COVID-19, vaccination and MS

DR.SAADAT

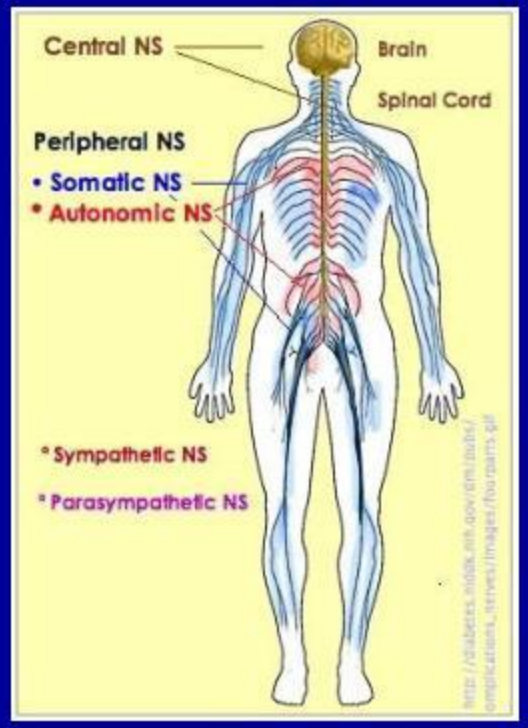
ASSOCIATE PROFESSOR OF NEUROLOGY

What is Multiple Sclerosis?

- Multiple Sclerosis (MS) is an chronic inflammatory demyelinating disease of the brain and spinal cord.

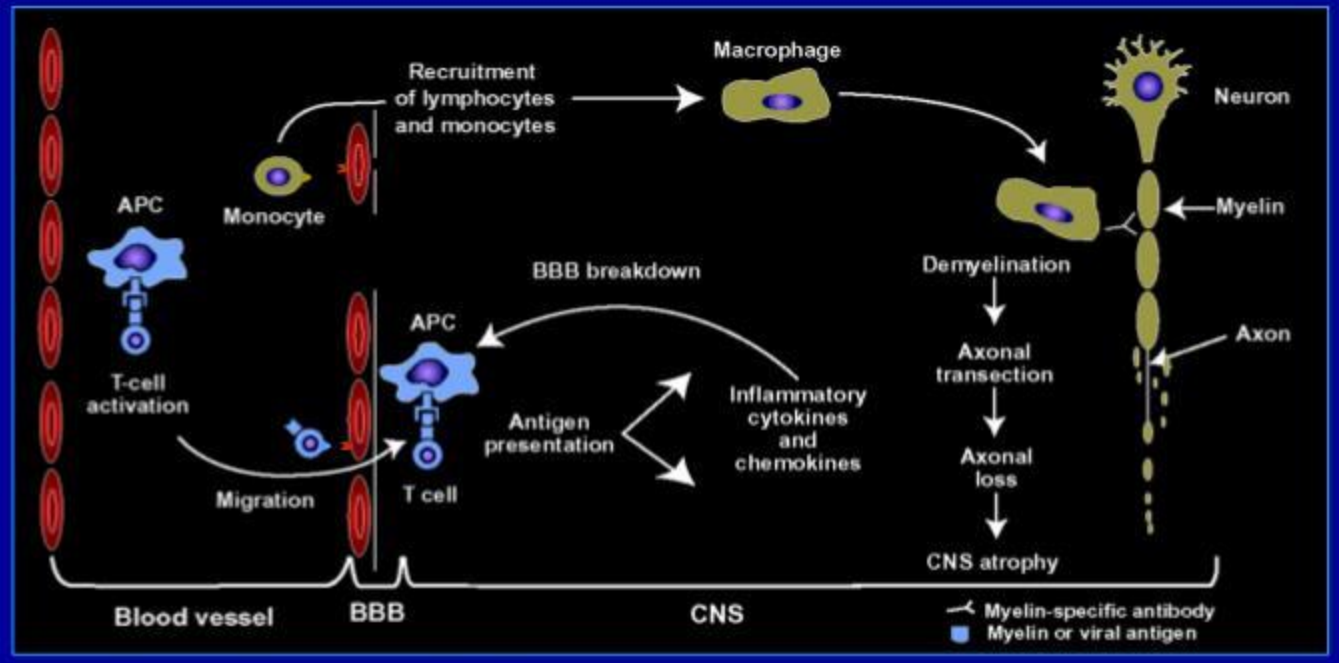
The Human Nervous System

- Areas affected by MS
  - Brain
  - Spinal cord
  - Optic nerves



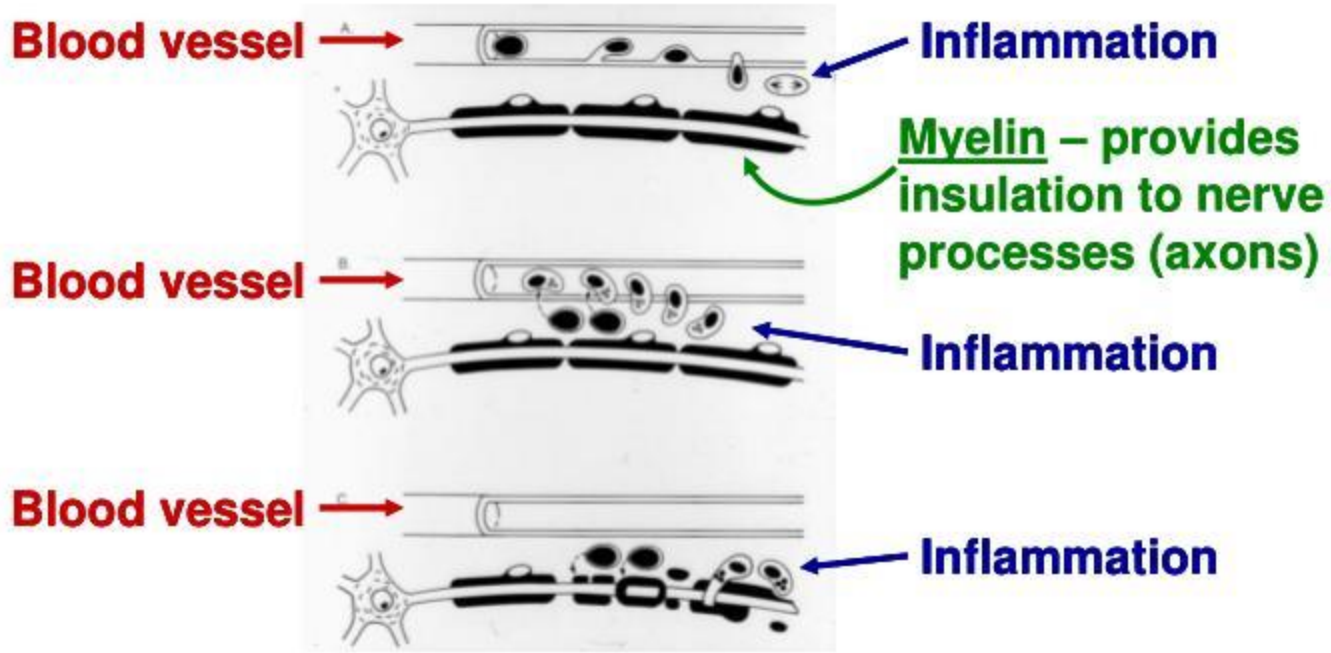
(http://web.lemoyne.edu/~hevern/psy340/lectures/psy340.04.2.ns.structure.html)

MS is an Immune-Mediated Disease



BBB=blood-brain barrier; APC=antigen-presenting cell.
Adapted from Miller et al. *Continuum: Multiple Sclerosis (Part A).* 1999;5:7.

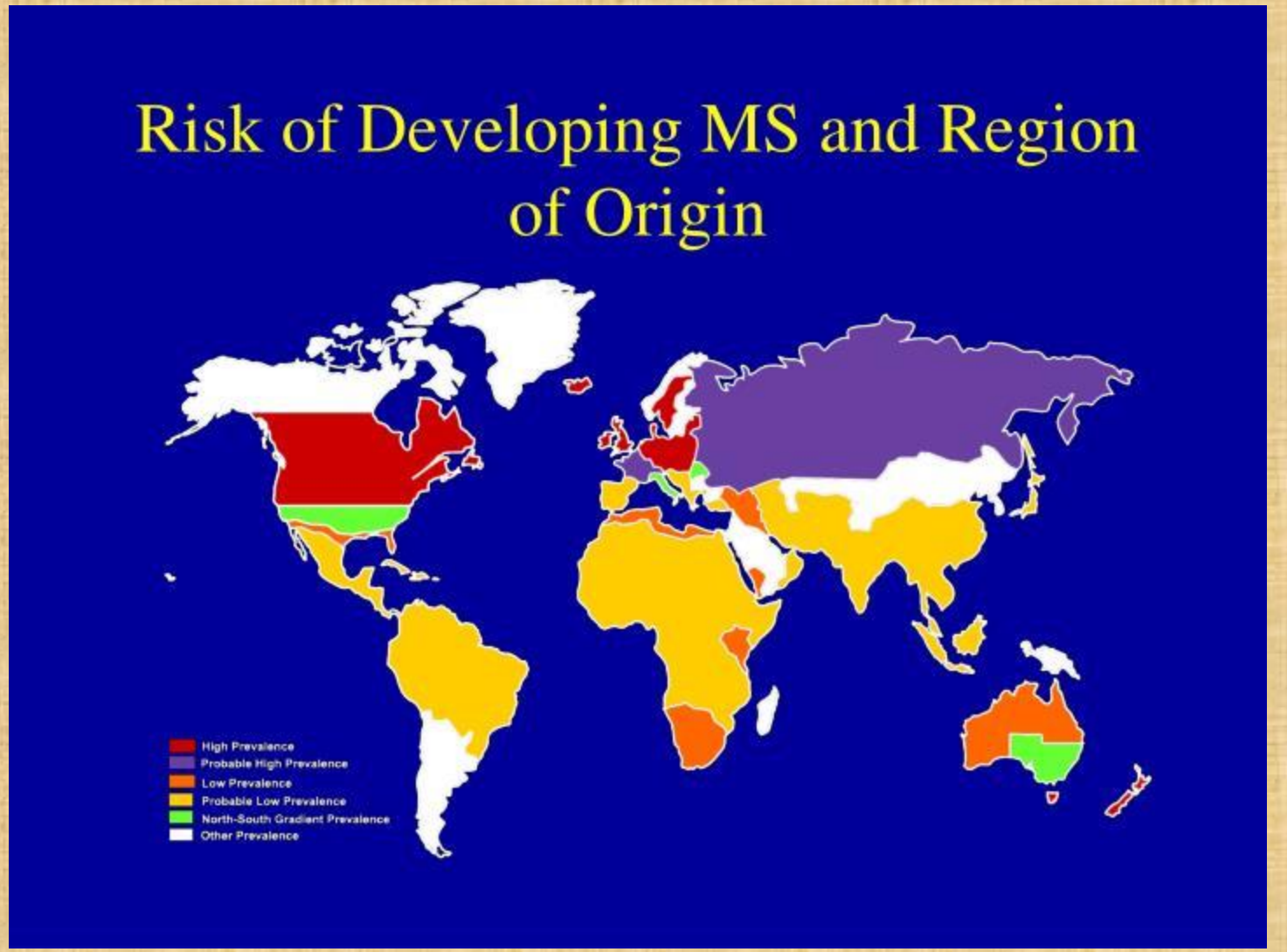
MS is a Demyelinating Disease



How Common is MS and Who Gets It?

- 8,000 – 10,000 new cases are diagnosed annually
- Affects nearly 500,000 individuals in the U.S.
- Occurs most frequently between ages 25 - 35
- Female: male ratio = 2:1
- More frequent in populations native to areas further away from the equator

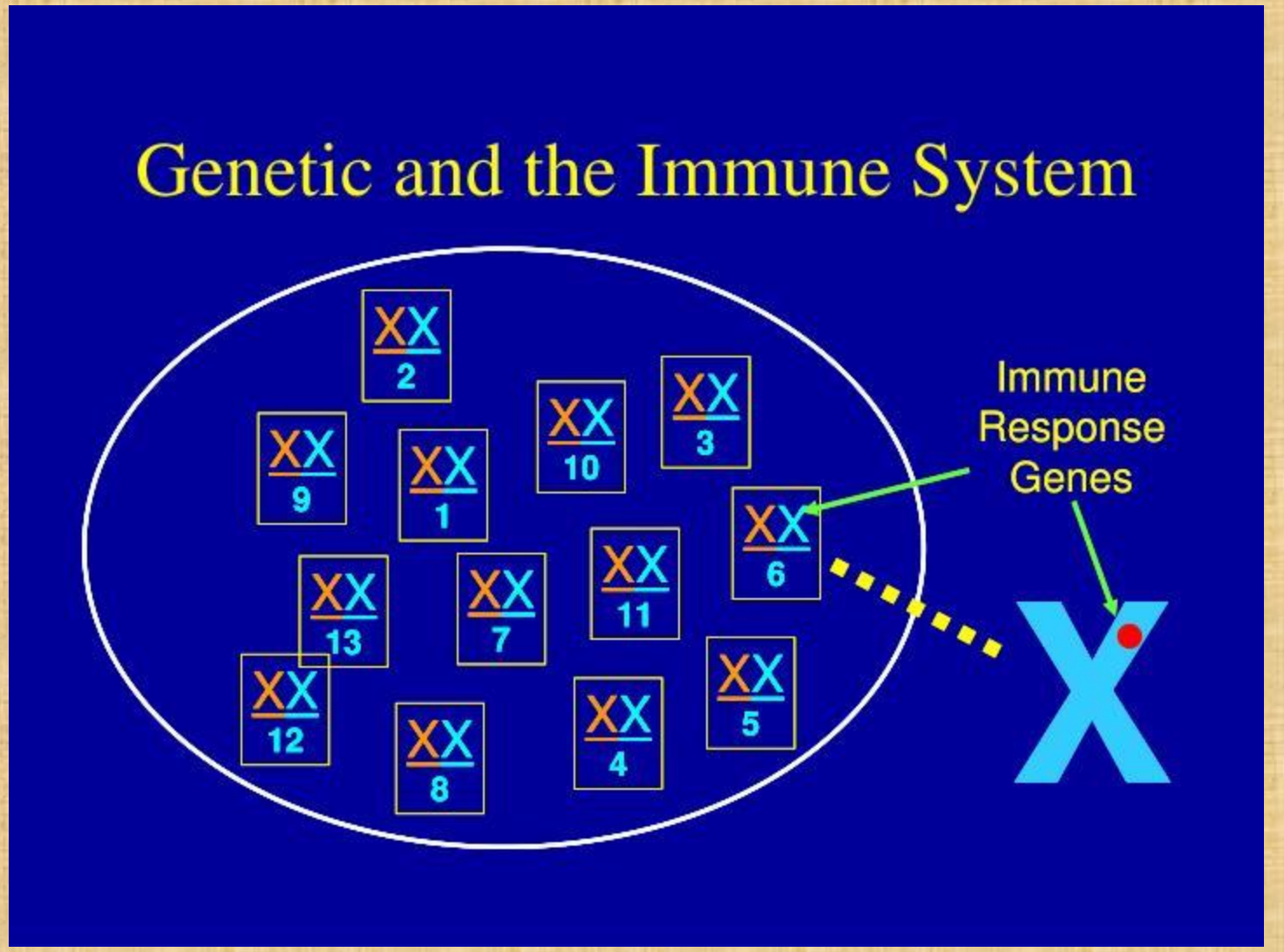
Risk of Developing MS and Region of Origin



What Causes MS?

- Genetics
- Environmental factors

Genetic and the Immune System



Family Studies

Up to 19% of patients have an affected relative

• Monozygotic (identical) twins	25 – 30%
• Dizygotic (non-identical) twins	3 – 4.5%
• Child of parent with MS	1.9%
• Sibling of person with MS	0.9%

Not Everyone with a Genetic Risk Will Develop MS – Why?

- Risk is modified by Environmental factors
  - Sunlight
  - Diet (e.g., vitamin D)
  - Other lifetime experiences (infections?)

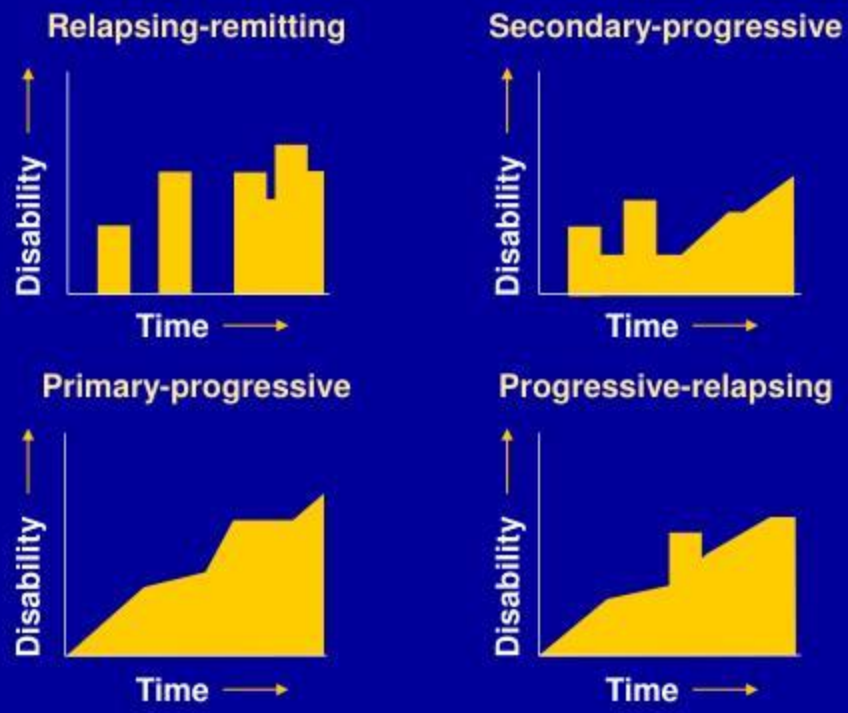
Initial Presentation of MS

	Incidence (%)
Optic nerve inflammation	14–29
Poor balance (ataxia)	2–18
Dizziness (vertigo)	2–9
Weakness	10–40
Double visions (diplopia)	8–18
Bladder, bowel dysfunction	0–14
Pain	21–40
Sensory loss	13–39

Other Common Symptoms of MS

- Fatigue
- Spasticity
- Sexual dysfunction
- Cognitive impairment
  - –Generally occurs later in the disease

Multiple Sclerosis Clinical Subtypes



Lublin FD et al. *Neurology*. 1996;46:907-911.

How Is MS Diagnosed?

- At least two episodes of symptoms
  - Occur at different points in time
  - Result from involvement of different areas of the central nervous system
- Absence of other treatable causes for the symptoms
- Results of neurological testing

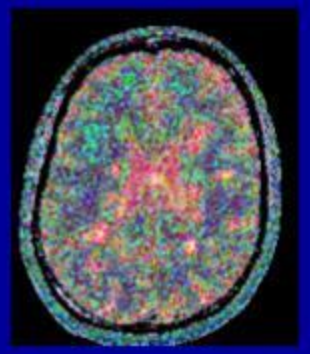
Other Potential Causes of MS-like Symptoms

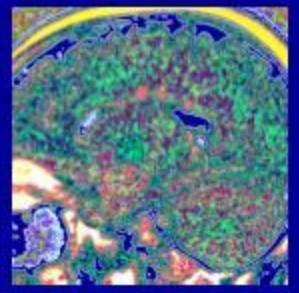
- Lyme disease
- Lupus
- Migraine
- Non-recurrent inflammatory process
- Encephalitis
- Stroke
- Tumor of the brain or spinal cord

How Is MS Diagnosed?

- Neurological examination
- Magnetic resonance imaging (MRI) Scan
- Blood tests
- Lumbar Puncture (spinal tap): occasionally performed
- Other testing: infrequently performed

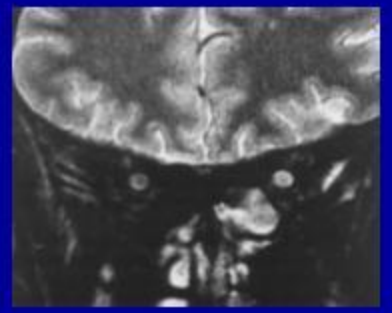
Magnetic Resonance Imaging in MS





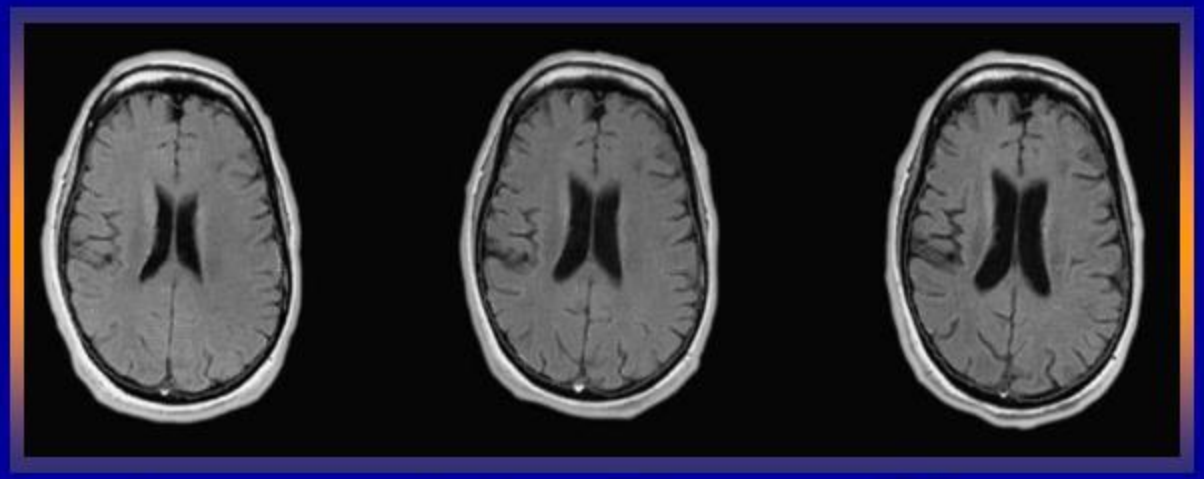
Brain

Spinal cord



Optic nerve

Brain Atrophy (Shrinkage) in Untreated MS



Images acquired over the course of 7 years
from a single person with untreated MS

How is MS Treated and Managed?

- Drug therapy
  - Treat new attacks (exacerbations)
  - Prevent the occurrence of future attacks
  - Slow or prevent disease progression
  - Treat the chronic symptoms of the disease
- Physical therapy
- Psychosocial support

Treatment of New MS Exacerbations

- Drug therapy
  - Corticosteroids
  - Intravenous immunoglobulin
  - Plasma exchange
- Physical therapy

Prevention of Future Attacks and Disease Progression

- Immune modulating drugs
  - Beta-Interferon
  - Glatiramer acetate
  - Humanized monoclonal antibodies
- Immunosuppressant drugs
  - Anti-cancer agents
- Combination therapies

Symptom Management – Examples

- Pain control
- Management of impaired bladder and bowel function
- Anti-spasmodic drugs
- Treatment of fatigue
- Splinting for contractures
- Counseling

MS Therapies: What Lies Ahead?

- Neural protection
- Regenerative therapies
- Cell replacement (stem cells)
- Dietary approaches (vitamin D)

Timing MS Medications with COVID-19 Vaccines

The Pfizer BioNTech, Moderna and Janssen/J&J vaccines are safe for people with MS, and they are safe to use with MS DMTs. The vaccines are not likely to trigger an MS relapse or have any impact on long-term disease progression. The risks of COVID infection far outweigh any potential vaccine risk, and persons with MS are encouraged to get the vaccine as soon as possible. Most DMTs are not expected to affect the responses to these vaccines, though some may make the vaccines less effective. Coordinating the timing of vaccine administration with these DMTs may provide the best vaccine response.

Given the potential serious health consequences of COVID-19, getting the vaccine as soon as possible may be more important than optimally timing the vaccine with DMT.

The decision of when to get the COVID-19 vaccine should include an evaluation of risk of COVID-19, including occupation, and the current state of MS. If the risk of MS worsening outweighs or is equal to risk of COVID-19, do not alter DMT schedule and get the vaccine as soon as possible. If MS is stable, consider the following adjustments in the administration of DMT to enhance the effectiveness of the vaccine:

Beta interferons (Avonex, Betaseron, Extavia, Plegridy, Rebif), any glatiramer acetate (Copaxone, Glatopa and generic glatiramer), Aubagio, Bafiertam, generic dimethyl fumarate, Tecfidera, Vumerity, and Tysabri

Do not delay starting one of these medicines for vaccine injection. If you are already taking one of these DMTs, no adjustments of your DMT administration are recommended.

Interferons:

With reference to regional recommendations, live vaccines are not contraindicated during therapy with interferon-ß preparations, but a risk–benefit assessment should be carried out.Regarding inactivated vaccines, there is no increased risk in view of the mode of action. Concerning vaccine efficacy, the immune response to an influenza vaccine in patients with MS did not differ from controls. Overall, based on the comparability of inactivated vaccines and gene-based vaccines, no heightened risk is expected with mRNA as well as non-replicating viral vector vaccines and a comparable immune response can be assumed.

Glatiramer acetate:

There is no contraindication for live vaccines during glatiramer acetate treatment, but a risk–benefit assessment is required. Concerning inactivated vaccines, a similar immune response after vaccination compared with controls could be shown. Overall, no increased risk is expected with mRNA and non-replicating viral vector vaccines as it is also the case for inactivated vaccines.

Dimethyl fumarate:

Based on regional recommendations, there is no absolute contraindication for live vaccines during therapy with dimethyl fumarate (DMF). Overall, given the mechanism of action of both inactivated and gene-based vaccines, no increased risk is therefore expected with mRNA and non-replicating viral vector vaccines.

Teriflunomide:

Live vaccines are contraindicated during treatment with teriflunomide and according to the prescribing information for at least 6 months after the end of therapy. However, if necessary, a washout with active carbon (50 g four times daily for 11 days) or cholestyramine (8 g three times daily for 11 days) can be performed. Regardless of the washout procedure, a subsequent check of the plasma level by two separate tests at least 14 days apart and a latency of 1.5 months between the first measurement of a plasma level below 0.02 mg/L and injection of the live vaccine is required. For inactivated vaccines, there are generally no safety problems regarding DMTs Overall, no elevated risk is expected with mRNA and non-replicating viral vector vaccines, although reduced immune response may occur.

Sphingosine 1 phosphate receptor modulators (Gilenya,Fingolimod, Mayzent, Zeposia, Ponvory)

If you are about to start one of these medicines, consider getting fully vaccinated* 2-4 weeks or more prior to starting your medicine. If you are already taking Gilenya, Mayzent, Zeposia or Ponvory, continue taking as prescribed and get vaccinated as soon as possible.

*Fully vaccinated= two doses of the mRNA (Pfizer BioNTech or Moderna) or one dose of the vector vaccine (J&J)

Alemtuzumab (Lemtrada)

If you are about to start Lemtrada, consider getting fully vaccinated* 4 weeks or more before starting Lemtrada. If you are already taking Lemtrada, consider getting vaccinated 24 weeks or more after the last Lemtrada dose[2]. If you are due for your next treatment course, when possible, resume Lemtrada 4 weeks or more after getting fully vaccinated. This suggested scheduling is not always possible and getting the vaccine may be more important than coordinating timing of the vaccine with your Lemtrada dose.

*Fully vaccinated= two doses of the mRNA (Pfizer BioNTech or Moderna) or one dose of the vector vaccine (J&J)

Oral cladribine (Mavenclad)

If you are about to start Mavenclad, consider getting fully vaccinated* 2-4 weeks prior to starting Mavenclad. If you are already taking Mavenclad, the currently available limited data does not suggest that timing of the vaccine in relation to your Mavenclad dosing is likely to make a significant difference in vaccine response. Getting the vaccine may be more important than coordinating timing of the vaccine with your Mavenclad treatment. If you are due for your next treatment course, when possible, resume Mavenclad 2-4 weeks after getting fully vaccinated*

*Fully vaccinated= two doses of the mRNA (Pfizer BioNTech or Moderna) or one dose of the vector vaccine (J&J)

Anti-CD20 monoclonal infusions (Ocrevus and Rituxan and biosimilars)

If you are about to start Ocrevus or Rituxan, consider getting fully vaccinated* 2-4 weeks or more prior to starting the infusions. If you are already taking Ocrevus or Rituxan, consider getting vaccinated 12 weeks or more after the last DMT dose[3]. When possible, resume Ocrevus or Rituxan 4 weeks or more after getting fully vaccinated*. This suggested scheduling is not always possible and getting the vaccine may be more important than timing the vaccine with your MS medicine.

*Fully vaccinated= two doses of the mRNA (Pfizer BioNTech or Moderna) or one dose of the vector vaccine (J&J)

Ofatumumab (Kesimpta)

If you are about to start Kesimpta, consider getting fully vaccinated 2-4 weeks or more prior to starting Kesimpta. If you are already taking Kesimpta, there is no data to currently guide timing of the vaccine in relation to your last DMT injection. When possible, resume Kesimpta injections 2-4 weeks after getting fully vaccinated. This suggested scheduling is not always possible and getting the vaccine may be more important than timing the vaccine with your MS medicine.

*Fully vaccinated= two doses of the mRNA (Pfizer BioNTech or Moderna) or one dose of the vector vaccine (J&J)

Glucocorticoids:

For live vaccines, no therapy stop is required under glucocorticosteroid treatment if (1) local therapy or (2) short-term (<14 days) and low-dose therapy (prednisone equivalent <20 mg/day in adults) is used. For therapy durations, longer than 14 days and above the prednisone equivalent mentioned, an interval between last intake and vaccine administration of 1 month is recommended for live vaccines to avoid an increased vaccination-related reaction. Inactivated vaccines do not bear an increased risk at all. However, they should only be administered after therapy has been stopped or the dose reduced to the prednisone equivalent mentioned due to the possible reduced efficacy. No data regarding patients with MS are available to date. In conclusion, no increased risk is expected with mRNA and non-replicating viral vector vaccines.

High-dose steroids

Consider starting the vaccine injection(s) at least 3-5 days after the last dose of steroids.

Mitoxantrone

Live vaccines are contraindicated during immunotherapy with mitoxantrone. A minimum interval of 3 months after the end of therapy is recommended. This also seems reasonable for inactivated vaccines in order to be able to develop sufficient immunity. In summary, no increased risk is expected with mRNA and non-replicating viral vector vaccines as it is with inactivated vaccines, although vaccine immunogenicity may be compromised.

Table 1. Disease modifying therapies in Multiple Sclerosis patients with COVID-19.

Drug	COVID-19 Cases		Death See text for details	Total (%)	References
	Confirmed	Suspected			
Beta-interferon	144	74	4	218 (4.9)	[7–25]
Glatiramer acetate	196	73	4	269 (6.1)	[8,10,11,15,16,18–25,29–31]
Dimethyl fumarate	408	195	19	603 (13.7)	[8,11–25,29,31,35,40,41]
Teriflunomide	202	49	4	251 (5.7)	[7,8,10,13,15–25,31–39]
Dimethyl fumarate/teriflunomide §	-	108	-	108 (2.4)	[30,31]
Fingolimod	268	146	1	414 (9.4)	[7,8,10,11,14–20,22–25,30,31,35,37,43–49]
Siponimod	19	-	2	19 (0.4)	[11,25]
Ponesimod	-	1	-	1 (0)	[18]
Non-specified S1P [1] modulator	29	-	-	29 (0.7)	[21]
Natalizumab	325	136	20	461 (10.4)	[8,11,13–16,18–25,30,31,35,50–52]
Alemtuzumab	35	23	1	58 (1.3)	[8,13,16–25,31,72–77]
Cladribine	195	140	1	335 (7.6)	[8,17–20,23,25,31,78–84]
Alemtuzumab/cladribine §	-	15	-	15 (0.3)	[30]
Ocrelizumab	1042	173	35	1215 (27.5)	[8,11,13,15,16,18,19,22–25,29,35,53–63]
Rituximab	211	25	8	236 (5.3)	[7,8,11,12,15,22–25,54,59,64–68]
Ofatumumab	13	-	-	13 (0.3)	[70,71]
Non-specified anti-CD20	123	49	-	172 (3.9)	[21,30,31]
Total	3210	1207	99	4417 (100)	

[1] S1P-sphingosine-1-phosphate; § Two studies [30,31] reported patients suspected to have COVID-19 on either Dimethyl fumarate/teriflunomide (n = 108) or Alemtuzumab/cladribine (n = 15) (non- specified).

Table 2 DMT and vaccination recommendations for live/non-live/gene-based vaccines as well as the recommended time of administration and expected immune response

DMT	Live vaccines[178,s180–s182]	Non-live vaccine	Gene-based vaccine [s181,s182]		Timing of vaccine after DMT is stopped*	Timing of vaccine after DMT†	Timing of DMT after vaccine‡[s182]	Immune response§
			mRNA	Vector				
HDMP	Contraindicated	Yes	Yes	Yes¶	≥1 month[s184]	Therapy stopped**	≥2–4 weeks‡	May be reduced[s185]
Interferon	Strict indication	Yes	Yes	Yes¶	Anytime[s186]	Anytime	≥2–4 weeks‡	Similar[s187]
Glatiramer acetate	Strict indication	Yes	Yes	Yes¶	Anytime[s186]	Anytime	≥2–4 weeks‡	Similar[s188]
Dimethyl fumarate	Strict indication	Yes	Yes	Yes¶	Not specified	Anytime	≥2–4 weeks‡	Similar[s189]
Teriflunomide	Contraindicated	Yes	Yes	Yes¶	≥6 months[s190]††	Anytime	≥2–4 weeks‡	Slightly reduced [s191,s192]
S1P modulators‡‡	Contraindicated	Yes	Yes	Yes¶	≥2 months[s193]	Anytime	≥2–4 weeks‡	Reduced[s194–s196]
Natalizumab	Contraindicated	Yes	Yes	Yes¶	≥3 months[s186]	Anytime	≥2–4 weeks‡	Similar[s197,s198]
B cell-depleting agents§§	Contraindicated	Yes	Yes	Yes¶	Specified¶¶	≥3–6 months***	≥2–4 weeks‡	Reduced[s196,s199,s200]
Alemtuzumab	Contraindicated	Yes	Yes	Yes¶	Not specifieds178,s201	≥3–6 months***	≥2–4 weeks‡	Reduced[s202]
Cladribine	Contraindicated	Yes	Yes	Yes¶	Specified†††	Specified‡‡‡	≥2–4 weeks‡	Similar[s196,s203]
Mitoxantrone	Contraindicated	Yes	Yes	Yes¶	≥3 months[s204]	Not specified	≥2–4 weeks‡	May be reduced[s178,s204]

*Recommended timing of vaccination for *live/attenuated vaccines* after stopping DMT, with timing meant to avoid the risk of infection from the vaccine itself in immunocompromised individuals.

†Recommended timing of vaccination for *non-live/gene-based vaccines* with already established DMT (concerning cyclical therapies after last administration of DMT) to generate the most protective vaccine response possible.

‡Recommended timing of the start of a DMT/next dose of a DMT (especially concerning cyclical therapies) after completion of the vaccine to enable a protective vaccine response before the immune response is possibly affected by the DMT/next dose of DMT—at least *2 weeks for non-live/gene-based vaccines* and at least *4 weeks for live/attenuated vaccines* (here also for safety reasons).

§Data only for non-live vaccines available.

¶II Non-replicating viral vector vaccines.

**III After end of therapy or after dose reduction of prednisone equivalent <20 mg/day in adults.[s184]

††IV Washout option with active carbon or cholestyramine, regardless of the washout procedure chosen, a subsequent check of the plasma level by two separate tests at least 14 days apart, and a waiting period of 1.5 months between the first measurement of a plasma level below 0.02 mg/L and the live vaccination is required.[s190]

‡‡a Sphingosine-1-phosphate (S1P) receptor modulators including fingolimod, siponimod, ozanimod and ponesimod.

§§b Including rituximab, ocrelizumab and ofatumumab.

¶¶V At least 6 months for revaccination and 12 months for primary vaccination, if possible[s184] respectively until B cell recovery.[s178]

***VI At least 3–6 months apart depending on regional recommendations.[s94,s205–s207]

†††VII Until white cell counts are within normal limits.[s208]

‡‡‡VIII Available limited data do not suggest that timing the vaccine in relation to your cladribine dosing is likely to make a significant difference in vaccine response.[s94,s196,s203]

DMT, disease-modifying therapy; HDMP, high-dose methylprednisolone; mRNA, messenger RNA.

Table 2. Impact of Multiple Sclerosis disease modifying therapies on vaccination and expert recommendations.

Drug	Impact on Vaccination Response	Recommendation
Interferons	No impact	Similar to other vaccines
Glatiramer acetate	Some studies have suggested a blunted humoral response to Influenza vaccine. No data for other vaccines.	If possible, vaccination must be administered previously to first drug administration
Terifluonomide	Possibly no impact	If possible, vaccination must be administered previously to first drug administration
Dymethil fumarate	Response to toxoid, conjugate and polysaccharide vaccines was not affected	If possible, vaccination must be administered previously to first drug administration, due to lymphopenia risk
S1P modulators [1]	Reduced response to inactivated, toxoid and polysaccharide vaccines with fingolimod Slightly blunted response to Influenza vaccine with Siponimod	If possible, vaccination must be administered previously to first drug administration
Cladribine	No specific studies but MS [2] patients under cladribine have mounted immune response to influenza vaccine after four weeks from vaccination, without additional adverse events. COVID-19 vaccine three months after the second cycle of treatment promoted a protective antibody response despite an incomplete immune reconstitution.	A three-month gap after the treatment cycle until vaccination is recommended (or until the recovery of lymphocyte count)
Natalizumab	Possibly no impact	If possible, vaccination must be administered previously to first drug administration
Anti-CD20	Attenuated humoral responses to tetanus, seasonal flu, pneumococcus and SARS-CoV-2 vaccines were observed	Ocrelizumab/rituximab: vaccination should be deferred toward the end of the cycle (12 weeks or more after the last drug dose) and the next drug dose administered at least 4–6 weeks after completing vaccination. Ofatumumab: vaccination might be delivered toward the end of the monthly cycle and the next two ofatumumab doses skipped.

Table 2. *Cont.*

Drug	Impact on Vaccination Response	Recommendation
Alemtuzumab	Blunted immune response until six months after last treatment cycle, but retained after that period	Vaccination should be delayed for at least six months after the last treatment cycle and the second cycle adjusted to ensure an optimal vaccination response.
All	-	Live vaccines are generally contraindicated. Pre-vaccination lymphocyte count is advised. Treatment withdrawal to promote vaccination response is not recommended. Post-vaccination serology status checking is encouraged.

Vaccine Effectiveness and MS

Some DMTs may reduce the effectiveness of the COVID-19 vaccines

People taking certain DMTs (ocrelizumab, rituximab, ofatumumab, and possibly fingolimod and others) will have a reduced and possibly undetectable antibody response to the COVID-19 vaccines. If you use one of these DMTs and take an antibody test following your vaccine, it may show a decreased or undetectable antibody level. Even if your antibodies are undetectable or low, you could be protected from COVID-19 since other components of the immune system are triggered by the vaccine and could contribute to your protection.

While easiest to measure, antibodies are not the only post-vaccine response which helps protect us. Research is underway to explore these other components of the immune response to the vaccine and how they might play a role in protection against COVID-19

FDA states that antibody tests should not be used to determine immunity or protection against COVID-19

Antibody tests are helpful to determine if someone may have been exposed to the SARS-CoV-2 virus (the virus that causes COVID-19) and may have developed an immune response. Antibody tests should not be used to determine immunity or protection against COVID-19, especially after a person has received a COVID-19 vaccination

Even after you've been fully vaccinated, continue to take precautions against COVID-19

Even though the current COVID-19 vaccines are highly effective, some people can still become infected with COVID-19 and give it to others. While research on the immune response to the vaccines in MS is underway, the safest approach is to ensure those closest to you are vaccinated. When in settings where you are unsure of the vaccination status of those around you, continue to wear a mask, practice physical distancing, wash your hands frequently and follow local rules about getting tested for COVID-19 when necessary.

COVID-19 Vaccine Boosters and Additional Doses

Those age 18 and older who have received two doses of an mRNA vaccine [Pfizer BioNTech (Comirnaty) or Moderna] will be eligible for a COVID-19 vaccine booster starting in September. The booster is expected to be available eight months after their second dose of the mRNA vaccine. **People with MS age 12* and older who are fully vaccinated with an mRNA vaccine may be eligible to receive an additional vaccine dose now. Talk with your healthcare provider to determine the best time to get your additional dose.**

* Only the Pfizer BioNTech (Comirnaty) vaccine is authorized for age 12 and older and approved for age 16 and older.

People with MS may be eligible for an additional dose now

FDA has authorized an additional COVID-19 vaccine dose for people who are not expected to have normal and/or adequate immune responses after two doses of the vaccine. Studies of the COVID-19 vaccine responses in MS have shown a reduced or absent antibody response to the vaccine among those who use certain disease modifying therapies (DMTs).

People with MS using the following DMTs may benefit from an additional dose:

- sphingosine 1-phosphate receptor modulators (Gilenya,Fingolimod),
- alemtuzumab (Lemtrada) and
- anti-CD20 monoclonal antibodies (Ocrevus, Kesimpta, Rituxan and biosimilars)

Boosters are different than an additional dose

An additional dose is intended to improve immunocompromised people's response to their first and second dose of vaccine. A booster dose is given to people when the immune response to the first and second dose is likely to have waned over time. An additional dose can be administered as soon as 28 days following your second vaccine injection. Boosters are expected to be available eight months after the second dose of an mRNA vaccine.

Timing vaccines with DMTs

A recent study of people with MS who use B cell depleting DMTs showed a better antibody response when the vaccine was administered three months or more after the last dose of DMT.

Having MS does not make you immunocompromised, but some DMTs do reduce your immune responses to vaccines

Having MS does not compromise our immune system. Current evidence shows that having MS does not make us more likely to develop COVID-19 or to become severely ill or die from the infection than the general population. However, some DMTs used to treat MS do alter your immune system and certain groups of people with MS are more susceptible to having a severe case of COVID-19, including people taking B cell depleting DMTs.

COVID-19 antibodies in people with MS

Antibody tests are helpful to determine if someone may have been exposed to the SARS-CoV-2 virus (the virus that causes COVID-19), but antibody tests are not recommended by the FDA to determine immunity or protection against COVID-19.

An additional dose of the mRNA vaccines produces more robust immune responses against the SARS-CoV2 virus (the virus that causes COVID-19). These responses can include an increase in antibodies (produced by B cells) as well as an increase in the immune cellular responses (T cells)– both of which offer protection from serious illness due to COVID-19.

People who lack B cells, such as those on B cell depleting therapies, may have reduced or even absent antibody responses to the additional dose as well, though other aspects of their vaccine response (T cells) are likely to be increased. A recent study of people with MS who had a reduced or absent antibody response to the COVID-19 vaccine showed increased T cell responses. This finding shows the importance of vaccination for all people with MS regardless of the anticipated antibody response.

Vaccine side effects

Data from currently available studies indicate that the side effects of the third dose of mRNA vaccine [Pfizer BioNTech (Comirnaty) or Moderna] were similar to prior doses. Any vaccine can cause side effects, including a fever. A fever can make MS symptoms worse temporarily, but they should return to prior levels after the fever is gone.

The COVID-19 vaccines are not expected to cause MS or trigger an MS relapse

None of the available vaccines contain live virus and the vaccines will not cause COVID-19. There is nothing to indicate that the vaccines will cause MS. For youth with MS, the vaccines are not likely to trigger an MS relapse or have any impact on long-term disease progression. The risk of getting COVID-19 far outweighs any risk of having an MS relapse from the vaccine.

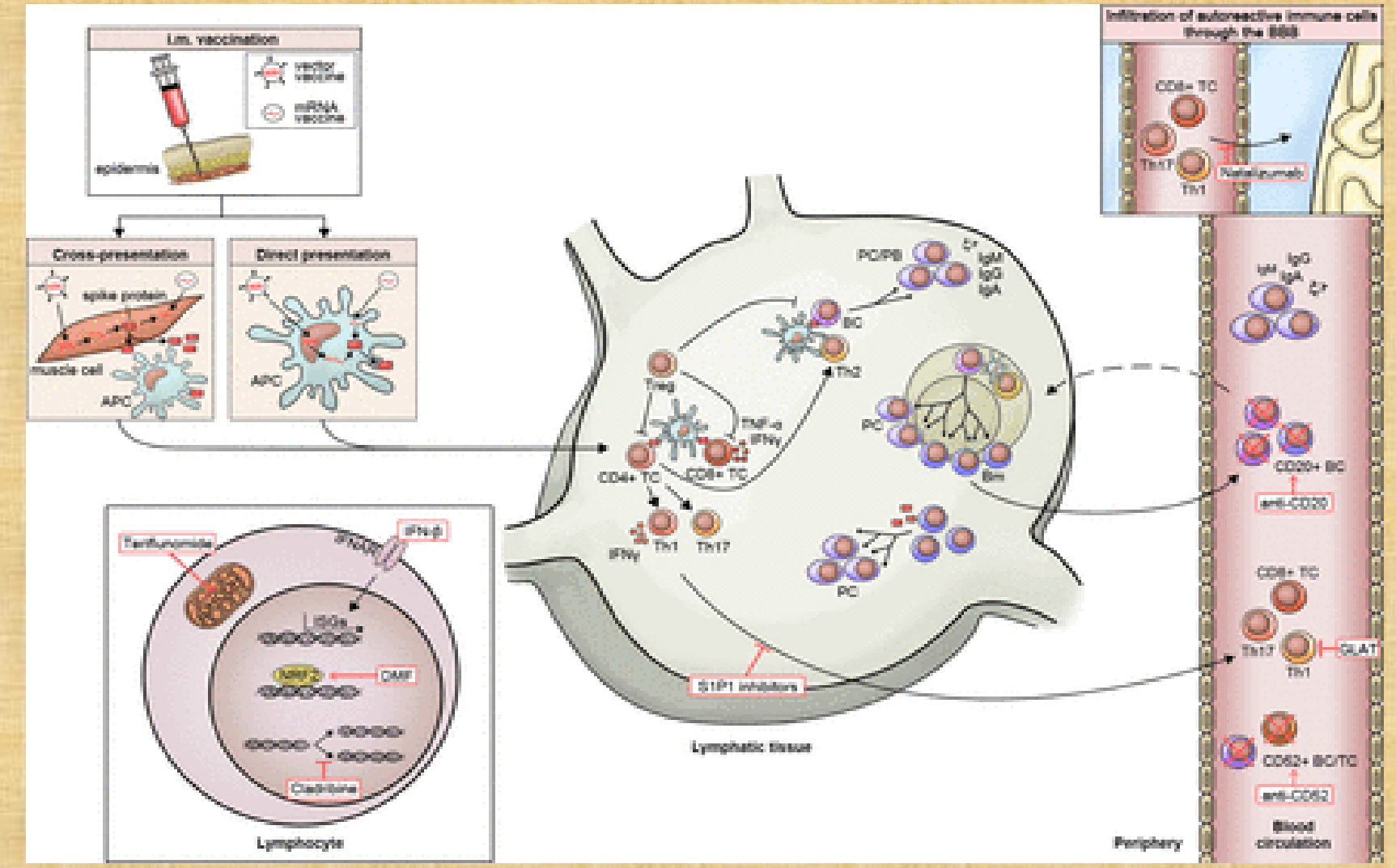
There is no evidence that the vaccines will affect fertility

There is no reason to expect any COVID-19 vaccine to affect fertility.

CONCLUSION:

To efficiently fight the COVID-19 pandemic, it is of utmost importance to follow the general recommendations of the WHO and to achieve the fastest possible protection through comprehensive vaccination of the human population. This is particularly relevant to people with autoimmune diseases such as MS. Therefore, all people with MS should be vaccinated against SARS-CoV-2 according to regional recommendations and in accordance with their treating neurologist, not least in order to prevent the emerging problem of virus mutants as far as possible.

Regarding cyclical therapies (ocrelizumab, rituximab, alemtuzumab, cladribine) possible postponement of the next dose may be considered depending on individual circumstances (risk factors, age, MS disease activity and prognosis, and lymphocyte count). The risk of disease reactivation may greatly exceed the risk of COVID-19.


Im. vaccination
vector vaccine
mRNA vaccine
epidermis
Cross-presentation
spike protein
muscle cell
APC
Direct presentation
APC
Infiltration of autoreactive immune cells through the BBB
CD8+ TC
Th1?
Th1
Natalizumab
PC/PB
BC
Th2
Treg
TNF-α
IFNγ
CD4+ TC
CD8+ TC
IFNγ
Th1
Th17
PC
Brn
S1P1 inhibitors
Lymphatic tissue
IgM
IgD
IgA
IgG
CD20+ BC
anti-CD20
CD8+ TC
Th17
Th1
GLAT
CD52+ BC/TC
anti-CD52
Blood circulation
Periphery
Teriflunomide
IFNGR
IFN-β
JAK1
JAK3
STAT1
STAT2
DMF
Cladribine
Lymphocyte