

Proceedings of the 14th International Conference on Myasthenia Gravis and Myasthenic Disorders

Message from the Founding Facilitator

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I am delighted that the Proceedings of the 14th MGFA International Conference of Myasthenia Gravis and Myasthenic Disorders is being published in the RRNMF Neuromuscular Journal. This conference has a long, impressive, and impactful history. My understanding is that the conference began in 1954. For decades the proceedings were published in the Annals of the New York Academy of Science and these issues became a great source of information and authority for several generations of scientists and physicians involved in the field of myasthenia gravis (MG) and other disorders of the neuromuscular junction. Some of the biggest breakthroughs in the field were communicated at these meetings and in the published proceedings. As I type this I am in my library and looking at the proceedings from 1976 and the fifth annual conference. This was volume 274 in the NY Academy of Science series, and in that issue there were many papers on experimental autoimmune myasthe-

nia gravis by both the J. Lindstrom laboratory in southern California and E. Lambert and V. Lennon laboratory at Mayo Clinic. This conference was held just three years after the Lindstrom lab first produced EAMG and proved the immune basis of myasthenia gravis. This the fifth annual conference I see as a pivotal year in our understanding of the disease. In addition to papers by the scientists noted above, there were reports by M Seybold, A Engel, S Ringel, D Drachman, D Grob, E Stalberg, A Pestronk, K Toyka, S Appel, J Griffith, D Sanders, A Penn, R Lovelace, J Daube, WK Engel, TR Johns, HJHG Oosterhuis, M McQuillen, and many others that began the field of modern myastheniology.

We have come such a long way both in understanding MG and in treating patients with the disorder. Now we have a new generation of myasthenia experts who gathered in 2022, emerging from the Covid-19 pandemic. It is a privilege that the conference has chosen to publish the proceedings in this relatively new open access, on-line neuromuscular journal. When Drs. Carolina Barnett-Tapia and Kevin O'Connor approached me about this opportunity we immediately made the journal available for their use to publish the conference proceedings. I hope that the scientific communications published in this issue will be as impactful as those from the 5th conference in 1976.

As always, we abide by our mission to publish open access papers that the authors own, at no charge to the author or the reader.

- Rick

Proceedings Editors' introduction

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Myasthenia gravis (MG) is an autoimmune disease of the neuromuscular junction (NMJ) that specifically affects neuromuscular transmission. The clinical hallmark of MG is skeletal muscle weakness, worsened by physical activity. Early in their disease, most patients present with extraocular muscle weakness which can generalize to involve limb, bulbar, and respiratory muscles. The disability can be severe and muscle atrophy may occur over time. The immunopathology of autoimmune MG is directly attributed to circulating autoantibodies specifically targeting postsynaptic membrane proteins at the NMJ. In contrast to many autoimmune diseases, autoantibodies in MG are unmistakably pathogenic. Consequently, MG serves as an archetype for human autoantibody-mediated autoimmune diseases. Due to several recent approval of therapeutics, MG patients can now benefit from a wider spectrum of treatment options including biologics that target specific underlying immune mechanisms.

The MGFA International Conference on Myasthenia Gravis and Related Disorders is considered the *major* meeting focused on MG pathology, treatment, and epidemiology. The meeting brings together clinicians and scientists, covering different aspects of MG: from basic science to new treatments, to the personal and societal impacts of the disease. Thus, this meeting is driven by the shared goal to improve the care and lives of people living with MG and related disorders. The meeting had been held every five years, providing a unique opportunity to discuss advances in the field, while also serving as a venue for idea exchange, establishing collaborations, and the opportunity to refocus the field while moving forward. In addition, this international conference aims to engage the next generation of clinicians and investigators, nurturing their MG-specific investigative programs and clinical practices.

The 14th MGFA International Conference on Myasthenia Gravis and Related Disorders was held from May 10th - 12th, 2022 in Miami, Florida. The meeting was sponsored by the Myasthenia Gravis Foundation of America (MGFA). National presenting partners included argenx, Alexion, UCB, Takeda and national sponsors included Regeneron, Catalyst, Immunovant, Sanofi, CSI Pharmacy, Janssen, and Horizon. The importance of the meeting is demonstrated by its high attendance, with upwards of 360 scientists and clinicians from around the world. The plenary

sessions included 51 oral presentations and 102 posters were presented; there were 16 exhibit booths.

The Keynote address was given by Professor Angela Vincent, who has had a long-standing interest in understanding the pathophysiology of MG. She is credited with several major discoveries that have deepened our understanding of the disease. She also has trained and mentored many clinicians and scientists that have, in turn, made important contributions to the field. In her talk she shared her experience while attending the 5th International Conference on MG in New York City in 1975. She then provided her first-hand perspective of the last 50 years of MG-focused research, highlighting seminal discoveries made by Drs. John Newsom-Davis, Jon Lindstrom, Daniel Drachman, Vanda Lennon, Ricardo Miledi, her own lab and other key investigators.

Additional highlights from the sessions included new data on the role of autoantibody-mediated complement activity, and human monoclonal autoantibodies that revealed pathomechanisms underlying both AChR and MuSK MG. Topics that were also covered included ocular MG, experimental MG, biomarkers, fetal AChR autoantibodies, immune checkpoint inhibitor induced MG, sero-negative MG, cytokines and immune cells, and the biology of the NMJ.

The meeting also included an outstanding series of talks focusing on congenital myasthenia syndromes (CMS), which comprise a heterogeneous group of rare genetic disorders. Mutations underpinning CMS are found in genes encoding proteins with expression largely restricted to the neuromuscular synapse. Newly identified mutations were presented along with successful demonstrations of therapeutic intervention targeting the mutated proteins.

During the five years since the last conference, remarkable progress has been made in MG research. Perhaps most importantly is the approval of several biologic therapeutics that are highly effective in treating MG, and which are targeted, as opposed to traditional treatments. Therefore, we are entering a new era on how we treat people living with MG. This transition comes with new gaps in our scientific knowledge and healthcare systems, which will drive our research efforts in the next years. Highlighting these new therapeutics were presentations on complement inhibitors that interrupt autoantibody-mediated complement activity, neonatal FcRn inhibitors that decrease circulating autoantibodies, and cytotoxic therapeutics that target and deplete B cells by leveraging engineered T cells. Additional presentations focused on preclinical studies that investigated the induction of immune tolerance in experimental models of MG, shedding light on novel candidate treatments that represent a worthy focus of future research.

Given the growing interest in MG research and the accelerated pace of new treatments coming into clinical

practice, the MGFA has decided that the international conference will be held every three years. Additionally, to be able to reach a larger number of international clinicians, scientists and trainees, the next meeting will be outside of the United States, with the 15th International Conference scheduled to be held in Europe.

Finally, the co-chairs of the organizing committee would like to thank Dr. Richard J. Barohn, the editor of the RRNMF Neuromuscular Journal, for supporting the publication of these proceedings. Marianne Reed, Eric Bader and Jiji Oufattole at the journal were gracious and extremely helpful through all phases of developing these proceedings. We also thank Dova Levin and Samantha Masterson of the MGFA for managing the meeting logistics, and the steering committee members, Drs. Anna

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Myasthenia Gravis and Related Disorders