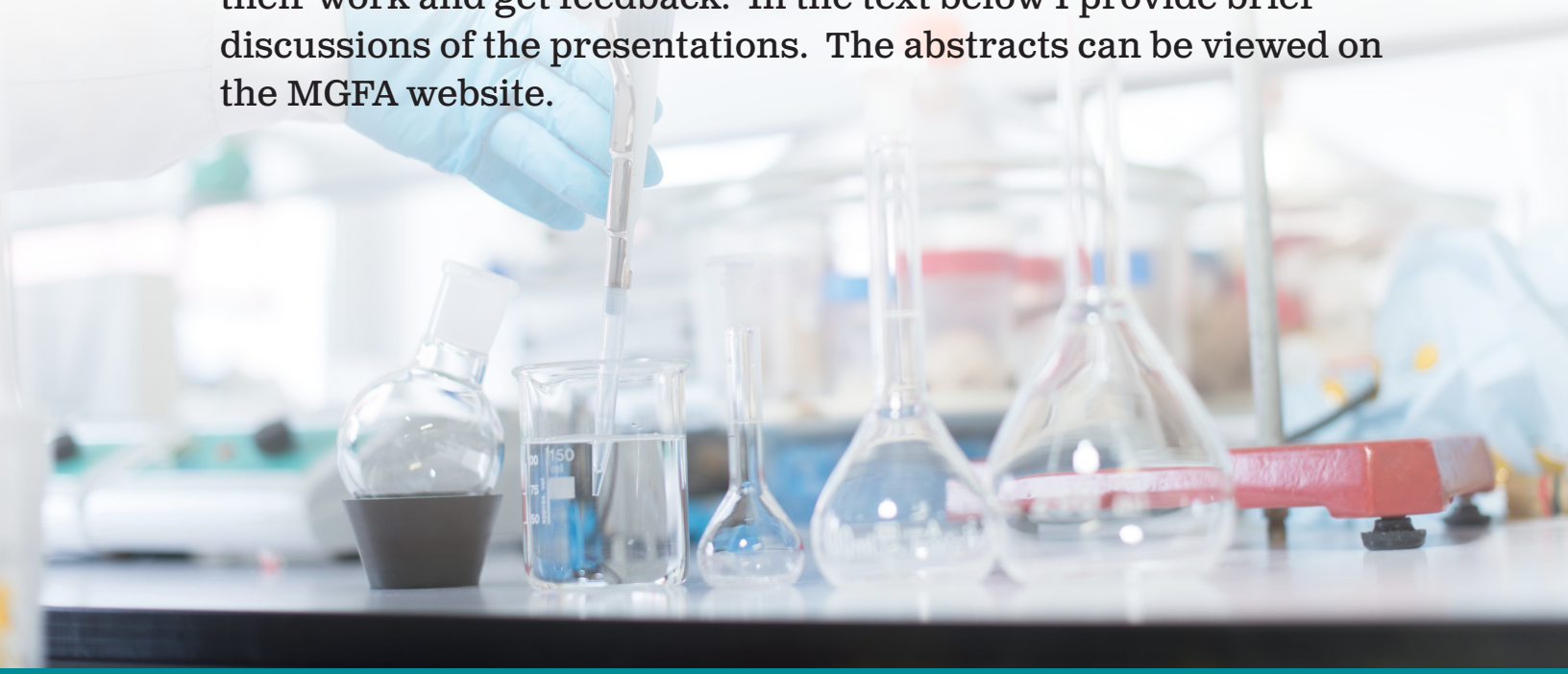
Overview: The 2017 Scientific Session of the MGFA was held at the Annual Meeting of the American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) on Wednesday, September 13th, 2017 in the conference center of the Marriott Desert Ridge Hotel. The meeting was chaired by Drs. Amanda Guidon, Jeff Guptill, and Mike Hehir. Drs. Guptill and Hehir were both recipients of MGFA/AAN Fellowships. There was an audience of about 200 people. The session provided a venue for young investigators to present data using talking and traditional posters. Posters give new investigators an opportunity to present their work without the pressure of standing in front of hundreds of people. I liked the attention paid to posters, which enable young investigators to present their work and get feedback. In the text below I provide brief discussions of the presentations. The abstracts can be viewed on the MGFA website.



PLATFORM PRESENTATIONS

KEYNOTE PRESENTATION

Incorporating Outcome Measures into Clinical Practice

S Muppidi, Stanford Univ, Palo Alto CA

This talk was aimed to encourage clinicians to use standardized measures to evaluate how MG is affecting a patient, how severe the symptoms are, and the direction of the clinical course (improve or worsen in response to a new intervention). The first described was the Quantitative MG index (QMG) which assesses 13 items that are graded in 5 increments from absent to severe. The score ranges from 0-39. A 3 point change is considered to be significant. Manual muscle testing (MMT) evaluates the strength of 18 selected muscle functions. MMT is one of the first measures used to assess the severity of MG. MG-ADL (activities of daily living) assesses how MG is affecting a person's ability to function independently. The MG-ADL is a good tool for following disease severity. MG-QOL (quality of life) measures how MG is affecting a patient's ability to carry out tasks required to live independently. The current version of MG-QOL evaluates 15 items. The MG composite score combines elements of MG-ADL, QMG and MMT to assess the severity of MG. The MG impairment index is being evaluated to comply with FDA guidelines used to evaluate medication efficacy (Neurology 87:979-886, 2016). This measure has been validated (measures what it is supposed to measure and the score reflects severity of disease determined by other measures). The responsiveness of the MG impairment index to clinical changes is being assessed now. These indices are best if used from the beginning of caring for a patient – continued use of these measures provides a "clinical video" of how a patient's MG is changing and responding to different interventions.

TALK 1

A Redcap Database for the MG Clinic and Multicenter Collaborations

D Sanders (Durham, NC), M Small (Durham, NC), S Budinger (Durham, NC), J Guptill (Durham, NC)

This talk was essentially the implementation of the Keynote talk. The group at Duke recognizes that the Electronic Medical Record (EMR) is becoming the standard in American healthcare and they have devised a tool (REDCap (Research Electronic Data Capture) to enable a uniform format for collecting information about MG which will allow information about patients from all over the US to be integrated into a single data set. This tool will facilitate national studies of MG as well as to encourage multisite clinical trials involving MG. The information that can be collected by this tool will complement the data in the MG Patient Registry about the distribution of various forms of MG. Patients who really want to help advance the understanding and treatment of MG are encouraged to enroll in the Registry. The trick is to get the REDCap system to work within the EMR due to the variety of EMR systems in use. An even greater limitation is that the EMR used in many large health care systems, known as the EPIC system, is not easy to alter because EPIC is optimized for billing, not collecting patient information in a manner that will be easily used for clinical studies.

"Patients who really want to help advance the understanding and treatment of MG are encouraged to enroll in the Registry."

TALK 2

Efficacy of Eculizumab is Sustained over 52 Weeks in Patients with Achr+ Refractory Generalized Myasthenia Gravis (Gmg): Interim Results from the Open-Label Extension of Regain

J Howard (Chapel Hill, NC), J Wang (New Haven, CT), F O'Brien (Lexington, MA), R Mantegazza (Milano, IT), REGAIN Study Group

Medical treatment has entered a new era with the emergence of biopharmaceuticals, which are chemicals produced in living cells, often yeast, that act on specific chemicals present in the human body. An important class of agents is the monoclonal antibodies (drug names that end in "mab"). Eculizumab is a human monoclonal antibody that specifically targets a key element in the complement pathway, complement element №5 or C5. The complement pathway is critical in causing damage to the postsynaptic membrane in most autoimmune forms of MG, with the exception of MuSK-MG. Therefore, Eculizumab has the potential to block the damage caused by the autoimmune attack on the endplate. The results, including those presented here, of the REGAIN study (Eculizumab) extension for the treatment of refractory AChR-MG, are very encouraging. The downside of Eculizumab is the current charge which may well be over $100,000 per year. If the price of treatment can be reduced, Eculizumab can become an extremely useful tool to fight and eventually cure MG.

TALK 3

Immune Profiling of Circulating Follicular Helper T Cells in Musk-Mg Patients

Y Li (Guangzhou, Guangdong), M Russo (Durham, NC), W Liu (Guangzhou, Guangdong) S Raja (Durham, NC), J Guptill (Durham, NC), J Yi (Durham, NC)

Note: Lay translation of the start of the abstract: "MG is an autoantibody-dependent, CD4 T-cell mediated autoimmune disease of the neuromuscular junction . . ." – There are two general classes of immune cell, aka white cells, specifically lymphocytes. B-cells produce antibodies and T-cells regulate the B-cells. A subset of CD4 T-cells (CD-4 refers to a specific marker (a distinct molecular element on the cell surface)) present on the surface of a T-cell. The B-cells produce the antibodies that target specific elements of the neuromuscular junction such as the acetylcholine receptor (AChR) or muscle-specific kinase (MuSK) – in addition, there are more antibody targets being recognized and discovered.

This talk focused on the role of Tfh cells, which are follicular helper cells. The Tfh cells are present in the lymphocyte germinal centers (sites where lymphocytes multiply) as well as in circulating blood. Tfh cells enhance the responsiveness of B-cells to T-cell signals. In a sense the Tfh cells change how well the B-cells listen to the T-cells (think of the T-cells as parents and the B-cells as children – what parent wouldn't love to have an effective Tfh to get children to do what you tell them?).

TALK 4

B-Cell Depletion in Late-Onset Myasthenia Gravis is Safe and Effective; A Case Series

S Sahai (Los Angeles, CA), R Lewis (Los Angeles, CA), A Maghzi (Los Angeles, CA)

Rituximab is a monoclonal antibody that targets a class of lymphocytes implicated in MG – B-cells with a CD20 surface marker. Rituximab has the potential to block the action of a class of immune cells that has been shown to be critical for many forms of MG. Most importantly, Rituximab has a much milder side effect profile compared to prednisone-like drugs. Several studies have shown Rituximab to be effective for MuSK-MG. This study targeted older patients with AChR-MG and appreciable side effects due to prednisone or who were refractory to prednisone. All patients greatly improved and either completely tapered off or greatly reduced their dose of prednisone. This was a small study of only 6 patients, but the findings are encouraging for future use of Rituximab as an alternative to prednisone, provided the cost of Rituximab can be brought down. Though the charge for Rituximab is currently much less than for Eculizumab, the current charge exceeds $50,000 per year.

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This is an ongoing study that re-evaluates the risk/benefit of using drugs that have been previously shown to exacerbate MG.

TALK 5

Prescribing Patterns and Implications of Medications Known to Exacerbate Myasthenia Gravis (MG)

K Weekes-Plante (Burlington, VT), N Kolb (Burlington, VT), M Hehir (Burlington, VT)

This is an ongoing study that re-evaluates the risk/benefit of using drugs that have been previously shown to exacerbate MG. This study evaluates how often contraindicated medications were prescribed. One aim of this study is to improve systems used to alert clinicians of possible side effects when a medication is being considered. This study will also consider new agents that may have contraindications for people with MG that are not on the list as yet. One such class of medications are agents used to enhance the immune system in people with cancer. This study is extremely important because many of the current restrictions/recommendations are based upon information that was collected decades ago. Medicine has advanced greatly and it is entirely appropriate to re-evaluate the list of contraindicated medications. This study will also evaluate why patients with MG are treated with contraindicated agents. The list of drugs to avoid is the dynamic MGFA list, which would be revised if this study shows the need to do so. See: http://myasthenia.org/LivingwithMG/DrugstoAvoid.aspx

TALK 6

Tele-Rehabilitation Improves Function and Balance in Myasthenia Gravis

C Macko (Ellicott City, MD) University of Maryland and Baltimore VAMC

This talk focuses on providing rehab for people with MG. Most of the patients have stable MG – meaning that the symptoms that are present are not changing. Tele-rehab was used because people with MG may have difficulty in getting to frequent treatment sessions, as is needed for effective rehab. The study focused on 5 exercises: sit to stand, forward lunge, marching, side-stepping and squatting. The tele-rehab program improved endurance and breathing function. The system uses a laptop or tablet that has a camera so that the patient can see the exercise and the therapist can see what the patient is doing – number of repetitions and quality of each rep. They developed an automated way to review the patient videos to determine how to individualize the treatment for each subject. Patients come in for clinical interventions periodically to go over how the exercise program is working and to modify based upon the patient's performance. The program was widely accepted. The most common need to change the program for an individual was knee pain.

The tele-rehab program improved endurance and breathing function.

TALK 7

Prolonged Post Tetanic Potentiation (PTP)

L Gutmann (Iowa City, IA), M Shy (Iowa City, IA)

The speaker was not able to be present, but I can provide background for this abstract. PTP refers to an enhanced release of ACh after a period of rapid stimulation of the motor nerve. There are two competing actions that affect the number of packets (vesicles) of ACh released in response to nerve stimulation. The first is reduction of readily releasable ACh vesicles. The second is a rise in nerve terminal calcium which increases the likelihood that an available ACh vesicle will be released (facilitation). PTP is not observed in normal neuromuscular junctions because the release of ACh appreciably decreases the number of releasable ACh vesicles, hence depletion overpowers facilitation. PTP is observed in conditions in which the release of ACh vesicles is low. Botulinum toxin (that's right the botox that some folks use to remove wrinkles or to reduce muscle spasm) reduces the likelihood of

release of ACh vesicles without impairing build-up of nerve terminal calcium. Therefore, PTP has been reported in association with botulinum toxin. This presentation documented that PTP can occur in a congenital disorder of neuromuscular transmission (congenital myasthenia gravis) in which the defect is a mutation of gene (SYT2) that provides the code for producing a protein (synaptotagmin II) involved in releasing vesicles of ACh. Functionally, the mutation of SYT2 compromises release of ACh in a manner similar to the way that botulinum toxin works.

POSTER PRESENTATIONS

TALKING POSTER 1

Clinicodemographic Predictors of the Impact of Infections on Myasthenia Gravis

N Kukulka (Columbia, MO), R Govindarajan (Columbia, MO)

The speakers were not present for this talking poster. This presentation was interesting to me because it addressed the triggers for MG exacerbations. Infections were responsible for almost more than one-third of the hospital admissions and close to half of visits to the Emergency Department associated with MG. Of the infections almost 30% could have been prevented if individuals received an appropriate vaccine such as flu vaccine or pneumovax – vaccine to prevent pneumococcal pneumonia. Therefore people with MG should get flu shots as well as pneumovax. To my knowledge even people receiving Rituximab and Eculizumab should get flu shots and pneumovax. People who will receive Eculizumab should receive vaccine to prevent meningococcal meningitis before they start Eculizumab. Consult your healthcare provider to make sure that you get all of the vaccinations that you should receive.

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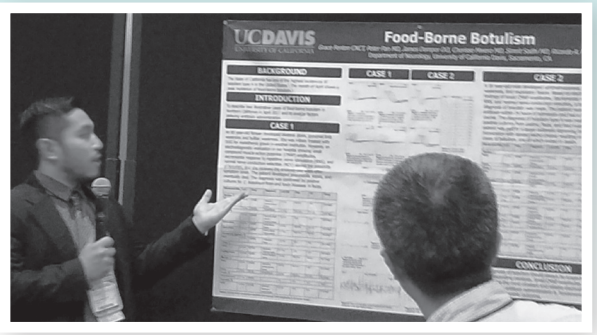

TALKING POSTER 2

The Benefits and Pitfalls of Next Generation Sequencing (NGS): 3 Illustrative Cases of Myasthenia

K Scherer (Tucson, AZ)

Next Generation Sequencing refers to a way of analyzing the DNA of people who may have a congenital myasthenic syndrome (congenital form of myasthenia gravis (CMG) that is due to mutations that alter the production of proteins essential for neuromuscular transmission). NGS looks at the sequencing of genes associated with recognized congenital myasthenic syndromes. The upside of NGS is that this technology can very quickly recognize mutations associated with CMG leading to rapid employment of the appropriate treatment for a known form of CMG. The downside was pointed out by one of the cases. Not all mutations greatly impair the function of the resulting protein. NGS may identify a mutation of a protein associated with CMG that does not impair the function of the specific protein. Therefore, when a clinician interprets NGS it is important that the findings be viewed carefully, particularly if the mutation identified has not been previously associated with CMG.

TALKING POSTER 3

Food-Borne Botulism: Diagnostic Challenges

R Maselli (Davis, CA), G Fenton (Sacramento, CA), P Pan (Sacramento, CA), J Dompor (Sacramento, CA), S Sodhi (Sacramento, CA), C Mwero (Sacramento, CA), Ricardo Maselli (Davis, CA)

This poster dealt with an unusual acquired cause for impaired neuromuscular transmission – food borne botulinum toxin. Botulinum toxin is the most potent toxin that I know of. A single toxin molecule can knock out one motor nerve terminal for months. The toxin blocks release of vesicles of ACh. The bacteria that produces botulinum

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toxin thrives in anaerobic (without air) conditions. Most cases of botulism occur in food that has been canned or stored improperly. In the first case the patient ate a can of her home canned creamed corn that was swollen due to the gas produced by the Clostridium botulinum that was in the can due to improper canning. In the second case the C botulinum grew in Nacho cheese sauce that was stored improperly. Don't eat anything from a can that is swollen or has a hole in it. Beware of fly by night taco stands!

TALKING POSTER 4

Curative Strategies in Myasthenia Gravis

J Sonett (New York, NY) Columbia Presbyterian Medical Center.

Dr. Sonett is a thoracic surgeon who was part of the International Myasthenia Gravis Thymectomy trial. He spoke about combining different treatments with thymectomy to perhaps speed the rate of achievement of, and the percentage of people who have, complete remissions following thymectomy. The approach suggested by Dr. Sonett is partnering between medical clinicians and surgeons to enhance the benefit of thymectomy, which is a natural extension of the Thymectomy trial.

TALKING POSTER 5

Pediatric Neuromuscular Junction (NMJ) Disorders

S Bhatia (Atlanta, GA), S Verma (Atlanta, GA)

The speaker was not present. The poster dealt with patterns of MG in infants and children (teens and younger). When I went to medical school, autoimmune MG was not recognized to occur in children (wrong). This poster indicated that in Atlanta, the most frequent presentation is generalized autoimmune MG followed by autoimmune ocular MG and then Congenital MG (CMG). Children with autoimmune MG respond to the same types of treatments that are used in adults.

TRADITIONAL POSTERS

A Case Report of Recurrent Takotsubo Cardiomyopathy in a Patient during Myasthenia Crisis

A Battineni (Columbia, MO), N Mullaguri (Columbia, MO), R Govindarajan (Columbia, MO)

Myasthenic crisis is a life threatening condition. In the setting of myasthenic crisis the body produces large amounts of adrenaline and related chemicals which over-stimulate and damage the heart (Takotsubo cardiomyopathy). This poster reported on a patient who had repeated episodes of Takotsubo cardiomyopathy triggered by myasthenic crisis.

West Nile Virus Induces a Prolonged Pro-inflammatory State that may Promote Myasthenia Gravis

A Arturo Leis (Jackson, MS), D Stokic (Jackson, MS), D Acharya (Hattiesburg, MS), A Paul (Hattiesburg, MS), R Kuwar (Richmond, VA), P Vig (Jackson, MS), M Ross (Scottsdale, AZ), G Szatmary (Hattiesburg, MS), F Bai (Hattiesburg, MS)

West Nile Virus (WNV) is most commonly associated with epidemics of encephalitis and other infections in people. WNV can also alter the immune system by inducing the production of chemicals that enhance inflammation. One chemical induced by WNV is RAGE (receptor for advanced glycation end products) this chemical has been associated with experimentally-induced MG. We do not know what triggers MG. There may be several factors including a genetic predisposition toward developing autoimmune disorders. Another potential trigger could be exposure to a virus such as WNV that can alter the immune system toward developing autoimmune conditions such as MG. A side note, viruses do more than causing diseases. About 20% of human DNA came from viruses. The virus DNA does not code for human proteins, but may regulate the activity of the DNA that codes for proteins.

Sequential Intravenous Immunoglobulin (IVIG) and Plasmapheresis Therapy in a Seronegative Myasthenia Gravis (Mg) Patient with Common Variable Immunodeficiency Disease (CVID) and Refractory Weakness

G Small (Pittsburgh, PA)

This poster addressed the treatment of people who clinically have MG, but do not have antibodies associated with MG (i.e. do not have antibodies against AChR, MuSK, and if testable other known proteins associated with MG such as LRP4 and agrin). Such patients are seronegative. About 10% of MG patients are seronegative. The patient in question had seronegative MG and was immunodeficient. The immunodeficiency made treatments that directly suppressed the immune system problematic. The treatment combination that helped this patient was to add plasmapheresis (PLEX) to IVIG. The importance of this abstract is that patients are different and treatment needs to be optimized to the needs of each patient.

About 10% of MG patients are seronegative.

Eculizumab in Refractory Myasthenic Crisis

C Yeo (Houston, TX), M Pleitez (Houston, TX)

This poster reports successfully treating MG crisis with Eculizumab in a seronegative MG patient who was in crisis in spite of treatment with prednisone-like medication, IVIG and mestinon.

Prognostic Factors of Thymectomized Patients with Acetylcholine Receptor Antibody Positive Myasthenia Gravis

H Kim (Seoul, KR), Y Lim (Seoul, KR), E Lee (Seoul, KR), Y Oh (Seoul, KR), K Kim (Seoul, KR)

This poster examined the relationships between AChR-antibody titer and thymus pathology in the outcomes of people with AChR-MG who had thymectomies. People who did not have a thymoma (a benign tumor of the thymus gland) were more likely to achieve clinical remission. Among the group of people who had thymomas, those with higher AChR-antibody titers were more likely to achieve clinical remission.

Autoimmune Limb Girdle Myasthenia

V Sreenivasan (Madison, MS), D Jabari (Flowood, MS), A Witt (Jackson, MS), L Davis (Brandon, MS), V Vedanarayanan (Jackson, MS)

Most people with MG have weakness of ocular muscles leading to double vision and ptosis (drooping eyelids). This paper discusses two young people (12 yo and 16 yo) who had MG diagnosed based upon fatigueable weakness, EMG findings consistent with MG and AChR-antibodies. What was different about these patients was that they did not have involvement of eye or throat muscles or the tongue. Their weaknesses involved the proximal muscles of the upper and lower extremities (shoulders, hips, upper arms and buttocks/thighs) – this pattern is referred to as limb-girdle. MG is characterized by having a variable presentation, this is why it is a snowflake disease (no two snowflakes or MG patients are exactly alike). Drs. Kaminski, Kusner and I investigated why the eye muscles are particularly susceptible in MG. There are probably differences in the muscles of the young folks described in this poster that resulted in the unusual pattern of their MG. Future studies may understand why their MG looked different.

An Institutional Retrospective Study of Rituximab Effectiveness in Myasthenia Gravis

R Roda (Baltimore, MD), A Corse (Baltimore, MD)

Dr. Roda is a fellow whose current training is supported by the combined support of the MGFA and American Academy of Neurology /American Brain Foundation. Rituximab is a relatively new treatment for MG that uses human-based antibodies grown in yeast to selectively kill a class of immune cells, CD20 B-cells, associated with autoimmune MG. Most studies of Rituximab have focused on specific subgroups of people with MG, such as people with MuSK-MG or people in crisis. This poster looked at the experience at Johns Hopkins University of using Rituximab for treating MG in people with MG. The findings were encouraging: 1) people tolerated the treatment, 2) people completely tapered off their prednisone-type of medication and 3) Rituximab was effective for all sub-types of autoimmune MG.

Reporting on Patient Reported Outcome Measures in Myasthenia Gravis Patients Prescribed Intraveneous Immunoglobulin in the Home Setting using CareExchange®

T Walton (Lenexa, KS), A Smith (Lenexa, KS), J Stacey (Lenexa, KS)

This poster was targeted to care providers. It described the utility of using a data collection system, Care Exchange, which monitors patient reported responses to treatment, data about the treatment type and dosage, and information collected by the person(s) delivering/monitoring the treatment. The presenters found that the data provided by CareExchange was useful in optimizing treatment for each patient.

Cost Comparison between Rituximab, Plasmapheresis and Intravenous Immunoglobulin for Refractory Musk Antibody Positive Myasthenia Gravis

A Wali (Fullerton, CA), C Park (La Jolla, CA), N Bello (La Jolla, CA), R Mandeville (La Jolla, CA)

This poster speculated the lifetime cost of three types of recurring therapies: Rituximab, plasmapheresis (PLEX) and IVIG. The aim of this proposal was to counter insurance refusals of Rituximab for MG. The information presented was that lifelong Rituximab treatment was half the cost of PLEX and about one-quarter the price of IVIG. Insurance companies usually approve PLEX or IVIG for MG treatment. If insurance companies bought into the data presented, this poster might provide reason for insurance companies to approve Rituximab treatment costs.

This poster speculated the lifetime cost of three types of recurring therapies: Rituximab, plasmapheresis (PLEX) and IVIG.

Features of Lambert-Eaton Myasthenic Syndrome with Repetitive Nerve Stimulation in a Patient with known Myasthenia Gravis

A Comer (Indianapolis, IN), C Bodkin (Indianapolis, IN)

This poster showed that an EMG pattern usually associated with Lambert-Eaton Myasthenic Syndrome (LEMS) was seen in persons with MG. The importance of this poster is that clinical findings cannot be regarded in isolation. The entirety of each person's clinical manifestations needs to be considered to achieve a proper diagnosis.