British Myology Society
Second Annual Meeting

2nd – 3rd September 2010
St Anne's College, Oxford

MRC | Centre for Neuromuscular Diseases

Contents

Welcome from the BMS organising Council

Dear Member,

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

The BMS background

The object of the BMS is to act as an independent multidisciplinary professional body of experts to promote the clinical practice, education and advancement of knowledge relating to muscle diseases, myasthenia gravis and spinal muscular atrophy in the British Isles and Ireland. The BMS was established in London in April 2008 and has registered for charitable status (number 5011301). Some rules have been drawn up and are contained in this brochure. 84 colleagues have accepted invitations to be members and we are very pleased that 63 are attending this second meeting in Oxford.

The specific aims of the BMS include:

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

Running the BMS

The BMS is a new venture which is untested. It has come together as a result of discussions and some meetings of the colleagues listed at the end of this introduction. At present the secretariat for the BMS is located at and sponsored by the MRC Centre for Neuromuscular Diseases in London. The organising group have agreed that initially there will be no subscription to be a member for the BMS. At the first annual BMS a brief AGM was held - see minutes. Since this was a new venture, and we needed to assess if it will be useful to colleagues, we considered it reasonable to simply ask colleagues if they are content for the initial organising group to continue to organise the next two meetings and to have a show of hands. This was agreed as indicated in the minutes.

The first BMS meeting

Based on discussions within council and a questionnaire of members (45 responses) we devised a programme of interactive sessions for the first annual BMS meeting.

The key themes that were covered in interactive sessions included:

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

The invited guest speaker was Professor Robert C Griggs, President of the American Academy of Neurology. Professor Griggs established the North American Muscle Study Group which has successfully facilitated neuromuscular translational research and delivered clinical trials.

This year the council have devised a programme which builds on the themes covered in the first meeting and we will also report on progress in the UK in each of these areas. This year we are delighted that Professor Marianne de Visser has agreed to be our guest speaker.

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

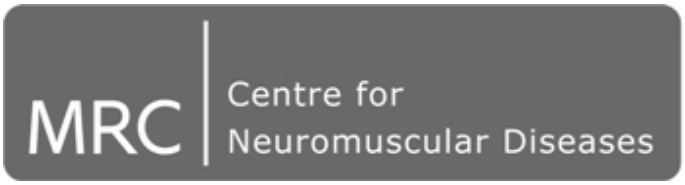
Michael Hanna, David Hilton-Jones, Francesco Muntoni, Kate Bushby,

Doug Turnbull, Janice Holton, Caroline Sewry,

Helen Roper, Mike Rose, Peter Baxter, Doug Wilcox

Professional Academic sponsor

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



About the MRC Centre for Neuromuscular Diseases

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

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

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

Professional and patient organisation partners

Second Annual meeting of the British Myology Society
2nd – 3rd September 2010
St Anne's College, Oxford

THURSDAY 2nd SEPTEMBER 2010 - Day 1

15:00 – 15:15	**Welcome and Introduction** The BMS progress to date	Michael Hanna

15:15 – 18:25 Neuromuscular Services in the UK

15:15 – 15:45	Review of regional commissioning Update from the Muscular Dystrophy Campaign	Robert Meadowcroft
15:45 – 16:00	Commissioning discussion	Michael Hanna
16:00 – 17:00	Update on NCG services:	Kate Bushby
	LGMD	Rita Barresi
	Muscle channel	Mike Hanna
	Congenital myasthenia	Jacqueline Palace
	Congenital muscular dystrophies and myopathies	Francesco Muntoni
	Mitochondrial	Bobby McFarland
	Enzyme replacement – Myozyme	Mark Roberts
17:00 – 17:30	NCG service round table discussion	Francesco Muntoni
17:30 – 17:45	Coffee break	
17:45 – 18:05	Muscle pathology services: new developments	Janice Holton
18:05 – 18:25	Pathology services discussion	Caroline Sewry

18:25 – 20:00	**Network updates and panel**	**David Hilton-Jones**
18:25 – 18:40	UK training update	Chris Turner
18:40 – 18:55	National database	Adnan Manzur
18:55 – 19:05	Scottish Network	Douglas Wilcox
19:05 – 19:15	TREAT-NMD	Kate Bushby
19:15 – 20:00	Round-table discussion with speakers and audience	Leads: Hanna, Muntoni, Hilton-Jones & Bushby
20:00 – 20:15	AGM	Michael Hanna/ Francesco Muntoni
20:15	Dinner at St Anne's College (main hall)	

FRIDAY 3RD SEPTEMBER 2010 – Day 2

07:30 – 08:15	Breakfast (main hall)	
08:30 – 09:20	**Invited lecture:** Neuromuscular services in The Netherlands	Marianne de Visser
09:20 – 12:30	**Muscle Interest Group**	Helen Roper
09:20 – 10:50	MIG unsolved cases: 3 adult/3 paediatric	
10:50 – 11:15	Coffee break	
11:15 – 12:30	MIG solved cases: 2 adult/2 paediatric	
12:30 – 13:15	Lunch (main hall)	

13:15 – 15:30	**Trials and translational research**	
13:30 – 14:10	Latest information on adult and paediatric clinical trials in the UK and beyond:	
13:30 – 13:50	Adults	Michael Hanna
13:50 – 14:10	Children	Kate Bushby
14:10 – 14:30	Muscle Quality of Life study in the UK	Michael Rose
14:30 – 14:40	Discussion	
14:40 – 15:30	Myasthenia Interest Group	David Hilton-Jones
	Management issues in childhood	Stephanie Robb
	Autoimmune myasthenia	Heinz Jungbluth
15:30 – 16:00	**Invited lecture** "Enzyme replacement therapy in the UK: evidence and current practice"	Robin Lachmann
16:00 – 16:15	**Conclusion and next steps**	Michael Hanna & David Hilton-Jones
16:15	Close	

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*Attending the BMS annual meeting

Rules of the BMS

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

23. The agenda for the Annual General Meeting of the Association shall be sent to Ordinary and
Honorary Members by the Honorary Secretary at least one week before the meeting is held.

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

Other Rules

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

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

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

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

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

Minutes from previous meetings from 2008

Monday 28th April 2008

Present:

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

Apologies:

Doug Turnbull, Kate Bushby

The following points were agreed:

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

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

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

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

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

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

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

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

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

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

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

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

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

It was noted the BPNS addressed all peripheral nerve diseases.

4th July 2008, Worcester College Oxford

Present

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

Apologies

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

Previous meeting minutes

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

Matters arising

Rules adjustments:

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

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

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

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

Membership of the BMS

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

It was agreed that trainees in myology should be associate members.
It was agreed that the BMS should be an independent professional body.

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

Invitation to be members:
It was agreed that a standard email should be sent to all colleagues potentially interested in being members of the BMS.
This email should be accompanied by the latest version of the rules.

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

HR will circulate to the MIG members

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

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

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

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

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

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

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

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

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

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

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

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

Action

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

AOB

None

Date of next meeting

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

WMS meeting of BMS council Newcastle 1 October 2008

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

Apologies: all other council members

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

BMS council telephone conference 11 March 2009

All council members called in and programme agreed.

Minutes of 2009 meetings

Conference call, 30 September 2009

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

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

The following points were agreed:

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

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

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

The purpose of the meeting is to

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

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

3) Colleague networking

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

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

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

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

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

Action Mike and Zoe to do a Doodle Date choice

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

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

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

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

Minutes of 2010 meetings

Conference call 14th April 2010

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

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

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

The following was agreed in relation to the programme:

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

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

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

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

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

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

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

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

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

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

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

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

Following lunch will be an optional Myasthenia Interest Group update.

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

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

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

The meeting will close at 16.00.

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

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

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

AOB
None.

AGM minutes from 2009 meeting

The 2009 AGM took place at 19.45 on Thursday 2nd July at St Anne's College during the first annual meeting of the BMS.

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

Agenda AGM 2010

To be tabled.

MRC BMS workshops 2009-2010

Management of foot deformity in CMT, London September 2009

Sponsored by the Muscular Dystrophy Campaign
Adnan Manzur

Exercise therapy in Neuromuscular Diseases, Newcastle 4-5 Nov 2009

Doug Turnbull, Mike Trenell, Mike Hanna

Respiratory Management of Congenital Myasthenic Syndromes, London 8 Dec 2009

Stephanie Robb, Anita Simonds

Planned MRC BMS workshops 2010-2011

MRC Myotonic Dystrophy Workshop

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

Workshops and other meetings continued

- Muscle Interest Group MIG 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@ion.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.parson@uclh.nhs.uk

Current UK Neuromuscular Clinical Trials

Clinical trials linked to the MRC Centre and supported by different funding agencies including the Medical Research Council, Muscular Dystrophy Campaign, UK Department of Health, National Institutes of Health (USA), Food and Drug Administration (USA), AVI Biopharma and PTC Therapeutics.

Completed Trials

RESTORING DYSTROPHIN EXPRESSION IN DUCHENNE MUSCULAR DYSTROPGY: A PHASE I/II CLINICAL TRIAL USING AVI-4658
Status: Completed (closed to recruitment)
Sponsor: Imperial College London
Funder: Department of Health (DoH)
PIs: Prof. Muntoni Bushby

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].

RANDOMISED DOUBLE-BLIND PLACEBO CONTROLLED TRIAL OF LONG-TERM ASCORBIC ACID TREATMENT IN CHARCOT-MARIE-TOOTH DISEASE TYPE 1A
Status: Follow-up phase (closed to recruitment)
Sponsor: University College London
Funder: Muscular Dystrophy Campaign (MDC)
PI: Dr. Reilly

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, randomized, double-blind, placebo-controlled study aiming to evaluate the efficacy of AA treatment in CMT1A.

The study has been running now almost for two years and it is now in the follow-up phase. Fifty participants were enrolled in the UK site at the National Hospital for Neurology and Neurosurgery.

For information about the study please contact Dr. Matilde Laura at m.laura@ion.ucl.ac.uk.

Open Trials

THERAPEUTIC TRIAL OF MEXILETINE IN NON-DYSTROPHIC MYOTONIA

Full Title: A Phase II Randomized, Double-Blind, Placebo controlled, Cross-Over Study to Investigate the Efficacy of Mexiletine in Patients with Non-Dystrophic Myotonia

Status: Open to recruitment
Sponsor: University College London (UCL)
Start date: June 2009
Funder: Food and Drug Administration (FDA – USA)
PI: Prof. Hanna

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 a total duration of nine weeks. Approximately fifteen participants will be enrolled in the UK at the National Hospital for Neurology and Neurosurgery.

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

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: Open to recruitment
Sponsor: Alexion Pharmaceuticals, Inc.
Planned start date: Dec 09
Funder: National Institutes of Health (NIH - USA)
UK 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. There are four stages in the study, the Screening Period, the first Treatment Period, the Wash-Out Period, and the second Treatment Period (the cross-over Treatment Period). 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.

Each patient who completes the study will receive approximately 22 infusions including 11infusions of eculizumab and 11 infusions of placebo. The estimated duration of a patient's participation is approximately 41 weeks.

For more information about the study please contact Dr. Jennifer Spillane at j.spillane@ion.ucl.ac.uk.

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

Status: Site Specific Approval pending
Sponsor: Newcastle NHS Foundation Trust
Planned start date: 2010
Funder: British Heart Foundation
PI: Dr John Bourke, Prof. Muntoni

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 characterized 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 randomized, 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 trial coordinator Rahela Choudhury at r.choudhury@ich.ucl.ac.uk.

ARIMOCLOMOL FOR SPORADIC INCLUSION BODY MYOSITIS (IBM)
Full Title: A Randomized, Double-blinded, Placebo-controlled Pilot Study Assessing the Safety and Tolerability of Arimoclomol in Adult Patients with Sporadic Inclusion Body Myositis

Status: Open to recruitment
Sponsor: University College London (UCL)
Planned start date: June 2010
Funder: Medical Research Council (MRC)
PI: Prof. Hanna

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

Arimoclomol is a new compound which acts by enhancing a normal, inbuilt protective cell reaction to stresses. The products of this response are 'Heat Shock Proteins (HSPs) which counteract processes that end up leading to abnormal protein deposition and to damage mediated by inflammation.

This proposal involves a multi-centre, double-blind, placebo-controlled parallel study of total duration twelve weeks.

This study proposal aims to assess the safety and tolerability of Arimoclomol (100 mg TDS) as compared with placebo over 4 months of treatment in patients with IBM.

Recruitment will take place at the National Hospital for Neurology and Neurosurgery and twelve patients will be enrolled.

For information on the status of recruitment please contact Dr Adrian Miller at a.miller@ion.ucl.ac.uk.

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

Status: Ongoing (closed to recruitment)
Sponsor: PTC Therapeutics
Funder: PTC Therapeutics
PIs: Prof. Bushby, Prof Muntoni

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 approximately10 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, randomized, 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 were followed for a period of 12 months. At the completion of the blinded treatment, eligible and compliant participants went on to receive PTC124 (Atularen) in an open-label extension study. However, this study was prematurely discontinued based on a decision made by the Data Monitoring Committee, following the analysis of 6-minute walk-test (primary endpoint) data showing no statistical difference in placebo and active treatment in the main study. Dystrophin expression data is yet to be fully analysed.

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

New PTC 124 in non-ambulant DMD has been suspended
PI Prof Katie Bushby

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.

DOSE-RANGING STUDY OF AVI-4658 TO INDUCE DYSTROPHIN EXPRESSION IN SELECTED DUCHENNE MUSCULAR DYSTROPHY (DMD) PATIENTS – (Systemic study)Status: Ongoing (closed to recruitment).
Sponsor: AVI Biopharma
Funder: Medical Research Council (MRC) and AVI Biopharma
PIs: Prof. Muntoni Bushby

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 is being conducted in London and Newcastle. All participants have completed treatment. Analysis of results is ongoing. For further information please contact Guru Ganeshaguru, MDEX Clinical Trials Coordinator (Dr K. Ganeshaguru k.ganeshaguru@ich.ucl.ac.uk) or Geoff Bell, Trials Coordinator (MRC centre Newcastle site) at geoff.bell@nuth.nhs.uk.

CCRN 165 (NDS mito function)
Status: Open to recruitment
PI: Prof Chinnery

A phase 2a, double blind, randomised, placebo-controlled, 28 day, two-arm, parallel group study of A0001 in patients with the A3243G mitochondrial DNA point mutation and evidence of impaired mitochondrial function.

PI – Professor P.F. Chinnery, Department of Neurology, Newcastle University, and Newcastle upon Tyne Foundation Hospitals NHS Trust.

The primary objective of this study is to establish proof of concept of the efficacy of A0001 in the treatment of patients with an established mitochondrial disorder using metabolic imaging, a number of functional assessments, biochemical measures and patient/clinical-rated scales.

Secondary objectives of the study are to evaluate the tolerability and safety of A001 in this patient population and to establish pharmacokinetics of A0001 in this patient population.
Patients will be invited to participate if they fit the inclusion criteria which briefly consists of aged 18 – 70 (male or female), confirmed carriers of the A3243G mitochondrial DNA point mutation, with one or more of the associated symptoms and are capable of performing the required tests associated with this study (MRI,MRS, 6 minute walk test).
The study will recruit approximately 30 patients, which should ensure 21 (14 on treatment, 7 on placebo) evaluable patients, which will give sufficient power to detect an improvement of 50% on one of the outcome variables, the primary endpoint being improvement in the rate of ATP recovery in cardiac muscle as measured by P-MRS.
Following informed consent and screening, patients will be randomized to receive 28 days of either A0001 capsules (to be taken orally) at dose level of 0.75g BID (1.5g total daily dose) or placebo.
PK samples will be collected at Baseline and days 4,7,11,14,21 and 28
Safety will be evaluated by history updates, physical examinations, vital sign assessments, 12 lead ECG, routine blood lab analysis and adverse event assessments.
This study is open to recruitment, for further information contact P.F.Chinnery p.f.chinnery@newcastle.ac.uk, Dr G Gorman Grainne.Gorman@newcastle.ac.uk or Mr G Bell Geoffrey.bell@ncl.ac.uk

Exercise Studies

STRENGTHENING HIP MUSCLES TO IMPROVE WALKING DISTANCE IN PEOPLE WITH CHARCOT- MARIE-TOOTH DISEASE
Status: Closed to recruitment
Sponsor: University College London Hospitals
Funder: Muscular Dystrophy Campaign (MDC)
PI: Dr. Reilly
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, randomized 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 included 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. For further information please contact Dr Gita Ramdharry, Research Physiotherapist at g.ramdharry@ion.ucl.ac.uk.

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

Open Natural History – Longitudinal Studies

NON-DYSTROPHIC MYOTONIAS: GENOTYPE AND PHENOTYPE CORRELATION AND LONGITUDINAL STUDIES
Status: Closed to recruitment
Sponsor: University College London
Funder: National Institutes of Health (NIH – USA)
UK PI: Prof. Hanna
This multi-centre project involves a prospective, cross-sectional and longitudinal natural history in non-dystrophic myotonias (NDM).
The aim is to collect standardized data from NDM patients, to include clinical symptoms, exam findings, as well as the results of strength, functional, and electrophysiological testing. Genetic testing will permit precise identification of individual NDM subtype. This information will allow for the identification and implementation of appropriate endpoints in studies of potential treatments.
This is a NIH funded study. Twenty patients were enrolled at the National Hospital for Neurology and Neurosurgery.
For more information about the study please contact Dr Dipa Raja Rayan at d.rajarayan@ion.ucl.ac.uk.

ANDERSEN-TAWIL SYNDROME: GENOTYPE AND PHENOTYPE CORRELATION AND LONGITUDINAL STUDY
Status: Open to recruitment
Sponsor: University College London
Funder: National Institutes of Health (NIH – USA)
UK PI: Prof. Hanna
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 characterized 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.
Eight patients have been enrolled so far at the National Hospital for Neurology and Neurosurgery.
For more information about the study please contact Dr Dipa Raja Rayan at d.rajarayan@ion.ucl.ac.uk.

CHARCOT-MARIE-TOOTH DISEASE AND RELATED DISORDERS: A NATURAL HISTORY STUDY
Status: Open to recruitment
Sponsor: UCLH NHS Foundation Trust
Funder: National Institute of Health, USA
PI: Dr M Reilly
Co-PI: Prof F Muntoni, Dr M Laura
The main aims of this study are to:
Collect natural history data on CMT and related disorders Identify genetic factors that cause and modify Charcot-Marie-Tooth neuropathies.
CMT is the most common inherited neurological disorders for which there are no established treatments and there is a need to fully characterise the disease and the different genetic components.
Other aims are to:
Establish a scoring system for quantifying impairment in young children with various forms of CMT (most patients with CMT develop their first symptoms in the first two decades of life - in childhood).
The success of the paediatric scoring system will be determined by whether it can reproducibly quantify disease progression in children with various types of CMT.
Establish a Website Resource for the Inherited Neuropathies for patients, families and investigators.
For further information, please contact Rahela Choudhury at r.choudhury@ich.ucl.ac.uk.

Planned Trials

HYP HOP: DICHLORPHENAMIDE vs. PLACEBO FOR PERIODIC PARALYSIS
Status: Open to recruitment
Sponsor: University College London (UCL)
Funder: National Institutes of Health (NIH - USA)
UK PI: Prof. Hanna
This is a phase III trial into Periodic Paralysis planned to start in 2010. This proposal involves a multi-centre, double-blind, placebo-controlled parallel group, nine-week studies comparing the effects of dichlorphenamide(DCP) vs placebo in patients with period paralysis (Hyper, Hypokalaemic periodic paralysis). The 9-week studies will investigate the prevention of attacks of weakness and it will be followed by 1-year double-blind extensions without placebo to compare the long term effects of DCP vs ACZ on the course of the diseases and on inter-attack weakness. Approximately 40 participants will be recruited from the United Kingdom.

For information on the status of recruitment please contact Dr. James Burge at James.burge@uclh.nhs.uk.

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: Set-up phase
Sponsor: GlaxoSmithKline
Funder: GlaxoSmithKline
PI: Profs F. Muntoni, V. Straub & K. Bushby
GSK2402968 has been explored at doses up to 6mg/kg subcutaneous (s.c.) weekly initially for 5 weeks in ambulant subjects with Duchenne Muscular Dystrophy (DMD). An open-label extension protocol is ongoing, and to date subjects have received GSK2402968 6mg/kg/week for at least 3 months. GSK2402968 appears to be well-tolerated, and has the potential to be efficacious based on the dystrophin expression previously observed in muscle biopsies. However, more information is needed to determine dosing regimens for optimal therapeutic safety margin in relation to efficacy.

This study is designed to explore efficacy and safety of GSK2402968 given as a continuous regimen over 24 and 48 weeks. For further information please contact Rahela Choudhury, Clinical Trials Coordinator at r.choudhury@ich.ucl.ac.uk. .
NOTE: GSK2402968 formerly know as PRO051

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)
UK PI: Prof Hanna
Andersen-Tawil Syndrome (ATS) is a rare form of periodic paralysis that is associated with serious heart-rhythm abnormalities. ATS is characterized by a triad of episodic muscle weakness, long-QT syndrome with potentially fatal cardiac dysrhythmias and skeletal developmental anomalies. The underlying cause of this potentially fatal condition is only partly understood and there are no established treatments. Mutations in the KCNJ2 gene encoding Kir2.1, an inward-rectifying potassium channel account for

approximately 60% of ATS cases (termed ATS1), the remaining 40% are presumed to have an as yet undetermined gene lesion and are designated ATS2. ATS1 and ATS2 are phenotypically indistinguishable.
The treatment of ATS has been largely anecdotal and empirical.
This proposal involves a multi-centre, placebo-controlled 'n of 1' study design of total duration 45 weeks. The expected total enrolment for this multi-centre study is 16 participants.
The aim of this study is to determine whether potassium supplements and/or acetazolamide alter the duration of muscle weakness and potentially life-threatening heart rhythm abnormalities in patients with ATS.
For information on the status of recruitment please contact Dr. James Burge at James.burge@uclh.nhs.uk.

OUTCOME MEASURES IN SMA TYPE II AND III
Status: Set-up phase
Funder: SMA Europe
PI: Profs Muntoni, Straub, Bushby
This project provides an excellent opportunity as for the first time, ten leading neuromuscular centers in Europe which have been involved in the development and validation of functional scales for SMA will collaborate to validate and cross validate measures that have been suggested to be the most suitable for multicentric trials by a large international consensus, but have not been tested in large multicentric studies yet.
One hundred and thirty patients affected by type II and type III SMA will be enrolled and assessed at baseline and 6 and 12 months later. Non ambulant patients will be assessed using the modified version of the Hammersmith Motor Functional Scale while ambulant patients will be assessed using the extended module of the Hammersmith Motor Functional Scale and timed items, the 6 minute walk and a step activity monitor. All patients will also be assessed using the MFM, that covers the whole range of activities for both ambulant and non ambulant patients. All measures will undergo a process of validation including inter observer reliability. This information will be most valuable for any future trial and will make the groups involved ready to participate to future collaborative studies saving a lot of time on the preliminary aspects (validation, reliability, training) that will be fulfilled by the present study. The study will also provide natural history data for a 12 month period on patients. Please contact Rahela Choudhury, Clinical Trials Coordinator at r.choudhury@ich.ucl.ac.uk for further details.

PERIPHERAL NEUROPATHY OUTCOME MEASURES STANDARDISATION STUDY (PERINOMS)
Status: set-up phase
Sponsor: Erasmus Medical Center
PI: Dr M. Lunn

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.

Imaging Studies

MRI in IBM and CMT
Full Title: A Study of Quantitative Magnetic Resonance Imaging and the Clinical Features of Inclusion Body Myositis and Charcot Marie Tooth
Disease Status: Open to recruitment
Sponsor: University College London Hospitals
Funder: Medical Research Council
PI: T Yousry/J Thornton/ MM Reilly/ M Koltzenburg/MG Hanna
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) will be recruited and 40 patients with genetically confirmed Charcot Marie Tooth Disease (CMT) will be recruited. 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 characterize 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.

Full-Title: A study using Magnetic Resonance Imaging (MRI) and Magnetic Resonance Spectroscopy (MRS) in Patients with Limb Girdle Muscular Dystrophy 2I; an assessment of muscle damage.
Status: Open to recruitment
Sponsor: Newcastle upon Tyne NHS Trust
Funder: MRC Centre for Neuromuscular diseases
PI: Prof. Volker 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.uk.

Future Meetings

MRC Centre for Neuromuscular Diseases/Muscular Dystrophy Campaign UK translational Research conference 2011
Tuesday 29th & Wednesday 30th March 2011
UCL Institute of Child Health, London
Contact Zoë Scott on z.scott@ion.ucl.ac.uk for further details

Date of BMS Annual Meeting 2011: tbc

Industry Sponsor:
Genzyme

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http://www.myology.org.uk/

RCP and RCPCH CPD approval has been applied for
RCP code: 58961

BMS 2010 Conference brochure prepared by
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