COVID19 and the MS patient

Tirisham Gyang MD
Assistant Clinical Professor

March 8th 2021

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Disclosure

- Personal compensation for consultation with EMD Serono and Genentech, unrelated to the topic of presentation

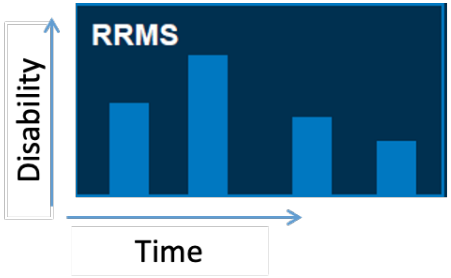
Outline

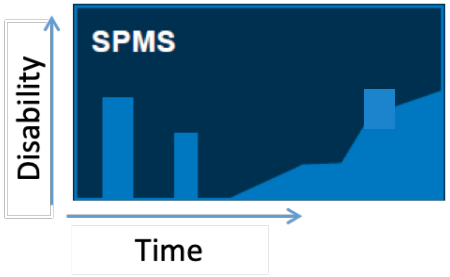
- Introduction to MS
- COVID19 pandemic
- COVID19 Vaccines
- COVID19 in MS
  - Risk factors
  - Impact on disease modifying therapies (DMT)
  - COVID19 vaccine in patients with MS

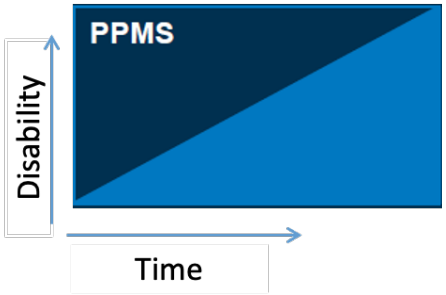
Multiple Sclerosis

- Most common inflammatory demyelinating disorder of the central nervous system (CNS)
- Second leading cause of disability in young adults

- MS phenotypes



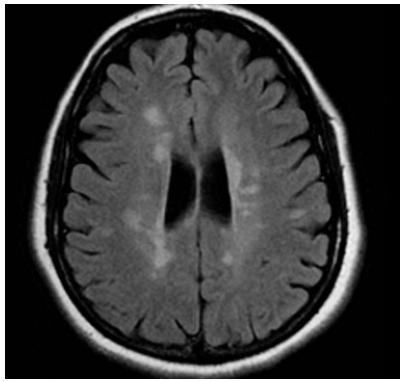


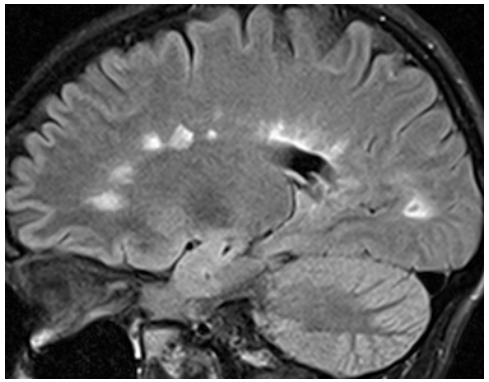


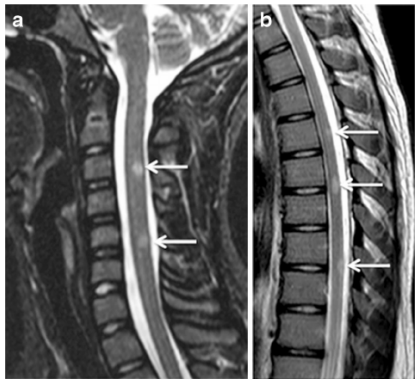
THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Diagnosis of MS

- Clinical symptoms
  - vision loss, weakness, numbness, walking difficulty, dizziness
- MRI scan – lesions in the brain, spinal cord or optic nerves
- Other tests - spinal tap, evoked potentials





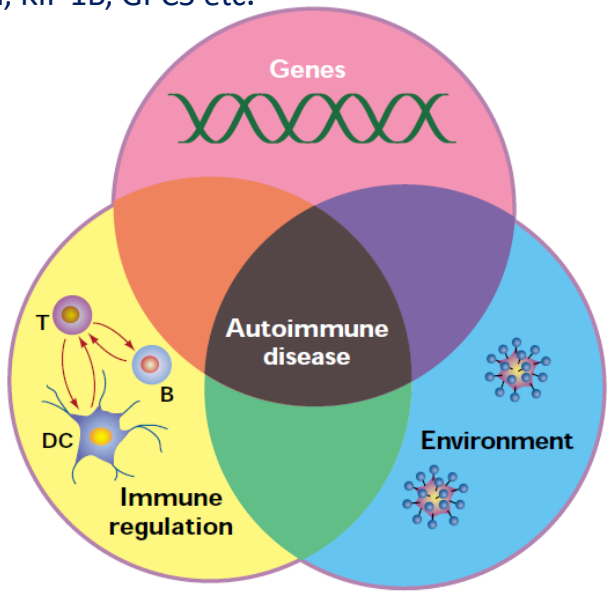


Etiology of MS

Over 200 immune gene SNPs are implicated in the risk of MS

- HLA-DR2, IL-2 receptor, IL-7 receptor, OAS1 polymorphism, AA genotype, CBLB in Sardinia, KIF 1B, GPC5 etc.

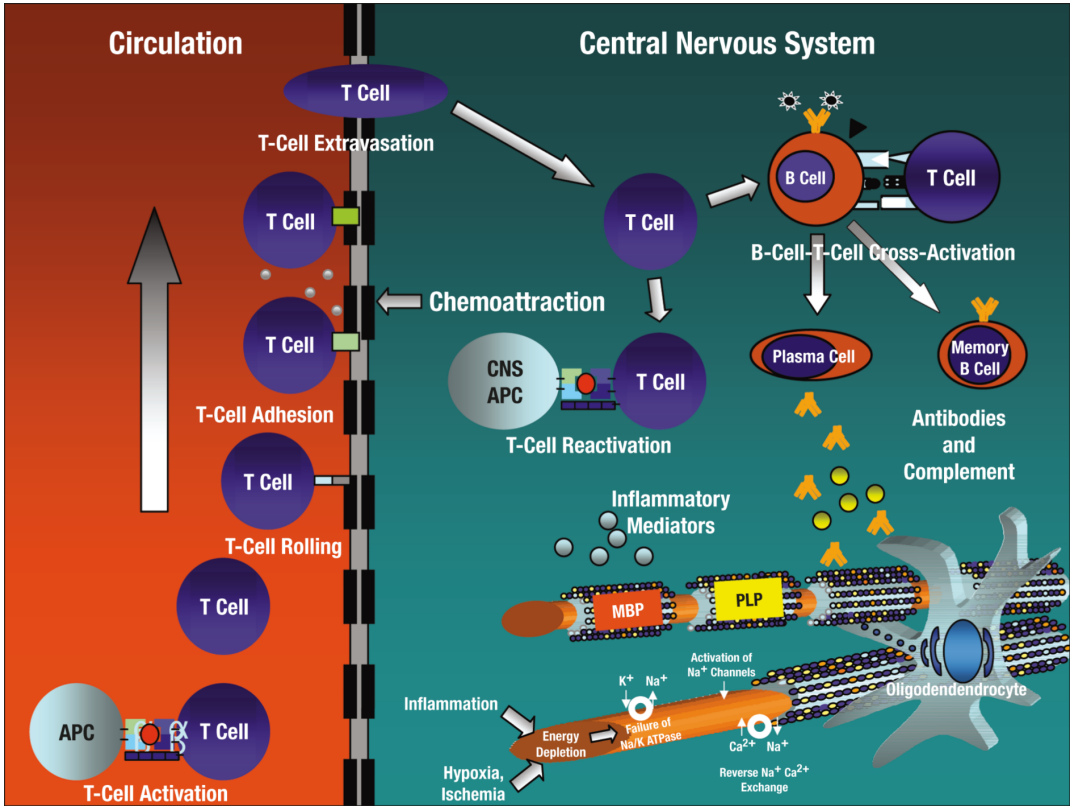
Immune dysregulation
- Innate and adaptive immune response



Latitude
Obesity
Microbial Agents
Viruses - EBV
Gut microbiome
Vitamin D
Smoking
High salt intake

Ermann J, Autoimmune diseases: genes, bugs and failed regulation. Nat Immunol. 2001 Sep;2(9):759-61.

Pathogenesis of MS

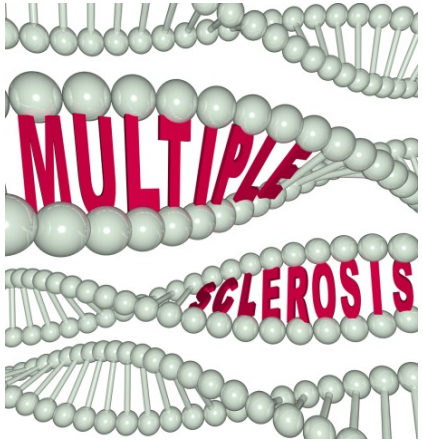


Frohman EM, et al. *Arch Neurol.* 2005;62(9):1345-1356

Epidemiology of MS

- Female to Male ratio (F:M)
  - Relapsing remitting MS – 3:1
  - Primary progressive MS – 1.2:1

- Mean age of MS onset
  - Relapsing remitting MS ~ 30 years
  - Primary progressive MS ~40 years



- Genetic susceptibility
  - HLA-DRB1*1501 haplotype
  - Concordance: monozygotic twins -30%, dizygotic twins- 5%
  - 20- to 40-fold increased risk of MS in first-degree relatives of patients with MS

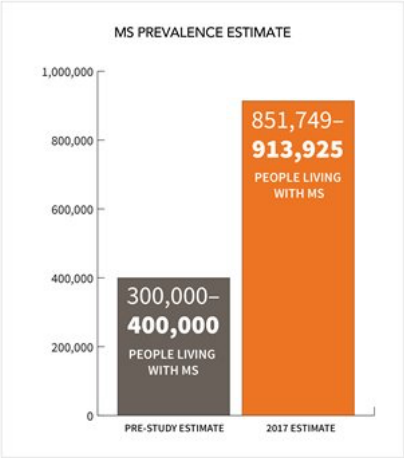
The prevalence of MS in the United States

A population-based estimate using health claims data

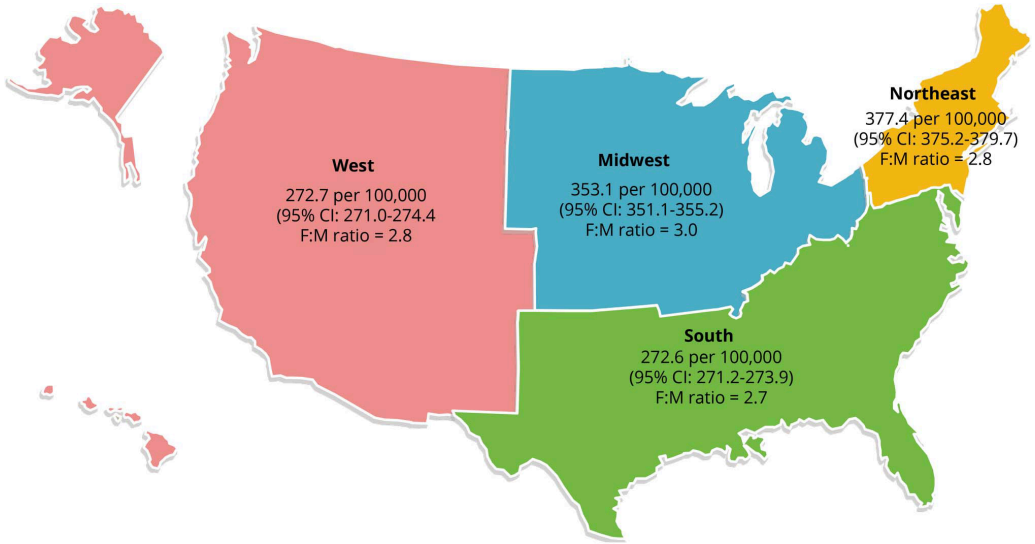
Mitchell T. Wallin, MD, MPH, William J. Culpepper, PhD, Jonathan D. Campbell, PhD, Lorene M. Nelson, PhD, Annette Langer-Gould, MD, PhD, Ruth Ann Marrie, MD, PhD, Gary R. Cutter, PhD, Wendy E. Kaye, PhD, Laurie Wagner, MPH, Helen Tremlett, PhD, Stephen L. Buka, ScD, Piyameth Dilokthornsakul, PharmD, PhD, Barbara Topol, MS, Lie H. Chen, DrPH, and Nicholas G. LaRocca, PhD, on behalf of the US Multiple Sclerosis Prevalence Workgroup

Correspondence
Dr. Wallin
mitchell.wallin@va.gov

Neurology® 2019;92:e1029-e1040. doi:10.1212/WNL.0000000000007035



Source: Wallin, Mitchell T. "The prevalence of MS in the United States: A population-based estimate using health claims data." *Neurology*. February 2019. *Neurology Journal* Web. http://n.neurology.org/lookup/doi/10.1212/WNL.0000000000007035



Wallin MT. The prevalance of MS in the United States.
Neurology. 2019 Mar 5;92(10)

Demographic distribution

- MS has been reported in most ethnic/racial groups
- Prevalence is highest in Caucasians of northern European ancestry
- **Growing incidence in ethnic minorities**
  - higher risk of MS than their ancestral countries of origin
  - higher risk of MS than previously thought

Table 1
Incidence of multiple sclerosis in diverse minority populations

Incidence of MS	Cohort	Period	Whites	African American	Hispanic	Asian	Native American
Langer-Gould	Kaiser Permanente Southern California	2008–2010	6.9	10.2	2.9	1.4	n/a
Wallin	US military-Veteran population	1990–2007, 2000–2007 for Hispanics	9.3	12.1	8.2	3.3	3.1

Rivas-Rodríguez E, Amezcua L. Neurol Clin. 2018 Feb;36(1):151-162

Disease modifying therapies

Interferon Beta
- Rebif
- Betaseron
- Avonex
- Plegridy

Glatiramer Acetate
- Copaxone
- Glatopa

Teriflunomide
- Aubagio

Fumarates
- Tecfidera
- Vumerity
- Bafietram

S1P1inhibitors
- Gilenya
- Mayzent
- Zeposia

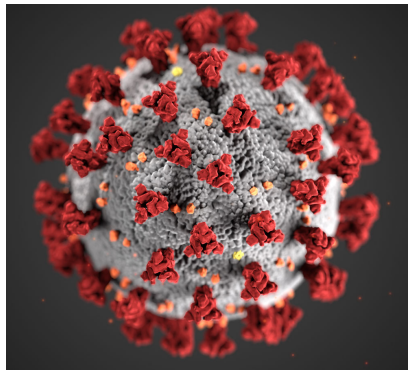
B cell depleting therapies
- Ocrevus
- Kesimpta
- Rituxan

Natalizumab
- Tysabri

Others
- Lemtrada
- Mavenclad

COVID 19 Pandemic

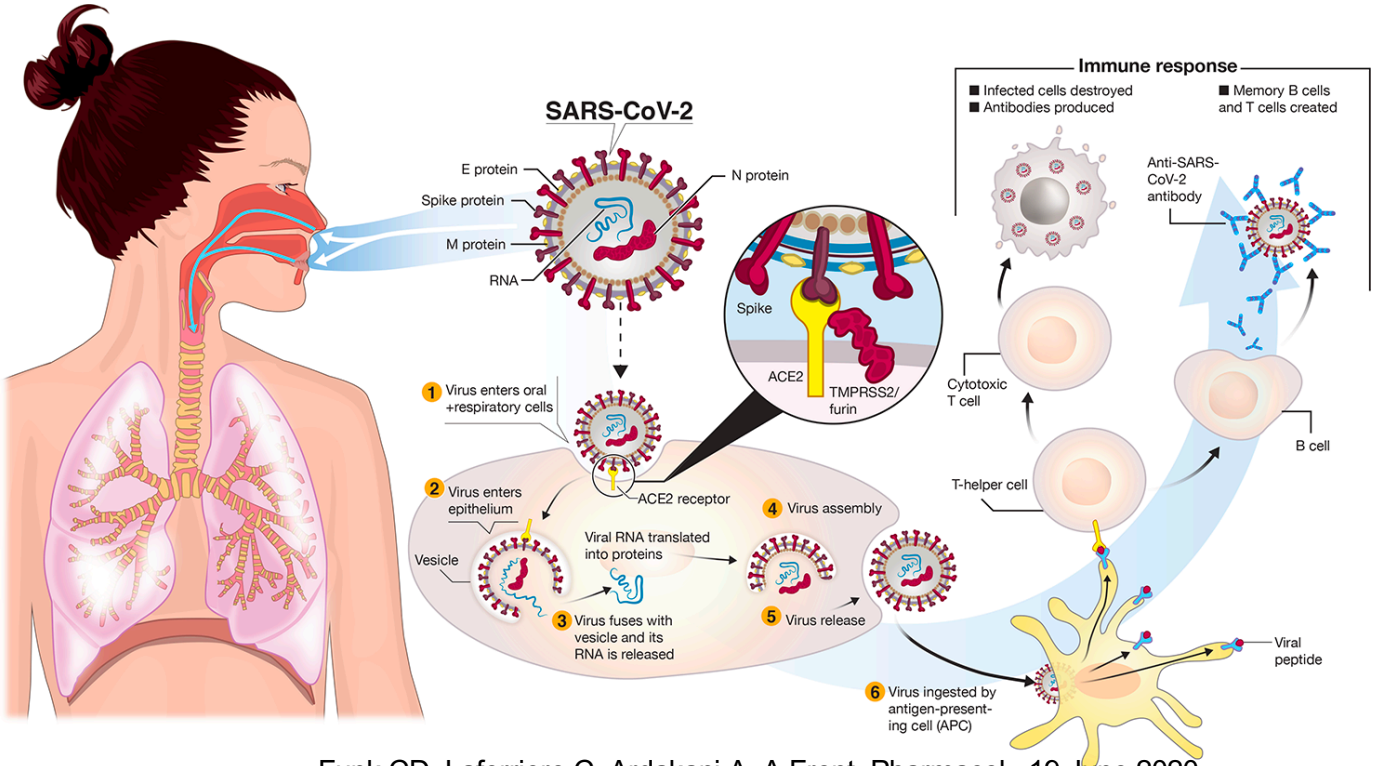
Subhead goes here



- Coronavirus disease 2019 (COVID19)
  - Caused by SARS-CoV-2
    - severe acute respiratory syndrome corona virus 2
- December 2019 – Hubie province, China
  - Zoonotic transfer – bats, pangolins
- Declared pandemic by WHO – March 7th, 2020
- In the US
  - over 500,000 deaths (as of February 26th 2021)

COVID19 – Pathogenesis

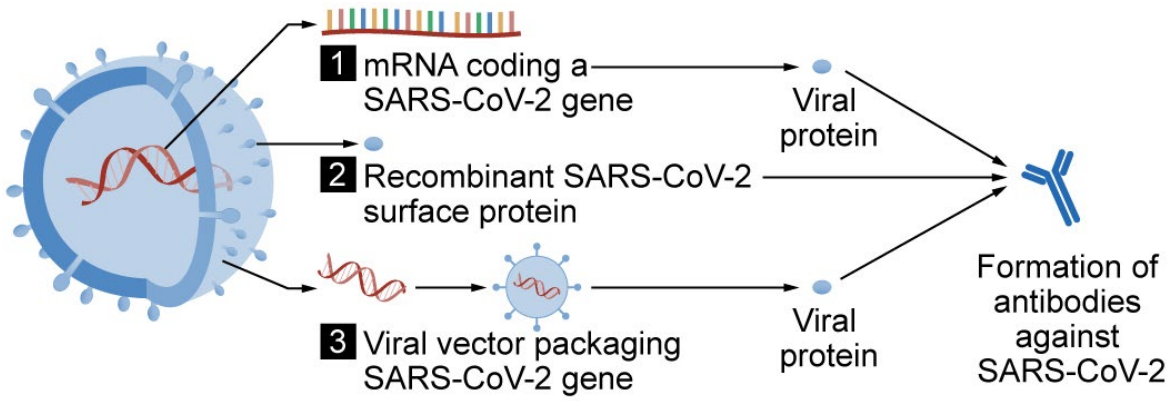
Viral Spike glycoprotein receptor binds to host cell angiotensin-converting enzyme 2 (ACE2)



Funk CD, Laferriere C, Ardakani A. A Front. Pharmacol., 19 June 2020

COVID19 vaccines

- Primary antigen – spike protein
- Pfizer, Moderna – mRNA vaccines
- Johnson & Johnson – viral vectored vaccine



Source: GAO. | GAO-20-583SP

COVID-19 Vaccines in the United States

Pfizer / BioNTech & Moderna Vaccines

- Emergency Use Authorization
- Non-Live mRNA Vaccines

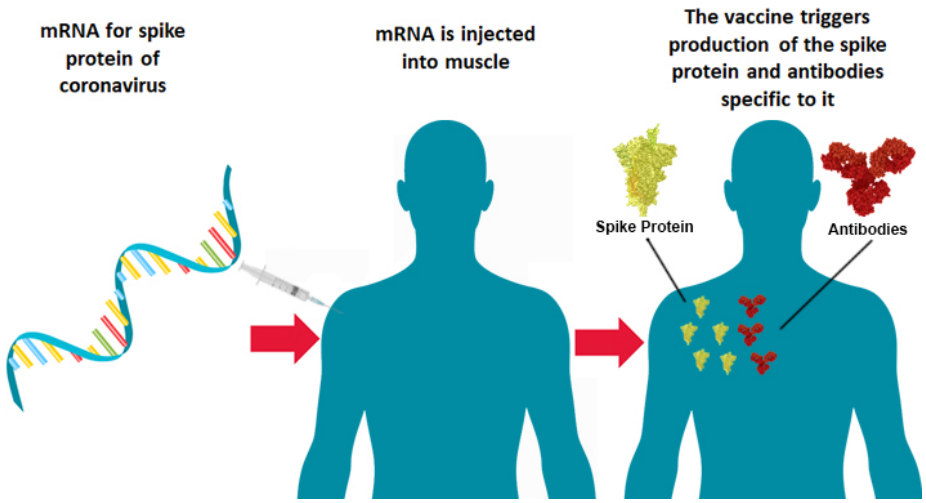


Image: NIH

COVID-19 Vaccines Clinical Studies

Pfizer / BioNTech & Moderna Vaccines

- Pfizer Participants: 43,548
- Moderna Participants: 30,420
- Included: age 16 and older who were healthy or had stable chronic conditions
- Excluded: previous COVID-19 infection, immunosuppressive medication or immunocompromising condition, pregnant and breast feeding women
- Study Outcomes: effectiveness and safety of two doses of COVID-19 vaccine to prevent confirmed cases of COVID-19 infection

MS and COVID19

- Many questions arise
  - Are MS patients at higher risk for COVID infection?
  - Is MS a risk factor for severe COVID19 infection?
  - Are there DMTs that increase the risk of COVID19 infection?
  - Should DMTs be stopped or switched to prevent infection
  - Should MS patients be given the COVID19 vaccine?
  - How will patients with MS respond to the COVID19 vaccine?
  - …..?

COVID19 in MS registries

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Risk of COVID19 infection in MS individuals

- The incidence of COVID 19 in MS population mirrors the general population
- Simply having MS does increase the risk for COVID-19 infection
- UK MS registry (5,309 subjects)
  - No association was found between disease modifying treatment, MS disease duration or degree of disability and the likelihood of contracting COVID19

Factors associated with severe infection

- The risk of severe outcomes from COVID-19 infection in patients with MS also mirrors the general population

- *COVISEP French study* (347 subjects)
  - Patients with more severe infection (hospitalization) were older, more neurologically disabled, more likely to be obese
  - No association between severity of disease with DMT exposure

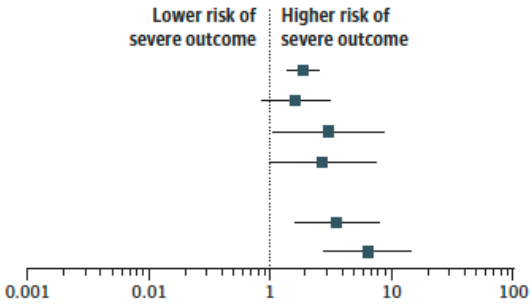
- *COViMS N. American Registry* (858 patients):
  - African American (AA) MS patients had a 3-fold higher risk for ICU admission or mortality compared with non-Hispanic white MS patients after adjusting for co-variates
  - AA patients were younger and more likely to have comorbidities than White MS patients

JAMA Neurology | Original Investigation

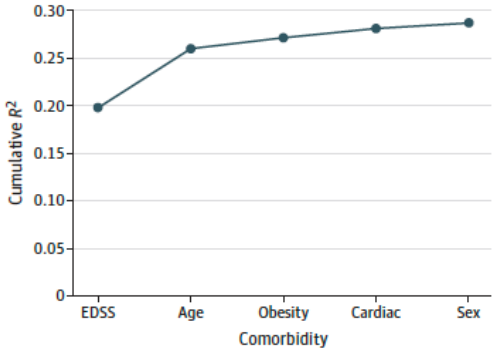
Clinical Characteristics and Outcomes in Patients With Coronavirus Disease 2019 and Multiple Sclerosis

B Multivariate analysis

Group	OR (95% CI)
Age per 10 y	1.85 (1.39-2.46)
Male	1.61 (0.83-3.11)
Obesity	2.99 (1.03-8.70)
Cardiac comorbidity	2.68 (0.97-7.40)
EDSS <3	NA
EDSS 3-5.5	3.48 (1.55-7.84)
EDSS ≥6	6.33 (2.78-14.39)



C Cumulative variability of severe COVID-19



DMTs and COVID19 severity

- UK MS registry (5,309 subjects)
  - No association was found between disease modifying treatment, MS disease duration or degree of disability and the likelihood of contracting COVID19

- *COVISEP French study* (347 subjects):
  - Most of the severe COVID19 infections occurred in patient on no treatment.
  - Some severe cases occurred in patients on teriflunomide or rituximab.
  - Patients on injectable DMTs had a lower risk of severe COVID19 than untreated patients.

DMTs and COVID19 severity

- *MuSC-19 Italian study* (784 subjects):
  - Over-representation of MS patients on ocrelizumab in the MS COVID19 cohort and under-representation of patients on IFNβ.
  - Patients on rituximab and ocrelizumab had a 2.7x higher likelihood of severe COVID19 versus patients on dimethylfumarate.

- *COVID19 & MS Global Data Sharing Initiative* (1,540 subjects):
  - Compared to other DMTs, Rituximab was associated with higher rates of hospitalization, ICU admission and mechanical ventilation, but not death,
  - Ocrelizumab showed similar trends but of lesser magnitude

Vaccination response and DMTs

- Based on studies on the prior vaccines, certain DMTs may affect the response to vaccinations

- S1P1 modulators – Fingolimod, Siponimod and Ozanimod
  - Fingolimod – reduced the response to several vaccines
    - Tetanus toxoid, influenza and H1N1 vaccines

- B cell depleting therapies – Ocrelizumab, Rituximab, Ofatumumab
  - Ocrelizumab and Rituximab – significantly affected the response to several vaccines – flu, pneumococcal, KLH

Vaccination response and DMTs

- Vaccine responses were reduced to varying degrees in those treated with glatiramer acetate, teriflunomide, and natalizumab.
  - Glatiramer acetate (GA) – Copaxone, Glatopa
    - In studies, patients on GA had similar response to healthy controls to the influenza vaccine
    - In one study, patients treated with GA had lower response rates than patients on interferon beta
  - Teriflunomide – Aubagio
    - In some studies, patients treated with Aubagio had mildly reduced response to the influenza vaccine
    - Aubagio may have a modest negative effect on the effectiveness of vaccines.

Disease modifying therapies

Interferon Beta
- Rebif
- Betaseron
- Avonex
- Plegridy

Glatiramer Acetate
- Copaxone
- Glatopa

Teriflunomide
- Aubagio

Fumarates
- Tecfidera
- Vumerity
- Bafietram

S1P1inhibitors
- Gilenya
- Mayzent
- Zeposia

B cell depleting therapies
- Ocrevus
- Kesimpta
- Rituxan

Natalizumab
- Tysabri

Others
- Lemtrada
- Mavenclad

National MS Society

Recommendations/guidelines for COVID19 vaccine

National Multiple Sclerosis Society

- Based on expert consensus and available data
  - Pfizer BioNTech and Moderna vaccines are safe for people with MS and they are safe to use with MS DMTs
  - Most DMTs are not expected to affect the responses to the Pfizer BioNTech or Moderna vaccines

- Given the potential serious health consequences of COVID-19 disease, getting the vaccine when it becomes available to you may be more important than optimally timing the vaccine with your DMT

Timing of the vaccine

National Multiple Sclerosis Society

- Rituximab and ocrelizumab
  - Initiation – get vaccine at least 4 weeks before starting these therapies
  - Already on therapy – get vaccine 12 weeks or more from last infusion and at least 4 weeks before next infusion

- Ofatumumab
  - Initiation – complete vaccine at least 4 weeks before starting therapy
  - Already on therapy – resume therapy at least 4 weeks or more following the second vaccine injection

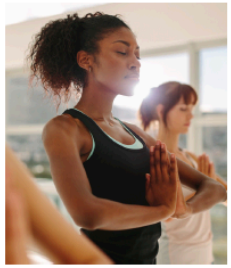
Timing of the vaccine

- Fingolimod, Siponimod and Ozanimod (S1P1 inhibitors)
  - Initiation – wait at least 4 weeks after vaccine completion to start therapy
  - Already on therapy – get vaccine once available without changing dosing
- All other DMTs
  - No change in dosing of DMT
  - No delay in starting vaccine
- High dose steroids
  - Wait 3-5 days after steroids before getting vaccine

Contact information

- Misty Green
  - 614-293-6486
  - Misty.green@osumc.edu
- Contact your provider
  - mychart
- Neurology clinic
  - 614-293-4969

THE OHIO STATE UNIVERSITY WEXNER MEDICAL CENTER



Multiple Sclerosis and the COVID19 vaccine

- Do you have multiple sclerosis (MS) or a similar disorder like neuromyelitis optica (NMO) or MOG-antibody related disorder?
- You may qualify for an interesting study with the OSU MS center.

The Ohio State Department of Neurology is currently enrolling for a research study to determine the effectiveness of the COVID19 vaccine in patients with MS and similar diseases.

YOU MAY QUALIFY IF:

- You are age 18 years and above
- You have a diagnosis of MS, NMO or MOG-antibody related disorder
- You plan on taking the COVID19 vaccine when it becomes available

Participants will have blood samples taken before and after they receive the COVID19 vaccine.

For more information, please call 614-293-6486 or email misty.green@osumc.edu

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Summary

- MS by itself is not a risk factor for COVID19 infection
- Risks of COVID19 severity is similar in MS patients as with the general population
- Some DMTs may affects the response to the COVID19 vaccinations
- General guidelines recommend giving the vaccine to individuals with MS to avoid infection

References

- Funk CD, Laferriere C, Ardakani A. **A Snapshot of the Global Race for Vaccines Targeting SARS-CoV-2 and the COVID-19 Pandemic.** Front. Pharmacol., 19 June 2020
- Louapre C, Collongues N, Stankoff B, et al. Clinical Characteristics and Outcomes in Patients With Coronavirus Disease 2019 and Multiple Sclerosis. JAMA Neurol. 2020 Sep 1;77(9):1079-1088. doi: 10.1001/jamaneurol.2020.2581.
- Salta A, Cutter G, Fox R, et al. Comparison of COVID-19 outcomes between racial groups in the COViMS registry. MS Virtual 2020. SS02.20

Thank You

wexnermedical.osu.edu