# FcRn and Myasthenia Gravis: Pathophysiology

Richard Nowak, MD
Associate Professor of Neurology
Yale School of Medicine

Accredited Continuing Education

# Continuing Education Information

In support of improving patient care, this activity has been planned and implemented by American Academy of CME, Inc. and CheckRare CE. American Academy of CME, Inc. is Jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

American Academy of CME, Inc., designates this enduring material for a maximum of 0.75 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Planner/Faculty Educator Dr. Nowak discloses the following relevant financial relationships with ineligible companies:

- Advisory Board/Consultant: Alexion (part of AstraZeneca), argenx, Amgen, Cour Pharmaceuticals, Immunovant, Janssen, UCB
- Grant/Research Support: Alexion (part of AstraZeneca), argenx, Amgen, Cour Pharmaceuticals, Immunovant, Janssen, UCB

Planners for this activity have no relevant financial relationships with any ineligible companies.

All relevant financial relationships listed have been mitigated.

This program is supported by an independent medical education grant from argenx.

# What Is Myasthenia Gravis (MG)?

Rare autoimmune disease.

Often due to the presence of antibodies against acetylcholine (AChR-Ab+).

Prevalence not well established but it is increasing due to improvements in suspecting and diagnosing MG.

Trademark: fluctuating weakness in specific muscle groups – such as bulbar weakness, limb weakness, and ocular weakness.

Ocular weakness - most common initial presentation of MG.

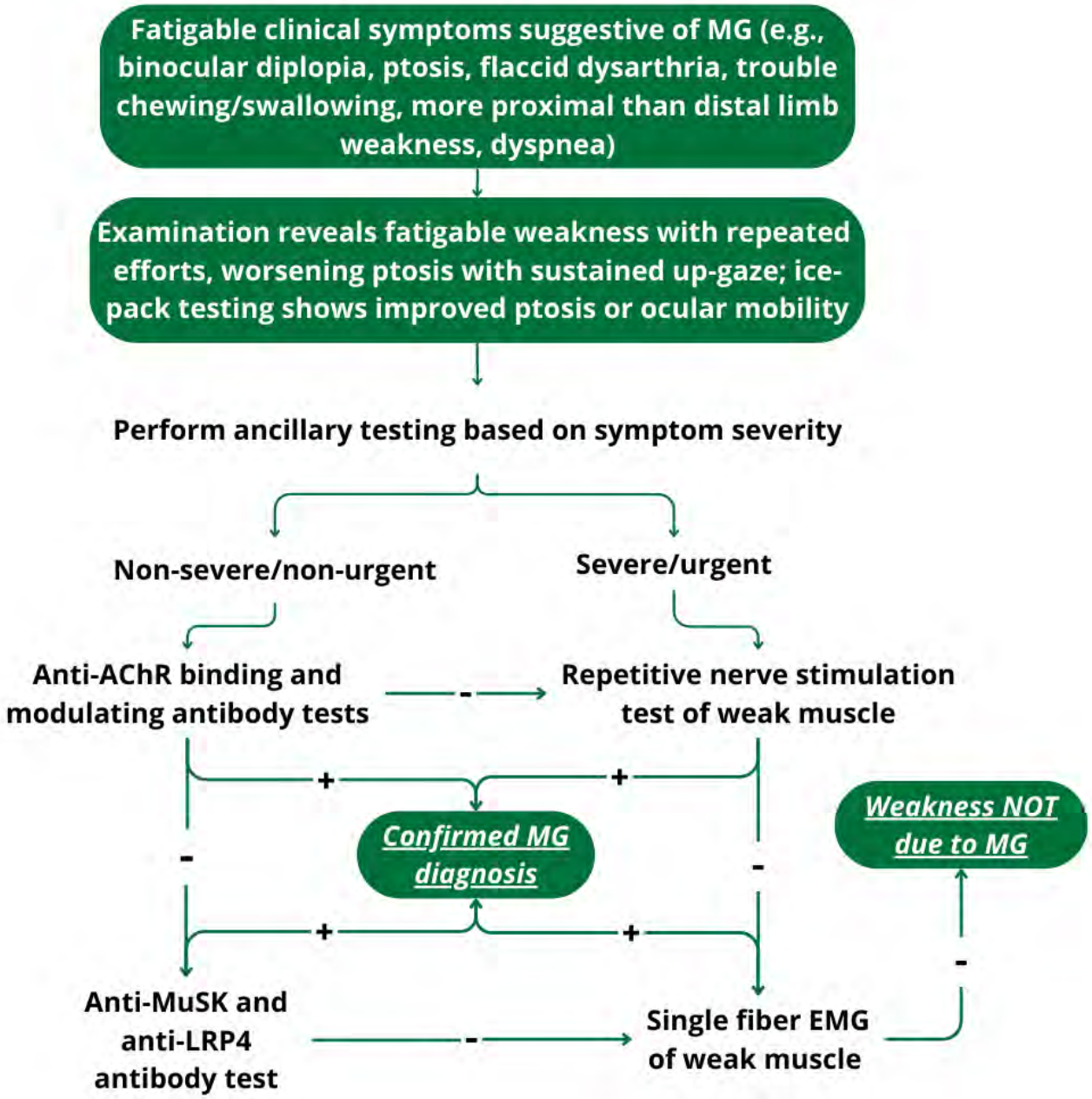
Treatment highly individualized and often includes off-label medications.

Five drugs approved by the FDA:

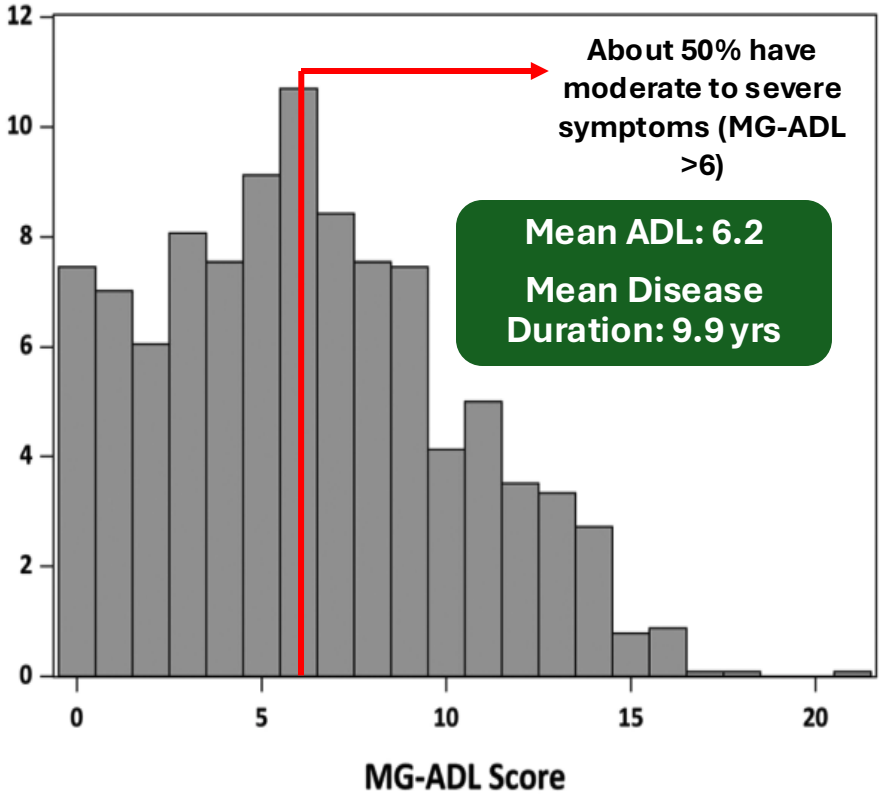
- Eculizumab (Complement)
- Efgartigimod (FcRn)
- Ravulizumab (Complement)
- Rozanolixizumab (FcRn)
- Zilucoplan (Complement)

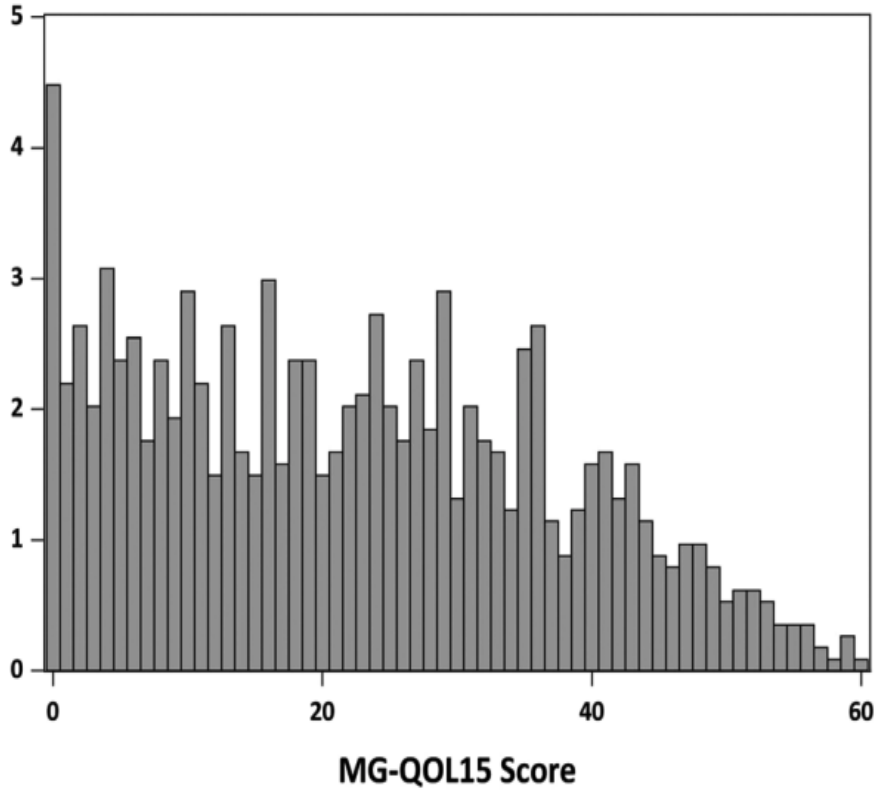
# Symptoms and Diagnosis

Figure adapted from Moreen JA, Li Y. *Cleveland Clin J Med. 2023; 90: 103-13. [creative* commons]



# Disease Burden




Distribution of MG-ADL (N=1138) and MG-QOL15 (N=1140) scores in patients in myasthenia gravis. The majority of patients reported moderate to severe impairment in activities of daily living.

Figures from Cutter G et al. *Muscle Nerve, 2019;* 60: 707-15. [creative commons]

# Immunopathogenesis and MG

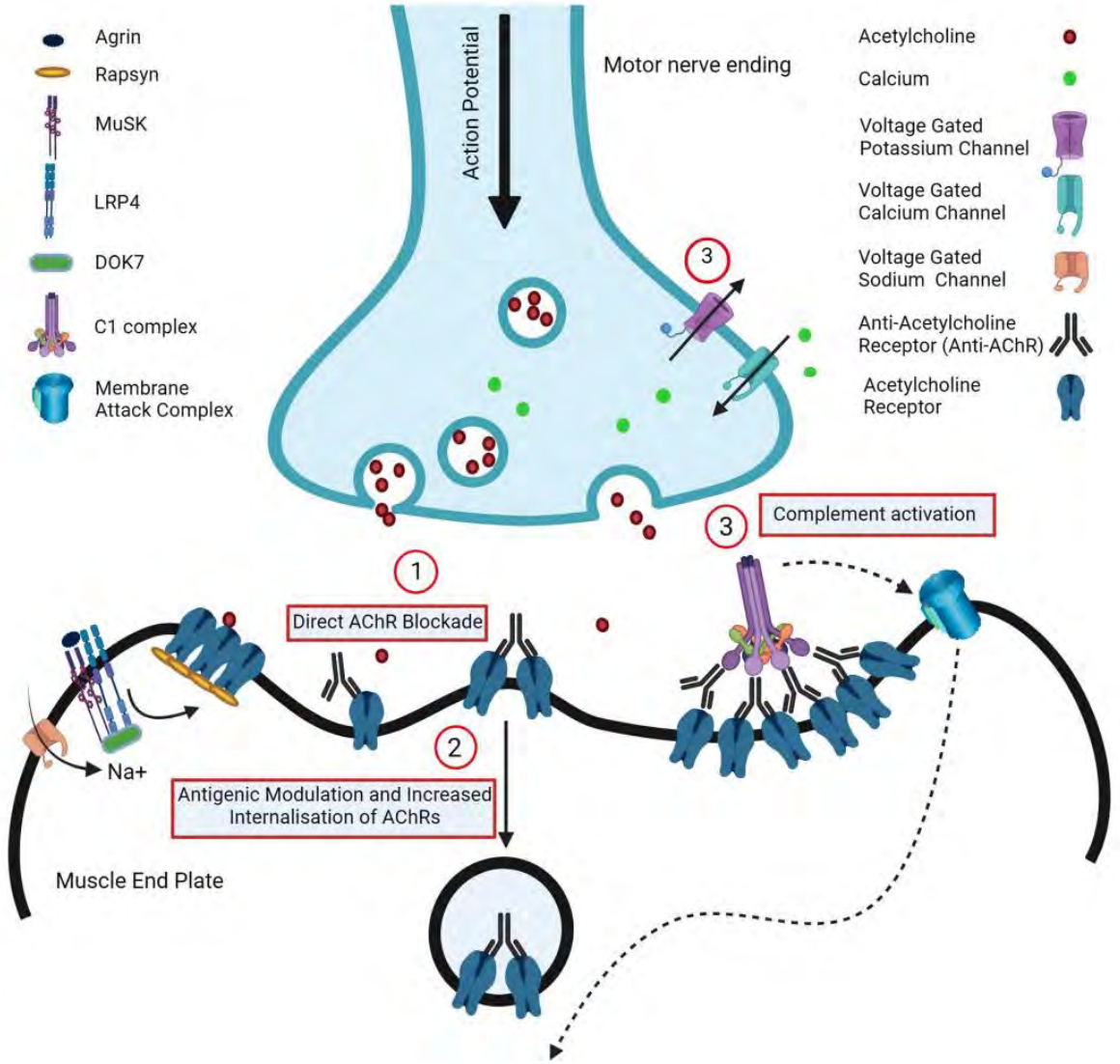



Figure from San PP, Jacob S. *Front Neurol.* 2023; 14: 1277596. [creative commons]

# FcRn and IgGs

- Endogenous IgG bind to FcRn and reduces IgG from entering lysosomes
- Abdegs (antibodies that enhance IgG degradation) bind to FcRn and prevent IgG-FcRn interactions – leading to increased IgG degradation in lysosomes

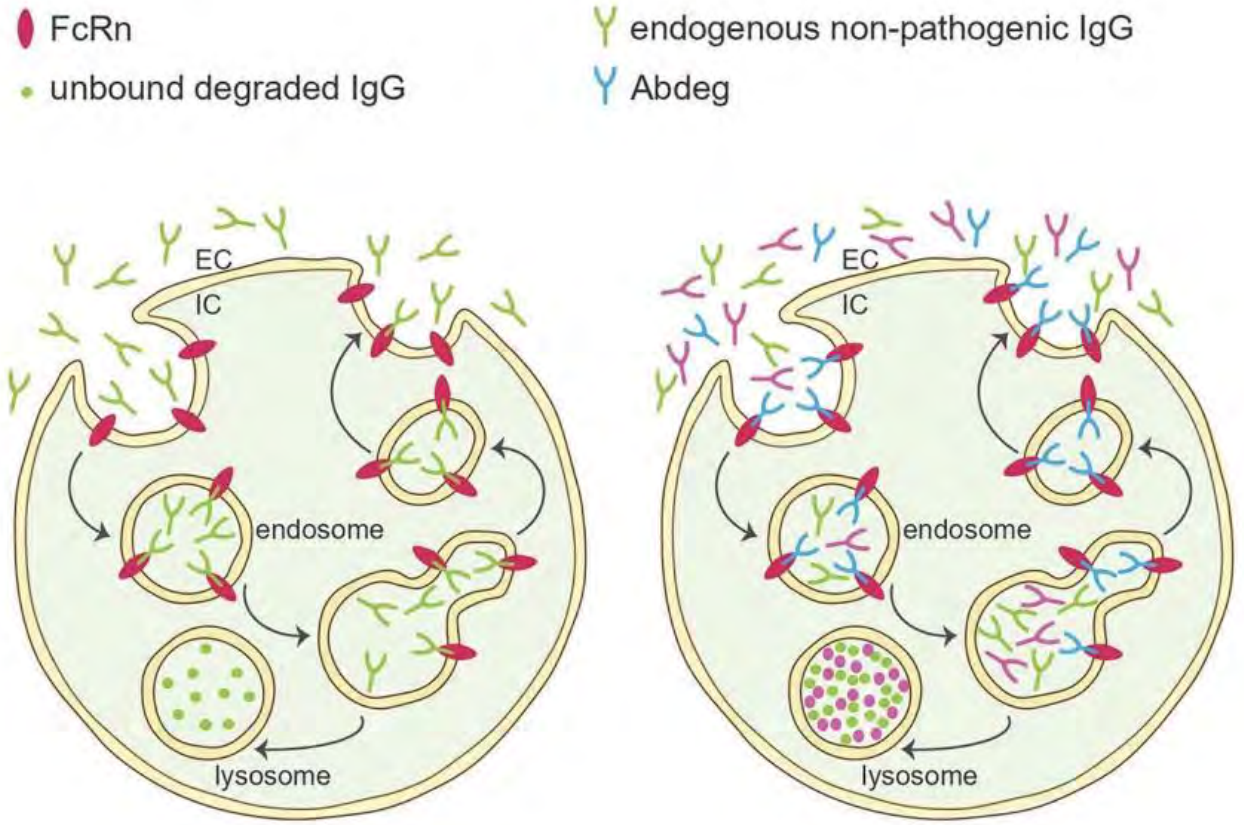



Figure from Nelke C et al. *Neurotherapeutic.* 2022; 19: 729-740. [creative commons]

# FcRn and IgGs (another view)

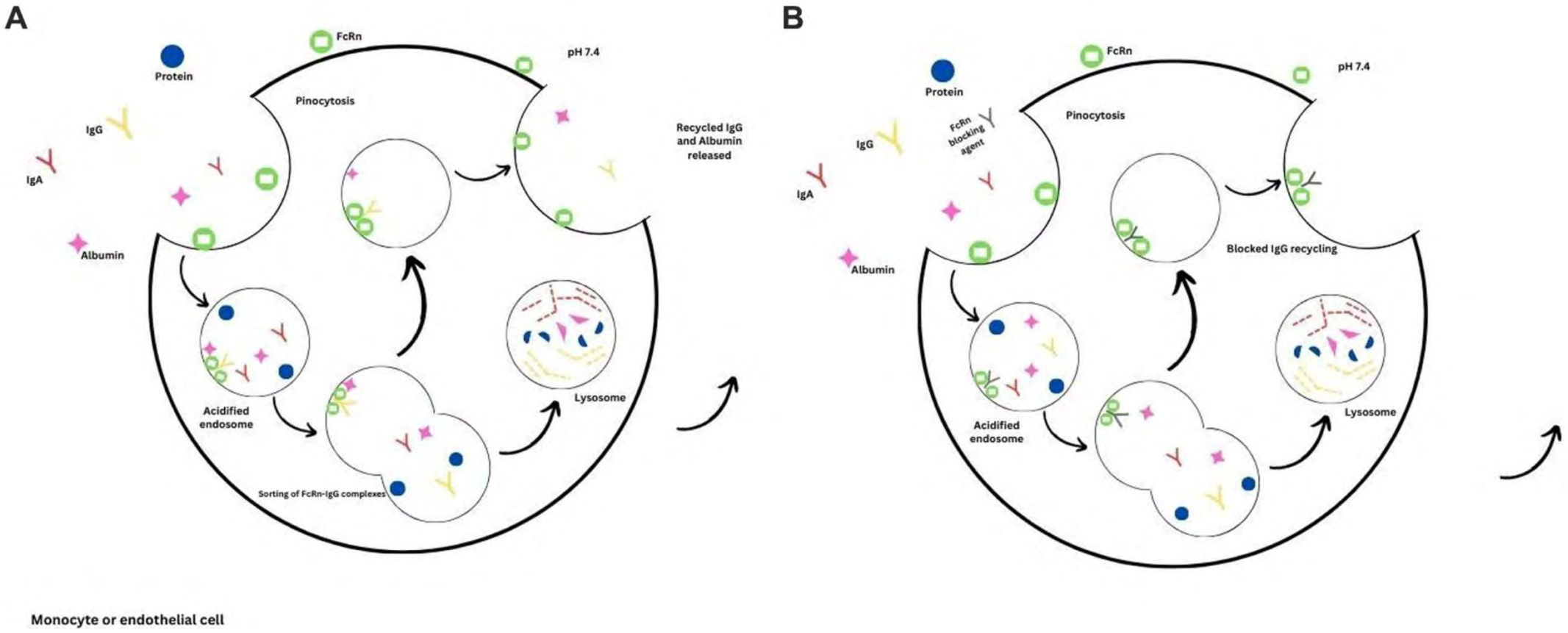
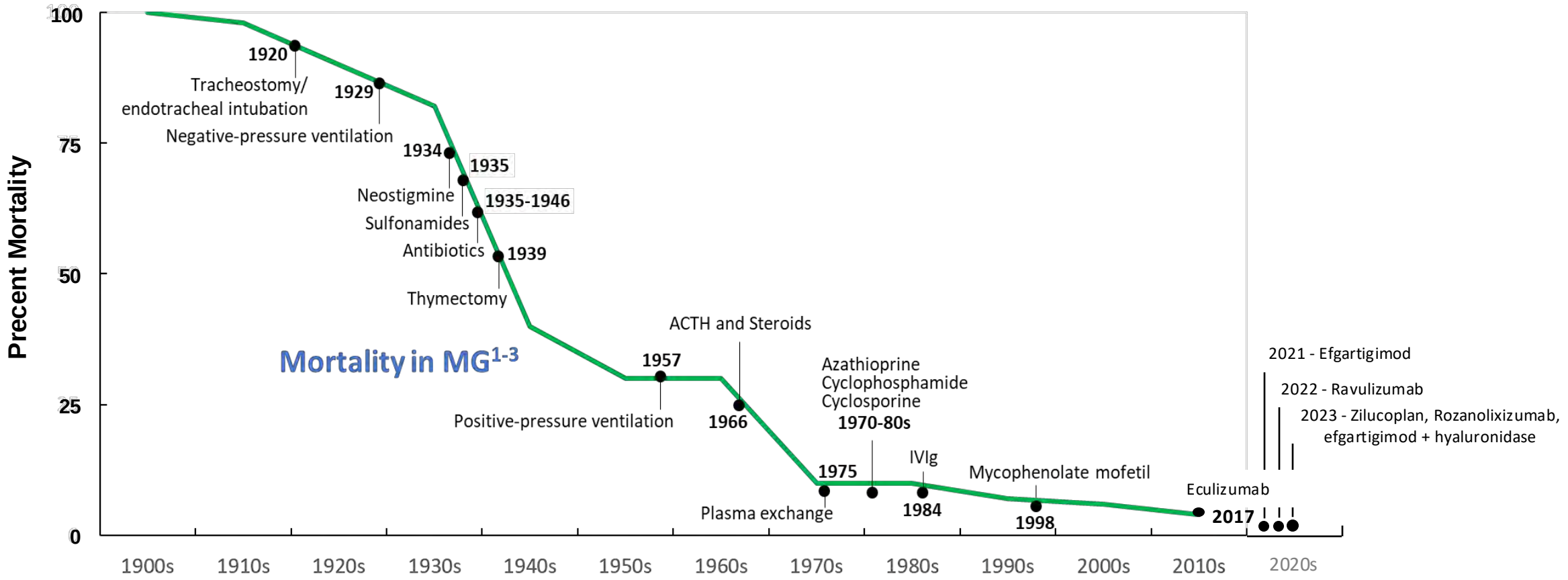



Figure from Bhandari V, Bril V. Front Neurosci. 2023; 14; *1229112*. [creative commons]

# History of Treatment Options




1. Mantegazza R, Antozzi C. *Ther Adv Neurol Disord.* 2018;11:1756285617749134. 2. Grob D, et al. *Muscle Nerve.* 2008;37:141-149. 3. Keesey JC. *Semin Neurol*. 2004;24(1):5-16.

# Clinical Pearls

- FcRn prevents IgG degradation.
- Blocking or reducing FcRn activity increases IgG degradation.
- Numerous therapies are approved and in development that attack FcRn to reduce pathologic levels of IgG associated with MG.