MH provided update on specialist commissioning and the role of CRGs. There are three CRGs in which NM diseases are represented- multisystem CRG (Hanna chair and strong nm membership), Neuroscience CRG, paediatric neuroscience CRG. The function of CRG was outlined- potential opportunities to support nm service developments and resource allocation were outlined.

6) **AOB**

MH reported that a new BMS bank account had been set up to make sure the BMS complies with all Charities commission regulations.

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Conference brochure prepared by Mike Hanna and Christine Oldfield
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