The Congenital Myasthenic Syndrome (CMS) service at The John Radcliffe Hospital combines a specialist genetic analysis laboratory with a dedicated inpatient (funded locally) and outpatient clinical service to offer a multidisciplinary service for patients across the country.

The core CMS team comprises of the following professionals [Appendix 1]:

**Clinical team**

- **Dr Jackie Palace**: Consultant Neurologist (Service Lead)
- **Dr Sithara Ramdas**: Consultant Paediatric Neurologist
- **Dr Pinki Munot**: Consultant Paediatric Neurologist (GOSH)
- **Dr Ravi Knight**: Consultant Neurophysiologist
- **Dr Pedro M Rodriguez Cruz**: CMS Clinical Fellow
- **Marzena Hilarowicz**: CMS Service Co-Ordinator
- **Hayley Ramjattan**: Neuromuscular Physiotherapist
- **Mary Quirke**: Myasthenia Specialist Nurse
- **Julia Goodgame**: Neurological Clinical Services Manager

**Laboratory team**

**Weatherall Institute of Molecular Medicine**

- **Prof David Beeson**: Lead Molecular Geneticist
- **Dr Wei-Wei Liu**: Molecular Geneticist
- **Dr Judy Cossins**: Molecular Biologist
- **Dr Richard Webster**: Post-Doc Electrophysiologist Medical Researcher
- **Ms Susan Maxwell**: Research Assistant

**Oxford University Hospitals Team**

- **Dr Carolyn Campbell**: Director of Genetics Laboratories
- **Dr Tracy Lester**: Principal Clinical Scientist
- **Dr Mike Oldridge**: Clinical Scientist

**Service Overview**

The service sees about 220 patients each year as outpatients and offers remote advice to Doctors, patients and their carers around the country regarding the diagnosis and management of CMS patients. The clinical team review patients primarily in an outpatient setting, often performing additional investigations, such as QMG scores (Quantitative Myasthenia Gravis Score), pulmonary function testing (spirometry) and EMGs (Electromyogram).
Consultants
There are five Consultants in the service (three Paediatric Neurologists, one Neurophysiologist and one Adult Neurologist). This includes outpatient clinics, email/telephone advice, genetic reviews and inpatient reviews when necessary.

Dr Stephanie Robb, Consultant Paediatric Neurologist, retired this year from clinical work. We acknowledge her contribution over the years to the CMS service and to the field of myasthenia.

Clinical Training Fellow
The Clinical Fellow’s post is split between the NHS clinical service and the University laboratory service and works as a link between both services. The Clinical Fellow provides specialised assessments in clinic (QMG scores) and gives remote advice to patients and healthcare professionals and is in charge of data collection and database maintenance. Currently the clinical fellow is senior and is training with the aim of long term succession planning.

Molecular Genetics
Professor Beeson in his role as the lead for the CMS genetics service provides valuable input into directing appropriate testing and treatment. This includes determining the disease mechanism on all newly identified mutations in known CMS-associated genes and looking for novel genetic causes of CMS where mutations are not identified in the standard CMS-associated genes.

Consultant Neurophysiologist
Dr Ravi Knight and performs all neurophysiological studies, which include standard EMGs and single fibre EMGs. Dr Adam Molyneaux, Consultant in Clinical Neurophysiology has recently joined the Neurophysiology Department and will also be doing some of the studies.

Neuromuscular Physiotherapist
The CMS service has a dedicated 0.2 WTE Neuromuscular Physiotherapist, who attends both the adult and paediatric clinics. The role of the Neuromuscular Physiotherapist is to support the assessment and management of patients in clinics; using standardised assessment tools, specialist physiotherapy assessment and treatment skills, and offer guidance on exercise, activity levels and participation. This support is particularly important in the adult population where access to specialist physiotherapy in the community can be patchy. The role extends to care outside of clinics, with links to community therapists, direct contact with patients, offering guidance on exercise regimes and activity pacing, and supporting coordinated medical input during hospital admissions.

Specialist Nurse
The role of the Myasthenia Nurse is wide ranging, either providing direct or remote care, or practical advice to patients, families and the MDT. In clinic they are available to provide education and support to patients and families recently diagnosed or dealing with the long term psychological, physical and practical issues of chronic illness. They are a readily accessible point of contact for patients and
families via email or telephone contact, either providing advice or signposting. If patients and families are receiving input from the MDT, they are a reference point for specific condition related information to support care delivery and management to enable patients to live well. Patient education is also a large part of the role.

**CMS Service Co-Ordinator**

Marzena Hilarowicz, Co-ordinator oversees the administration of the service, the Patient Day, liaises regarding the CQUIN meetings, and has contact with other hospitals on a daily basis, and is the first point of contact for the patients and professionals. They are responsible for co-ordinating information from referring physicians prior to review by the Clinical Team. They liaise with the laboratory and multi-agency professionals who may be involved in the care locally.

**Clinical Service**

The clinics are half day adult/paediatric clinics led by the Oxford clinical team, and twelve full day joint clinics with the GOSH team, which alternates between Oxford and London. This allows good practice to be shared between the centres. In addition, we held a joint Paediatric clinic at St Thomas’ hospital on the 13 September 2018 with Dr Heinz Jungbluth. We also held an adult joint clinic at King’s College Hospital with Dr Fiona Norwood on the 29 September 2017 and we have scheduled the next one for January 2019.

We would like to expand our remote clinics to other locations in the future, such as Glasgow with Dr Maria Farrugia. We are in the process of liaising with the NHS Greater Glasgow and Clyde Trust to give the approval for the clinic to go ahead. Both the clinical and laboratory teams offer an advice service to Healthcare Professionals around the country and overseas. This involves e-mail, telephone and letter correspondence regarding numerous patients, including those seen in clinic who are under local follow-up and patients who are unable to be seen at the centre due to geographical access issues or severity of illness, and children/neonates in crucial care with possible or known CMS.

In 2016 we were awarded, in collaboration with the Newcastle Muscle Group, Healthcare provider status for the European Reference Network (ERN) for rare neuromuscular disorders. The European Commission (EC) is supporting Member States in the development of European Reference Networks (ERNs) to link existing highly specialised healthcare providers across Europe, such as the CMS service and other neuromuscular services in Oxford. The development of ERNs will facilitate timely access to care, both diagnosis and treatment, by centralising knowledge and experience, medical research and training, and resources for these diseases and conditions. A 2nd EURO-NMD Annual Meeting is taking place on the 29th and 30th November 2018 at the Motol University Hospital in Prague to discuss common strategies in neuromuscular disorders. Due to the current political uncertainty of “Brexit”, terms and conditions of ERNs might need to be revised in the future for UK
centres participating in these networks. However, the most likely scenario at present is that UK centres will continue as part of the ERN networks but do not lead them.

The CMS Service has Telemed appointments available within our clinics, where we contact patients who are unable to attend clinic due to travel difficulties or they are feeling well in themselves and prefer to travel long distance yearly with an interim telemed appointment. In the previous year we set up a “self-assessment QMG form to allow patients to do their own assessment to allow us to monitor patients evolution remotely more accurately. Currently we are discussing the possibility of developing a mobile phone app for this purpose that could be useful for both patients with CMS and autoimmune MG. The ultimate goal of this app would be to better patient disease monitoring and, therefore, prevent or reduce hospital admissions.

The clinical and genetic research teams offer an advisory service to the diagnostic genetic laboratory on specific genes that need testing usually after a questionnaire or clinical information from the referring clinicians. This part of the service reduces the gene screening activity and keeps the costs down. These are referred to as “genetic reviews”.

**Genetic service**

The Diagnostic Genetics Laboratory at the Churchill Hospital, Oxford provides specialised genetic screening for patients with suspected CMS or related rare neuromuscular conditions. There are currently a number of genes screened for that are associated with CMS: CHRNA1, CHRNB1, CHRND, CHRNE, CHRNG, RAPSN, COLQ, CHAT, DOK7, GFPT1 and DPAGT1. Each of these genes encodes proteins involved in maintaining the function of the neuromuscular junction.

In addition to these, further screening for MuSK, AGRN, ALG2, ALG14, COL13A1, GMPPB, SLC5A7, LRP4, TOR1AIP1 and SLC18A3 genes is available within Professor Beeson’s research group, based at the Weatherall Institute of Molecular Medicine.

If a mutation in the genetic code is identified, additional tests can also be undertaken in Professor Beeson’s laboratory to determine the pathogenicity. The current functional studies available include:

- Electrophysiology to assess AChR channel kinetics for fast or slow channel syndromes or reduced conductance syndrome.
- AChR cell surface expression to test for AChR deficiency syndromes
- AChR clustering assays to test pathogenicity of RAPSN, DOK7, MuSK and AGRN variants
- Exon trapping to test splice site mutations and synonymous intronic variants
- Reporter assays to test for promoter variants
- Expression assays to test \textit{CHAT}, \textit{GFPT1}, \textit{DPAGT1}, \textit{MUSK}, \textit{AGRN}, \textit{ALG2}, \textit{ALG14}, and \textit{GMPPB}.

Once the screening has been performed, the patients are either reviewed in outpatient clinic, or alternatively, the details of the case are reviewed by the clinical team and remote advice offered to the referring clinician.

In addition, whole screen Exome and whole screen genome screening is performed via Professor Beeson's group in selected cases of CMS, where the genetic cause remains unidentified and the diagnosis of CMS is undoubted. This technology helps the identification of novel variants in genes originally not CMS-related. In these cases, further studies to determine pathogenicity need to be undertaken.

As our understanding of these conditions increases, it has become apparent that treatment choice is determined by the underlying pathogenic mechanism of the CMS subtype the patient has. Some of the treatments used routinely in some CMS subtypes cause deterioration in other subtypes. Accumulated experience allowed us to develop a treatment algorithm, which is routinely used in our clinics [Appendix 2].

\section*{Service Objectives and Outcomes}

\textbf{The purposes and goals of the service}

- To provide easy access to our clinical services to patients in the UK
- Make a definitive CMS diagnosis (including prenatal diagnosis where requested)
- Treat effectively in collaboration with local clinicians
- Deliver high-quality health care to patients with CMS
- Provide special neuromuscular physiotherapy advice
- Provide information for patients, families and their schools and other health care professions about CMS. (See later - Page 11: Service Engagement and Communication)

\section*{Outcomes}

\textbf{Activity Levels}

The clinical team reviewed approximately 221 patients in the outpatients clinics (200 when excluding Northern Ireland, Scotland and Wales). In addition, the clinical team also reviewed the genetic results of 270 patients in the April 2017 - August 2018 period, offering advice on diagnosis and management to the referring Clinicians. We also had 2 CMS inpatients (17 occupied bed days) who were admitted electively to the ward in order to optimise their treatment regimes.
DNA samples: the number of DNA samples received by the diagnostic laboratory was 137, compared to 121 last year. This suggests sample numbers remaining stable over time. At the moment we screen a total of 11 genes, but we regularly expand this to include any new CMS related genes discovered.

**Activity Levels Recorded [Appendices]:**

- Number of new and follow-up outpatient visits and geographical information. *(Appendix 3a, 3b, 3c, 3d and 3e).* The number of new referrals this year was 33 compared to 188 follow-up appointments.
- DNA sample activity – number of patients *(Appendix 3f)*, DNA sample geographical data *(Appendix 3g).* Number of exons analysed *(Appendix 3h).*
- Day cases and inpatient activity is also reported, although this is actually outside of the Highly Specialised Funding
- Number of remote genetic reviews from April 2017 to March 2018 was 270 (steering specific genetic tests performed dependent on clinical information) *(Appendix 3i).* Number of genetic reviews per patient *(Appendix 3j).*
- Number of remote consultations from April 2017 – August 2018 was over 251 phone calls and 250 emails. This represents our continuous effort in communication with patients and healthcare Professionals.
- Number of Telemed appointments from April 2017 to March 2018 was 5.
- Overall, activity levels in both outpatients clinics and DNA samples received have remained stable over time in the last years *(Appendix 4)*

**Performance Indicators [Appendices]:**

- Clinic waiting times: patients are offered an appointment within 8 weeks. This objective is met regularly and those exceeding the target is usually their own choice.
- Patient satisfaction *(Appendix 5a and see later – page 8)*
- Overall percentage of patients with definitive diagnosis of CMS *(Appendix 5b)*
- Overall percentage of patients with genetic diagnosis of CMS *(Appendix 5b)*
- Overall percentage of patients with diagnosis of CMS ruled out *(Appendix 5b)*
- Percentage of genetic reviews within 8 weeks: approximately 95-98%
- Detection rate for genetic test: the approximate detection rate in CMS for this year was approximately 12%, which has remained stable compared to previous years. Overall, this result is similar to other rare genetic conditions.
- Turnaround time for DNA reporting: the approximate time for DNA reporting is two months per gene. However, if the result is required as urgent, then the turnaround is approximately 2 weeks.
- Percentage of patients involved in research (enrolled in existing registries and natural history studies, biological samples donated to biobank): all patients seen in the outpatient clinic with CMS or suspected CMS are offered to take part in research studies under ethical approval (OXREC B: 04.OXB.017 and
Oxfordshire REC C 09/h0606/74). The response is in general very positive with an overall percentage of CMS patients involved in research close to 100%.

- The overall percentage of patients with a final diagnosis of CMS reached on new patients being referred to the CMS service was 35.7% (Appendix 5c). A small percentage of patients were classified as “undefined”, which means that the clinical diagnosis is unclear.
- Safety incidents, mortality and morbidity outcomes: there were no safety incidents and no CMS-related deaths.
- Quality of Life Measures: this outcome was recently introduced and we still lack the necessary amount of data.

**Geographical Distribution**

- Geographical data of outpatient activity (Appendix 3c, 3d and 3e), DNA samples received (Appendix 3g) and remote reviews (Appendix 3k and 3l) are shown - We are reporting country of residence and NHS regions.

As a National Referral Centre for CMS, Oxford aims to offer equal access to patients from across the whole of England and Scotland. Some patients cite transport costs as a limiting factor. For patients living far from Oxford, we try to offer them the flexibility to schedule their appointments to fit in with leisure travel plans. In cases where the patients are physically unable to attend outpatient clinic, remote advice is offered to their local Clinician regarding their diagnosis and management.

As well as offering a national service, the team also offer advice on international patients. In the period April 2017 – March 2018, 10.37% of our genetic reviews came from overseas patients, compared to 9.65% last year. This confirms our efforts in establishing us as a centre of international expertise in CMS. We are receiving a number of enquiries from EU countries using the S2 EU Cross-border Healthcare Directive referral process although this might change in the future due to “Brexit”.

**Patient Satisfaction**

Feedback from patients, relatives and carers offers important insight into the quality of service provided. These views are collected in the form of a questionnaire that is given to the patients and their carers when they attend an outpatient clinic appointment. We give our patients a feedback questionnaire in order to capture more information about the performance of the CMS Service measured against the quality indicators and to identify any gaps in service provision. We have been using this questionnaire since April 2013 in all our outpatient clinics. This information is collated on to our database and any negative feedback is disseminated to the CMS team for positive action and steps (Appendix 5a).
We receive positive comments, as well as negative feedback. The negative feedback on our questionnaires mainly relates to the parking issues that the Trust experiences.

The Trust's new parking policy came into action in April 2017 and this resulted in released extra parking for both patients and staff. The Trust is also liaising with the County Council to try and negotiate further parking places for our patients.

Some of the positive comments received this year:

*Always helpful advice on the phone and fitted into clinic at short notice.*

*CMS dept always fabulous.*

*Great appointment. Very positive, helpful and full of new information.*

*It is always a pleasure to attend the John Radcliffe Hospital.*

**Financial Update**

To be presented by the OUH Financial team lead by Carol Ann Gourlay, Neurosciences Finance Manager.

**Service Developments**

**New quality-health care measures and indicators**

Over the last year we developed a set of new indicators to better measure the quality of the healthcare provided by our service. These were added to our previous ones, and incorporated into our questionnaires and databases. These can be found in the service outcomes measures. In addition, we recently started to use standardised health care questionnaires (EQ-5D-5L and PedsQL) to measure the quality of life in our patients. We aim to be able to tell in the near future whether we can improve patients' quality of life in addition to their muscle strength.

**Telemed clinics and remote monitoring of patients**

The Telemed clinics were set up in March 2015 as some patients were finding it difficult to attend clinic due to geographical access issues. These have been proved to be very useful for patients. The CMS Co-Ordinator liaises with the patient to arrange a convenient time for the team to call the patient from the CMS clinic. After the telephone consultation, a letter is dictated and sent to their doctor. We have used this method in eleven patients so far and this has proven successful. Therefore, this is a way to monitor patients more easily and for them to save on travel expenses, as some patients have difficulty covering the cost of travel. This also stops patients from being lost to follow-up. In addition, we have developed a simplified QMG form.
so that patients can do a self-assessment at home, and we can monitor their evolution even if they are not seen in clinic. We are discussing the possibility of developing a mobile phone app to monitor patients remotely more efficiently with the idea of preventing admissions to hospital.

**New Genetic commissioning arrangements**

It is not clear how the new commissioning of genetics will affect the service. We are keen for testing to only be performed in patients with clinically possible CMS because indiscriminate testing would lead to irrelevant mutations being identified requiring resource heavy functional testing.

**Clinical and translational research**

**Newly identified CMS-associated genes and next generation sequencing**

The CMS Service continues to incorporate a number of CMS patients without a current genetic diagnosis into next generation sequencing techniques. This is part of a preliminary trial into the use of next generation sequencing (as part of the Biomedical Research Centre funding) for the routine screening of genes in rare Mendelian genetic disorders. We have found mutations in a new gene not previously known to be related to CMS (TOR1PA1) and further studies are currently being undertaken to elucidate the underlying physiopathological mechanisms in this subtype of CMS. Previously, using the same methodology, we were able to identify DPAGT1, ALG2 and ALG14, GMPPB, and COL13A1 as causative genes for CMS.

We are currently leading an international collaboration to define the clinical spectrum of disease associated with COL13A1 mutations in CMS patients (unpublished). This will help clinicians around the world to recognise this condition more easily and give the appropriate treatment on time.

Given the number of new CMS-associated genes that are being identified Drs Michael Oldridge and Tracy Lester are actively exploring generating a Next Generation Sequencing CMS panel to be used in the screening. This would be designed to detect the more common CMS, variants in the genes described above, the less common CMS forms caused by mutations in large genes such as AGRN and MUSK that are currently screened for in the research laboratory, and the many new CMS-associated genes currently being identified by next generation sequencing (total approximately 30 genes).

Following the contribution of the NHS to the 100,000 genomes project and the recent creation of the NHS Genomic Medicine Service, we predict a potential restructuring of genetic services in England. However, most recent information suggest that genetic testing for common CMS genes will remain in Oxford with the creation of a CMS next generation sequencing panel. In addition, we anticipate the likely increase in the need of interpretation of genetic variants using functional studies following the implementation of genomic medicine in England.
Current translational research projects

As previously reported by our group, several forms of CMS show a marked beneficial response to Salbutamol or ephedrine. Recent research in our laboratory has shown that β2-adrenergic agonists have an specific positive effect in both neuromuscular junction structure and function (J Neuromuscul Dis. 2018;5(2):231-240). The specific molecular mechanisms are currently being studied. We believe that these drugs provide a compensatory mechanism to stabilise the motor endplate structures, improving neuromuscular transmission. A better understanding of it will help us to provide more efficient treatments.

Future translational research projects

As stated above, an understanding of the underlying molecular mechanism of disease due to the different mutations is fed back to the clinical team to direct appropriate therapy. Next generation sequencing is revealing a series of new CMS-associated genes and projects are underway to determine how the different mutations affect signal transmission at the neuromuscular junction. Further projects are being undertaken to study the beneficial effects of salbutamol. At present the precise mechanism through which Salbutamol improves neuromuscular transmission is not known, but research into the mechanism may provide a scientific pointer to similar compounds that have greater efficacy. Ongoing collaboration with Novartis Pharmaceuticals is helping in the development of more potent β2-adrenergic receptor agonist which, in preliminary work, has been found to be muscle-specific and therefore have markedly reduced side effects.

We are currently working in the identification of small molecules that could increase expression levels of the DOK7 protein as a novel therapeutic strategy. Preliminary work to set up an in-vitro drug screening system has been successful. This has been funded partly a Myaware prize studentship from October 2016.

Service Engagement and Communication

Website

A webpage for the service is hosted on the OUH website and includes: patient CMS booklet, referral information and pre-referral form, as well as points of contact for Clinicians. The website has recently been updated with the contact information for the CMS Team. Patients can also access our annual reports on the website, as well as information from the Patient Day we hold, including the presentations, which patients have asked for. We endeavour to continually update the website, so the information is as up to date as possible.

Pre-attendance Clinic Information Pack

The content has been approved by the Trust Media and Communications Department. The information pack is placed on the CMS service webpage. The information pack is sent to all new patients attending the service prior to their
appointment. This helps patients and families to know what to expect from their appointment. The booklet has been updated last year to include new staff members (Appendix 6).

**Information in clinic**

Newly diagnosed patients are given in clinic a CMS booklet, published by ‘Myaware’ (Appendix 7) with the latest relevant information regarding diagnosis, treatment and management of this condition. In addition, there are given a CMS-DVD with testimonies of several CMS patients, so that patients and families can understand their condition better. We also send these documents to school when requested by the parents of patients with CMS.

For patients with child bearing potential, we provide them with an information pack for Health Care Professionals regarding the safety of the most commonly used CMS drugs in pregnancy & breastfeeding (Appendix 8).

**Patient Day**

The CMS Patient Day took place on the 28th April 2018 in Oxford. A total of 18 patients and their family members attended (55 in total). The agenda consisted of overviews, presentations, and breakout sessions where patients interacted with each other and the CMS team (Appendix 9). This year we had Steve Bradshaw (Myaware Benefits and Welfare Officer) who covered Disability Living Allowance (DLA), Personal Independence Payment (PIP) and general information on benefits through a presentation and subsequent breakout sessions. This year we also had a special focus on exercise: Hayley Ramjattan (Neuromuscular Physiotherapist) talked about “why exercise is good for you” and then we had a Pilates session, which our patients found thoroughly enjoyable. In addition to educational objectives patients find this meeting socially and psychologically helpful because they meet with individuals who are in a similar situation as themselves and many make long-lasting contacts.

Patients completed a questionnaire feedback with a positive outcome (Appendix 10). The next National Congenital Myasthenia Patient Day is due to take place in the spring of 2019 in Oxford. ‘Myaware’ have been informed and representatives will be attending. We uploaded the presentations onto our CMS website, via the Trusts website, so the patients can refresh themselves and other patients can have easy access to them.

**CQUIN**

The CQUIN requirement is designed to encourage collaborative learning and Quality Service Development is based on long standing precedent in the highly specialised services (HSS).

The meeting includes discussions of clinical outcomes, comparison of centres’ outcomes, and identification of where providers need to adopt new ways of
delivering consistent outcomes across all clinical teams. The meeting to discuss the 2017-2018 report took place on 22nd June 2018 in Newcastle. The 2019-2020 HSS Rare Neuromuscular Disease Service Audit Meeting is currently being organised for the following year.

Service Problems

3,4-DAP supply

Although Biomarin has up to now tolerated the prescribing of the cheaper generic 3,4-DAP, in the UK we have some concerns this may change in the future. They are currently trying to obtain a licence for Firdapse in CMS in the USA and it is likely this will lead to a European licence.

Provision of Salbutamol

The problem with the manufacturing of Salbutamol modified release capsules (Ventmax®) persists. The product was discontinued in 2015 and is no longer available. There has been no replacement modified-release preparation. There are no current issues with the supply of normal formulation Salbutamol tablets or liquid formulation, which are manufactured by GSK. All our patients are doing well on the tablet or liquid formulations. However the higher costs of the salbutamol tablets compared to the previous MR version and the liquid versions has meant some GPs insisting on prescribing the liquid formulation which has a short half-life and is bulky/heavy to transport. The following information was obtained from our hospital pharmacy regarding the cost and half-life of the tablet and liquid formulations of salbutamol.

“Salbutamol s/f syrup is significantly cheaper compared to immediate release tablets (approx. 95% cheaper) but due to contract agreements and confidentiality reasons the hospital was unable to verify the precise figures. We believe the liquid is up to 100 times cheaper.

Salbutamol 2mg/4mg tablets (Activis): The manufacturer states 50% of the drug is excreted within 4 hours, and fully excreted in 24 hours. Other brands of immediate-release salbutamol tablets have been quoted to have different half lives in the range of 5 to 7.2 hours.

Salbutamol s/f syrup (Ventolin): The manufacturer does not state a half-life for its preparation. However other sources suggest is it 5 hours. For oral preparations, tablet and syrup, the bioavailability is about 50%. Here at the OUH we only keep 4mg (x28) tablets and the s/f 2mg in 5mL syrup (150mL).”

Meetings, Presentations and Publications

Meetings
Dr J Palace, Professor D Beeson, Dr Stephanie Robb, Dr Sithara Ramdas, Dr P Rodriguez Cruz, Dr. Tracy Lester, Dr Mike Oldridge. Highly Specialised Services Clinical Outcome Collaborative Audit Workshop, Newcastle upon Tyne. 22nd June 2018.

Collaboration with Newcastle and GOSH physiotherapists on outcome measures used in clinic. Newcastle upon Tyne. Hayley Ramjattan, Dr Pedro Rodriguez Cruz. 18th January 2018.

**Oral Presentations**


British Myology Meeting September 2018- ‘Autoimmune Myasthenia in Children- Not Just small adults’, Dr Sithara Ramdas

XV International Congress on Neuromuscular Disease, July 6 - 10, 2018 in Vienna, Austria. Workshop talk: DPAGT1, DOK7 and salbutamol. Looking for new treatment options in neuromuscular disease. Prof David Beeson


Physiotherapy Management of Congenital Myasthenic Syndrome – MDUK Care Conference, Nottingham. (June 2017) Hayley Ramjattan, NM Physiotherapist
Publications


Appendix 2

Treatment Algorithm

SUSPECTED CMS

Features of DOK7, COLQ or SCS? (awaiting genetic diagnosis)

No

Start Pyridostigmine

Yes

Avoid Pyridostigmine

Start in 3, 4-DAP* 

Add in 3, 4-DAP* 

Add in Salbutamol/Ephedrine 

Add in Salbutamol/Ephedrine 

Add in SCS 

Add in Pyridostigmine 

Add in Pyridostigmine 

Avoid Pyridostigmine

First line treatment

Second line treatment

Additional treatment

DOK7 COLQ SCF ChAT AChR-def FCS N-Glyc Rapsyn

Fluoxetine

Quinidine

Adidin
Appendix 3a:

Outpatient attendances 01 April 2017 – 31 March 2018 (12 months)

Outpatient attendances 01 April 2018 – 31 August 2018 (5 months)
Appendix 3b:

Outpatient attendances 01 April 2017 – 31 March 2018 (12 months) classified by type of clinic and hospital location. – Total = 200

![Bar chart showing attendances by type of clinic and hospital location. The chart includes categories such as Oxford adult apps, Oxford paed apps, Joint GOSH - Oxford, Joint GOSH - London, Joint Kings College, Joint St Thomas London, with values ranging from 79 to 4. Total = 200.]
Appendix 3c:

Regional outpatient geographical data 01 April 2017 – 31 Mar 2018 (12 months)

Total = 221

Regional outpatient geographical data 01 April 2018 – 31 Aug 2018 (5 months)

Total = 70
Appendix 3d:

Regional outpatient geographical data 01 April 2017 – 31 March 2018 (12 months) – Total = 221
Appendix 3e:

Regional outpatient geographical data 01 April 2018 – 31 Aug 2018 (5 months) – Total = 70
Appendix 3f:

DNA samples received 01 April 2017 – 31 March 2018 (12 months) – Total = 137

DNA samples received 01 April 2018 – 31 August 2018 (5 months) – Total = 34
Appendix 3g:

DNA samples received geographical data April 2017 – March 2018 (12 months)

Total = 137

DNA samples received geographical data Apr 2018 – Aug 2018 (5 months)

Total = 34
Appendix 3h:

DNA (exons analysed) 01 April 2017 – 31 March 2018 (12 months) – Total 5512

DNA (exons analysed) 01 April 2018 – 31 Aug 2018 (5 months) – Total 1462
Appendix 3i:
Remote Genetic Reviews by Clinical Team 01 April 2017 – 31 March 2018 (12 months) – Total = 270

Remote Genetic Review by Clinical Team 01 April 2018 – 31 August 2018 (5 months) – Total = 82
Appendix 3j:

Remote Genetic Review by Clinical Team 01 April 2017 – 31 March 2018 (12 months): number of genetic reviews per patient – Total = 270
Appendix 3k:

Remote Genetic Review by Clinical Team: geographical data 01 April 2017 – 31 March 2018 (12 months) – Total = 270
Appendix 3L:

Remote Genetic Review by Clinical Team: geographical data 01 April 2018 – 31 August 2018 (5 months) – Total = 82
Appendix 4:

Activity levels (outpatients appointments) 2012 - 2018

Activity levels (DNA samples received) 2012 - 2018
Activity levels (remote genetic reviews) 2012 - 2018
## Appendix 5a:

### Patient outcome results 01 April 2016 – 31 August 2017

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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>How do you feel your Query was dealt with?</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fully</td>
<td>60</td>
</tr>
<tr>
<td>Partially</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Do you feel involved in decisions about your care?</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>120</td>
</tr>
<tr>
<td>No not completely</td>
<td>4</td>
</tr>
<tr>
<td>No not at all</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Do you feel your care is well co-ordinated?</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>120</td>
</tr>
<tr>
<td>No</td>
<td>1</td>
</tr>
</tbody>
</table>
Additional comments

- VERY APPRECIATIVE FROM CLINICIANS INVOLVED. MANY YEARS OF VARIOUS SPECIALISTS. WHETHER A DIAGNOSIS OR NOT. IT HAS BEEN VERY DIFFICULT AS DIFFERENT SYMPTOMS AT DIFFERENT TIMES & FROM DIFFERENT ACTIVITIES.
- ALL STAFF REALLY HELPFUL AS USUAL
- ALWAYS GOOD TO COME TO JR. ALWAYS LOOKED AFTER WELL.
- THE WAITING ROOM LACKS TOYS/BOOKS FOR CHILDREN, WHICH MAKES IT VERY DIFFICULT TO KEEP THE CHILDREN PATIENT WHILST WAITING.
- I DON'T KNOW THE MEDICAL TERM OF MY CHILD'S CONDITION IN ENGLISH. NO ADDITIONAL COMMENTS.
- I THINK IT WELL MANAGED SO FAR.
- FIX TV IN WAITING ROOM
- IT WAS REALLY HELPFUL EXPLAINING WHAT/WHY THE PEOPLE WERE IN THE ROOM. HELPS CHILDREN TO UNDERSTAND WHAT THE APPT IS ABOUT AND FEEL PART OF IT.
- GREAT HOSPITAL FACILITIES. MANY THANKS
- I FEEL THAT THE SERVICE WE RECEIVE TODAY FROM ALL STAFF MEMBERS ARE VERY PROFESSIONAL AND HIGH STANDARD. I AM VERY PLEASED.
- GREAT VISIT AGAIN. ALL STAFF VERY HELPFUL AND ANSWERED MY QUESTIONS. HER DOSAGE WAS INCREASED, SO WE ARE MOVING FORWARD AGAIN.
- THE CMS CARE AT OXFORD IS BRILLIANT. HOWEVER, THE GP FOLLOW ONS AND THE PAEDIATRIC'S CAN BE DIFFICULT TO CONTACT IN TERMS OF GETTING PRESCRIPTIONS.
- VISIT EVERYTIME WITH THE TEAM IS EXCELLENT. CANNOT SAY ANYMORE.
- FIND THAT AFTERNOON APPOINTMENTS ARE EASIEST FOR US TO ATTEND GIVEN WE TRAVEL FROM BIRMINGHAM
- THE CONSULTANTS ALWAYS OFFER EXCELLENT ADVICE AND LISTEN TO US AS A FAMILY. SINCE OUR DAUGHTER HAS STARTED COMING HERE, HER HEALTH HAS PROGRESSED POSITIVELY.
- THANK YOU FOR YOUR TIME
- EVERYONE VERY HELPFUL AS USUAL
- BIRUTE V GOOD
- ALWAYS HELPFUL ADVICE ON THE PHONE AND FITTED INTO CLINIC AT SHORT NOTICE
- THIS IS MY FIRST VISIT TO THIS CLINIC AND I AM VERY SATISFIED WITH ALL THE FACILITIES.
- GOING TO SEND EXERCISES TO DO AS STRETCHING AS NOT USED
- IT HAS BEEN VERY USEFUL TO HAVE THE OPPORYUNITY TO DISCUSS MEDICATIONS WITH A NURSE
- ALWAYS FRIENDLY
- GREAT APPOINTMENT. VERY POSITIVE, HELPFUL AND FULL OF NEW INFORMATION.
- COULD USE A FEW MORE CHAIRS IN RECEPTION. APPOINTMENT HAS BEEN DELAYED 15 MINUTES
Appendix 5b:

Overall percentage of patients with confirmed diagnosis Apr 2017 – Mar 2018

Performance indicator and agreed outcomes

<table>
<thead>
<tr>
<th>Description</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Patients with a definitive diagnosis of CMS</td>
<td>72.51 %</td>
</tr>
<tr>
<td>% Patients with a genetic diagnosis of CMS</td>
<td>70.18 %</td>
</tr>
<tr>
<td>% patients with a diagnosis of CMS ruled out</td>
<td>20.47 %</td>
</tr>
</tbody>
</table>
Appendix 5c:

Overall percentage of patients with diagnosis of CMS in new referral events
Apr 2017 – Mar 2018
Appendix 6:
Front cover of CMS pre-clinical information booklet

[NHS]

Specialised Services

Diagnostic and Advisory Service for Rare Neuromuscular Diseases

Attending the Congenital Myasthenia Service, Oxford

Useful information about your appointment
Appendix 7:

Front cover of CMS booklet published by Myaware—updated in 2017
Appendix 8:

Front cover of booklet for healthcare professionals on the use of CMS drugs during pregnancy and breastfeeding.

NHS

Specialised Services

Diagnostic and Advisory Service for Rare Neuromuscular Diseases

Congenital myasthenic syndromes and pregnancy

Useful information for GPs and other healthcare Professionals

Version 1.0 (September 2018)
# CMS Patient Day Agenda 2018

**Saturday 28 April 2018**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.30 am</td>
<td>Coffee &amp; Registration</td>
</tr>
<tr>
<td>10.00 am</td>
<td>Clinical Overview Dr Pedro Rodriguez Cruz</td>
</tr>
<tr>
<td>10.20 am</td>
<td>Drug Treatment Overview Dr Jackie Palace</td>
</tr>
<tr>
<td>10.30 am</td>
<td>Research Update Professor David Breson &amp; Dr Pedro Rodriguez Cruz</td>
</tr>
<tr>
<td>10.50 am</td>
<td>Questions &amp; Answer Session</td>
</tr>
<tr>
<td>11.00 am</td>
<td>Coffee &amp; Tea Break</td>
</tr>
<tr>
<td>11.30 am</td>
<td>‘Why exercise is good for you’ - Measuring disease impact Hayley Ramjattan (Neuromuscular Physiotherapist)</td>
</tr>
<tr>
<td>11.45 am</td>
<td>DLA, MP and Benefits Steve Bradshaw (Benefits and Welfare Officer)</td>
</tr>
<tr>
<td>12.05 pm</td>
<td>Questions &amp; Answer Session</td>
</tr>
<tr>
<td>12.30 pm</td>
<td>Lunch (one to one 10 minute chats with Steve Bradshaw)</td>
</tr>
<tr>
<td>1.30 pm</td>
<td>Breakout Session A – CMS in Children Dr Sithara Ramdas, Dr Stephanie Robb, Dr Pinki Munot</td>
</tr>
<tr>
<td>2.15 pm</td>
<td>Breakout Session B – Pilates for all Hayley Ramjattan &amp; Jackie Birch (Pilates Instructor)</td>
</tr>
<tr>
<td>2.35 pm</td>
<td>Breakout Session C – myaware Workshop Ruth Ingledow – Social Networking Steve Bradshaw - Welfare</td>
</tr>
<tr>
<td>3.00 pm</td>
<td>Open Questions Chaired by Pinki Munot</td>
</tr>
</tbody>
</table>
Appendix 10:

CMS patient day 2018 feedback

<table>
<thead>
<tr>
<th>Please rate the say</th>
<th>#</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent:</td>
<td>9</td>
<td>69%</td>
</tr>
<tr>
<td>Very Good</td>
<td>1</td>
<td>8%</td>
</tr>
<tr>
<td>Good</td>
<td>2</td>
<td>15%</td>
</tr>
<tr>
<td>OK</td>
<td>1</td>
<td>8%</td>
</tr>
<tr>
<td>Poor</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Which part of the day did you enjoy most?</th>
<th>#</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research/Drug treatment overview</td>
<td>4</td>
<td>30%</td>
</tr>
<tr>
<td>Exercise sessions</td>
<td>1</td>
<td>8%</td>
</tr>
<tr>
<td>Psychology talk</td>
<td>1</td>
<td>8%</td>
</tr>
<tr>
<td>All of it</td>
<td>3</td>
<td>23%</td>
</tr>
<tr>
<td>Meeting people</td>
<td>1</td>
<td>8%</td>
</tr>
<tr>
<td>Lunch</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Breakout sessions</td>
<td>3</td>
<td>23%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Do you think this was a suitable venue?</th>
<th>#</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>YES</td>
<td>11</td>
<td>85%</td>
</tr>
<tr>
<td>NO</td>
<td>2</td>
<td>15%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Please rate the venue</th>
<th>#</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>4</td>
<td>33%</td>
</tr>
<tr>
<td>Very Good</td>
<td>4</td>
<td>33%</td>
</tr>
<tr>
<td>Good</td>
<td>3</td>
<td>25%</td>
</tr>
<tr>
<td>OK</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Poor</td>
<td>1</td>
<td>9%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Did you enjoy lunch &amp; refreshments?</th>
<th>#</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>8</td>
<td>89%</td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td>11%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Please rate lunch/refreshments</th>
<th>#</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>4</td>
<td>45%</td>
</tr>
<tr>
<td>Very Good</td>
<td>2</td>
<td>22%</td>
</tr>
<tr>
<td>Good</td>
<td>1</td>
<td>11%</td>
</tr>
<tr>
<td>OK</td>
<td>1</td>
<td>11%</td>
</tr>
</tbody>
</table>
Would you like to attend a similar day in the future?

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>10</td>
<td>100%</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

On future days what activities would you like?

- Advice on anaesthesia and how to avoid associated problems.
- Employment workshop, education workshop.
- Information on development of gene therapy.
- Pilates
- Exercise again – very beneficial.
- Dietician, employment workshop – MDUK do hold similar workshop.

Comments/suggestions

- Better venue next year.
- More talks in local groups + activities.
- Thank you for a lovely day!