Rare Neuromuscular Disorders Group

Congenital Myasthenic Syndromes: Oxford University Hospitals NHS Foundation Trust

Annual Report October 2016

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:

Clinical team

Dr Jackie Palace	Consultant Neurologist (Service Lead)
Dr Sandeep Jayawant	Consultant Paediatric Neurologist
Dr Stephanie Robb	Consultant Paediatric Neurologist (GOSH)
Dr Pinki Munot	Consultant Paediatric Neurologist (GOSH)
Dr Ravi Knight	Consultant Neurophysiologist
Dr Pedro M. Rodriguez Cruz	CMS Clinical Fellow
Birute Saul	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 Anneke Seller	Director of Genetics Laboratories
Dr Tracy Lester	Principal Clinical Scientist
Dr Mike Oldridge	Clinical Scientist

Service Overview

The service sees about 200 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 (spirometer) and EMGs (Electromyogram).

Monthly joint all day clinics with Dr Stephanie Robb and the Oxford clinical team are now established. Joint clinics alternate between GOSH London and Oxford, and allow good practice to be shared between centres The GOSH London clinics are also attended by Dr Pinki Munot from GOSH. The CMS

Service held a Joint Paediatric clinic with St Thomas's Hospital (Dr Heinz Jungbluth) on the 28 July and an Adult Clinic at King's College Hospital (Dr Fiona Norwood) in London on the 2 September. We are looking to offer remote clinics in Liverpool and Scotland within the next 6-12 months.

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.

This year, the CMS service has lead the application of the Oxford Neuromuscular Group (in collaboration with Newcastle muscle group), to become a European Reference Centre 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 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. However, due to the political uncertainty of "Brexit", terms and conditions of ERNs might need to be revised in the future for UK centres participating in these networks.

The CMS Service has established Telemed appointments 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 just want to chat to the team over the phone, and will defer their appointments until later in the year. This has been welcomed by patients. In addition, we are thinking about the possibility that some patients could do their own assessment, using a "self-assessment QMG form" (Appendix). This would allow us to monitor patients evolution remotely more accurately.

The clinical and genetic research teams have an advisory service to the diagnostic genetic laboratory on specific genes that need testing usually after consultation with 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".

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* and *GMPPB* 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. These 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 for intronic variants
- Reporter assays to test for promoter variants
- Expression assays to test *CHAT*, *GFPT1*, *DPAGT1*, *MUSK*, *AGRN*, *ALG2*, *ALG14,* and *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 to 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 1]**.

Service Objectives and Outcomes

The purposes and goals of the service

- Make a definitive CMS diagnosis (including prenatal diagnosis where requested) **[Appendix 4a]**
- Treat effectively
- 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 8: Service Engagement and Communication)

Outcomes

Activity Levels

In addition to seeing about 206 patients in the outpatient clinics, the clinical team also reviewed the genetic results of 350 patients in April 2015-April 2016 period, offering advice on diagnosis and management to the referring Clinician. We also had 1 CMS inpatient (2 occupied bed days) that was admitted electively to the ward in order to optimise their treatment regime.

DNA samples: the number of DNA samples received by the diagnostic laboratory was 123, compared to 121 last year. This suggest sample numbers remaining stable after the addition of new glycosylation genes, *DPAGT1* and *GFPT1,* to our screening panel two years ago. 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 **[Appendix 4]**:

- Number of new and follow-up outpatient visits and geographical information. **(Appendix 4b,4c, 4d and 4e)**
- DNA sample activity – number of patients **(Appendix 4f),** DNA sample geographical data **(Appendix 4g).** Number of exons analysed **(Appendix 4h).**
- Day cases and inpatient activity is also reported, although this is actually outside of the Highly Specialised Funding
- Number of remote genetic reviews in April 2015 - March 2016 was 309 (steering specific genetic tests performed dependent on clinical information). **(Appendix 4i)**
- Number of remote consultations from September 2015 – August 2016 was over 50 phone calls and 420 emails. This represents our effort in communication with patients and other medical professionals from the UK and abroad.
- Number of Telemed appointments from September 2015 to August 2016 was 15.

Performance Indicators

- Turnaround time for DNA reporting: The turnaround time for DNA reporting is approximately two months per gene. However, if it is urgent, then the turnaround is approximately two weeks.
- Clinic Waiting Times: 8 weeks for new patients
- Geographical Distribution
- Patient Satisfaction (see later – page 6)

Geographical Distribution

- Geographical data of outpatient activity (**Appendix 4d**) genetic tests (**Appendix**) and remote reviews (**Appendix 4i**) are shown - We are reporting Country of residence

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 and we have set up a Telemed service from March 2015.

We are planning a Joint clinic in Glasgow in the future.

As well as offering a national service, the team also offer advice on international patients. In the period April 2015 – March 2016, 6.67% of our genetic reviews came from overseas patients, compared to 8.23% last year. This confirms our efforts in establishing us as a centre of international expertise in CMS. We are receiving more enquiries regarding from EU countries using the S2 EU Cross-border Healthcare Directive referral process .We currently have a 4 patients coming through this process successfully.

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 5**).

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 has a new action plan that has just come into force and this is hoping to release more parking spaces for patients. Thus, reducing the complaints about parking.

The CMS Service updated our patient pre-clinic information booklet in March 2015, to include new staff members **[Appendix 8]**.

Financial Update

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

Service Developments

Development of new quality-health care measures and indicators

We are developing a set of new indicators to better measure the quality of the healthcare provided by our service. They will be added to our previous ones, and incorporated into our questionnaires and databases. They will be collected prospectively from this year. The new indicators include the following:

- Percentage of genetic reviews within 8 weeks
- Detection rate for genetic test
- Overall percentage of patients with a final diagnosis
- Overall percentage of patients with a final diagnosis reached on new patients without prior diagnosis
- Concordance with the diagnosis centres of origin (in cases of second opinion)
- Percentage of patients involved in research (patients enrolled in existing registries and natural history studies, biological samples donated to biobank)
- Safety incidents, mortality and morbidity outcomes.
- Quality of Life Measures

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. 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 in travel expenses, as some patients have difficulty affording the cost of travel. This also stops patients from being lost to follow-up. In addition, we have developed a simplified QMG form (appendix) so that patients can do a self-assessment at home, and we can monitor their evolution even if they are not seen in clinic.

Salbutamol protocol

Due to the higher number of CMS patients on salbutamol and ephedrine, we are receiving a relatively high number of queries from GPs regarding the use and monitoring of these drugs. Therefore, we are planning to develop in the

upcoming year a shared care protocol with GPs for the correct prescription and monitoring of these drugs.

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 often well received by the CMS cohort, especially in the adult population where access to specialist physiotherapy in the community can be patchy. This support also extends to care outside of clinics, with links to community therapists (for example; in supporting respiratory management and progression of motor development) and supporting coordinated medical input during hospital admissions.

The role of the Neuromuscular Physiotherapist has evolved over the past 12 months, with patients seeking more guidance on engagement in sport and exercise progression. Recent collaboration between the Physiotherapists from the 4 main High Specialist Services, has resulted in the development and roll out of an activity audit. This aims to understand the importance patients place on being physically active and the barriers they experience in achieving the activity levels they would prefer. The results of this will be fed back at the next CQUIN meeting, and will help to inform future projects in this area.

The Neuromuscular Physiotherapist in the Oxford clinic has also established links with the Physiotherapists supporting the CMS clinics occurring in both Newcastle and GOSH. Further collaboration is planned to look at revised outcome measures and further patient activity audits, which will enhance the care patients receive in Oxford.

Myasthenia 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. As education is a large part of the role, the myasthenia education resources have been reviewed and updated, and now medication advice leaflets (**Appendix 9 and 10**) are available for patients, families and carer for reference. To improve the visual accessibility of these resources charitable

funding supported the service to purchase information stands for the outpatient's clinic.

The patient pathway has also been improved with the service acquiring two pulse oximeters. Fatigue is a huge issue for patients and maximising the times they are resting is vital. We recognised that poor sleep patterns can exacerbate fatigue. Hence, if there is a concern about sleeping patterns, a pulse oximeter can be given directly from clinic for patients to have sleep studies. This means this is promptly undertaken as opposed waiting for an outpatient's appointment and necessary inventions actioned quickly to address this.

New patient Liaison and Project Nurse

The CMS Service appointed a new nurse in combination with our NMO service to work on projects, such as, keeping our website up to date, producing patient information literature, and analysing performance outcome questionnaires from the clinics. This person will lead on analysis of patient services and implement improvement projects where needed and in association with our Myasthenia & NMO Nurses. This was funded from income from the two services.

Multimedia equipment

In August 2016 we purchased a new IPad to replace our video recorder. This will allow us to not only record patient performing their QMGs, but we can show patients Information booklets and online access details at the "touch of a button" in clinic.

Pregnancy Packs

We are producing for all patients with child bearing potential, an information pack for Health Care Professionals & patients regarding the safety of the most commonly used drugs in pregnancy & breastfeeding.

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. Previously, using the same methodology, we were

able to identify DPAGT1, *ALG2* and *ALG14, GMPPB,* and *COL13A1* as causative genes for CMS.

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, and the more unusual CMS such as *AGRN* and *MUSK* that are currently screened for in the research laboratory.

Current translational research projects

As reported, several forms of CMS show a marked beneficial response to Salbutamol or ephedrine. At the moment we are studying the molecular mechanism of Salbutamol at the neuromuscular junction. We believe that this drug provides 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. We are exploring with Novartis the potential use of a more potent β2-adrenergic receptor agonist which, in preliminary work, has been found to be muscle-specific and to have markedly reduced side effects.

We have recently been awarded the Myaware prize studentship starting on October 1st 2016 aimed at identifying small molecules that can increase expression levels of the *DOK7* protein and thus could be used as an alternative therapeutic strategy.

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. Our CMS

booklets have been updated with the latest relevant information regarding recently identified CMS and therapy (**Appendix 2)**.

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 has been updated this year to include new staff members.

Information in clinic

Newly diagnosed patients are given in clinic a CMS booklet **(Appendix 2)** with the latest information about the diagnosis, treatment and management of this condition. In addition, there are given a CMS-DVD **(Appendix 3)** 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

Patient Day

The CMS Patient Day took place on the 8 April 2016 in Oxford. A total of 22 patients and their family members attended (69 in total). The agenda consisted of overviews, presentations, and breakout sessions where patients interacted with each other and the CMS team **(Appendix 6)**. This year the patients had made suggestions about the subjects they wished us to cover and with that in mind, we arranged for the RDAC (Regional Driving Assessment Centre) and a Personal Trainer to attend to give talks. Patients completed a questionnaire feedback with a positive outcome **(Appendix 7)**. The National Congenital Myasthenia Patient Day is due to take place in the Spring of 2017 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 are able to view 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 2014-2015 report took place on 26 January 2015 in Newcastle. The 2014-2015 HSS Rare Neuromuscular Disease Service Audit Meeting is

anticipated to take place in early 2017. This meeting took place on the 6 January 2016 in Newcastle.

Service Problems

Provision of 3,4-Diaminopyridine

The CMS Service had no supply issues during this period. The NHS Commissioning document states Firdapse will not be funded; this is meant to allow Physicians to prescribe the unlicensed cheaper version because there is no licensed formulation available.

Provision of Salbutamol

The problem with the manufacturing of Salbutamol modified release capsules (Ventmax®) persists. The manufacturer Chiese has discontinued the product. 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.

Meetings, Presentations and Publications

Meetings

Dr J Palace, Professor D Beeson, Dr Stephanie Robb, Dr P Rodriquez Cruz, Birute Saul, Hayley Ramjattan, Julia Goodgame, Dr. Tracy Lester, Dr Mike Oldridge

Highly Specialised Services Clinical Outcome
Collaborative Audit Workshop
Newcastle upon Tyne
6 January 2016

Oral Presentations

Society for Muscle Biology, Asilomar Conference Grounds, Pacific Grove, CA, USA**.** June 6-11, 2016. Hereditary myasthenic syndromes: new genes and better treatments. Professor David Beeson

9th UK Neuromuscular Translational Research Conference, 'The John Newsom-Davis Lecture' March 22nd-23rd 2016, Keble College, Oxford, UK. Congenital myasthenic syndromes. Professor David Beeson.

Rare Diseases Day Symposium on CDG. 25-27th February 2016, Sanford Burnham Prebys Medical Discovery Institute, La Jolla, California, USA. Myasthenic syndromes and congenital disorders of glycosylation. Professor David Beeson.

International symposium on myasthenia and thymoma, 6th-9th Jan 2016, St Anne's College, Oxford UK. Hereditary myasthenic syndromes: new genes and better therapy. Professor David Beeson.

"Update in Myasthenia". Talk to local Myaware group, 7 November 2015, Holiday Inn, Peartree Roundabout, Oxford. Professor David Beeson

Wellcome Trust Synaptopathies Symposium, Saturday 26 September 2015, UCL Institute of Neurology. "Synaptopathies of the neuromuscular junction – mechanisms and therapy' Professor David Beeson

10th International Paediatric EMG Congress, Magdalene College, Cambridge, 9-11 Sept 2015. Staying current with genetic discoveries in CMS. Professor David Beeson

Congenital Myasthenic Syndromes, UCL Neuromuscular Disorders MSc Course, February 2015. Dr Stephanie Robb

Myasthenia, assessment and fatigue, APCP Network (Association of Paediatric Chartered Physiotherapists).4 March 2016, London; Hayley Ramjattan

Paediatric Therapy Team Talk – Hayley Ramjattan April 2016

Congenital Myasthenic Syndrome Patient Day April 2016 – Dr Jackie Palace; Dr Rodriguez Cruz; Professor David Beeson; Hayley Ramjattan

Myasthenia in Childhood at GOSH Practical Neurology Study Days Course on 19 May; Dr Stephanie Robb

Limb-girdle syndromes: myasthenia or myopathy. Association of British Neurologist Annual meeting, Brighton, May 2016. Dr Pedro Rodriguez Cruz

IX Annual Neuromuscular Translational Research Conference. Clinical features of the myasthenic syndrome arising from mutations in GMPPB. March 2016. Dr Pedro Rodriguez Cruz

Publications

1. Mutations in GMPPB cause congenital myasthenic syndrome and bridge myasthenic disorders with dystroglycanopathies. Belaya K, Rodríguez Cruz PM, Liu WW, Maxwell S, McGowan S, Farrugia ME, Petty R, Walls TJ, Sedghi M, Basiri K, Yue WW, Sarkozy A, Bertoli M, Pitt M, Kennett R, Schaefer A, Bushby K, Parton M, Lochmüller H, Palace J, Muntoni F, Beeson D .Brain. 2015 Sep;138(Pt 9):2493-504

2. Salbutamol and ephedrine in the treatment of severe AChR deficiency syndromes. Rodríguez Cruz PM, Palace J, Ramjattan H, Jayawant S, Robb SA, Beeson D. Neurology. 2015 Sep 22;85(12):1043-7.

3. Congenital myasthenic syndrome type 19 is caused by mutations in COL13A1, encoding the atypical non-fibrillar collagen type XIII α1 chain. Colin A. Johnson, Clare Logan, Judith Cossins, Pedro Rodriguez Cruz, David Parry, Susan Maxwell, Pilar Martinez Martinez, Joey Riepsaame, Zakia Abdelhamed, Alice Lake, Maria Moran, Stephanie Robb, Gabriel Chow, Caroline Sewry, Philip Hopkins, Eamonn Sheridan, Sandeep Jayawant, Jacqueline Palace, David Beeson. Am J Hum Genet. 2015 Dec 3;97(6):878-85.

4. Clinical features of the myasthenic syndrome arising from mutations in GMPPB. Rodríguez Cruz PM, Belaya K, Basiri K, Sedghi M, Farrugia ME, Holton JL, Liu WW, Maxwell S, Petty R, Walls TJ, Kennett R, Pitt M, Sarkozy A, Parton M, Lochmüller H, Muntoni F, Palace J, Beeson D. J Neurol Neurosurg Psychiatry. 2016 Aug;87(8):802-9

5. Muscle magnetic resonance imaging in congenital myasthenic syndromes. Finlayson S, Morrow JM, Rodriguez Cruz PM, Sinclair CD, Fischmann A, Thornton JS, Knight S, Norbury R, White M, Al-Hajjar M, Carboni N, Jayawant S, Robb SA, Yousry TA, Beeson D, Palace J. Muscle Nerve. 2016 Aug;54(2):211-9

6. Congenital myasthenic syndromes: recent advances. Beeson D. Curr Opin Neurol. 2016 Jul 28. [Epub ahead of print]

7. Salbutamol-responsive fetal acetylcholine receptor inactivation syndrome. Allen NM, Hacohen Y, Palace J, Beeson D, Vincent A, Jungbluth H. Neurology. 2016 Feb 16;86(7):692-4.

8. Late presentations of congenital myasthenic syndromes: How many do we miss? Garg N, Yiannikas C, Hardy TA, Belaya K, Cheung J, Beeson D, Reddel SW. Muscle Nerve. 2016 Feb 22.

9. Next generation sequencing in a large cohort of patients presenting with neuromuscular disease before or at birth. Todd EJ, Yau KS, Ong R, Slee J, McGillivray G, Barnett CP, Haliloglu G, Talim B, Akcoren Z, Kariminejad A, Cairns A, Clarke NF, Freckmann ML, Romero NB, Williams D, Sewry CA, Colley A, Ryan MM, Kiraly-Borri C, Sivadorai P, Allcock RJ, Beeson D, Maxwell S, Davis MR, Laing NG, Ravenscroft G. Orphanet J Rare Dis. 2015 Nov 17;10:148.