



Immunization and Multiple Sclerosis

Recommendations from the French Multiple Sclerosis Society

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BACKGROUND

Vaccines have been suspected in the past to trigger MS or MS exacerbations. Other concerns arose more recently, with the extension of the immunoactive treatment arsenal, about an increased risk of infections or a decreased effectiveness of immunization in immunosuppressed patients.

OBJECTIVE

The objective of this work is to establish recommendations on immunization and multiple sclerosis (MS)

METHODS

The French Group for Recommendations in Multiple Sclerosis (France4MS) did a systematic review of articles from PubMed and universities databases (January 1975 through June 2018). The RAND/UCLA appropriateness method, which has been developed to synthesize the scientific literature and expert opinions on health care topics, was used for reaching a formal agreement. Twenty-four MS experts worked on the full-text review and a group of 110 multidisciplinary health care specialists validated the final evaluation of summarized evidences.

REFERENCES

- Lebrun C and Vukusic S for SFSEP. Immunization and multiple Sclerosis. Recommendations from the French Multiple Sclerosis Society. Revue Neurologique 2019 and coediting Multiple Sclerosis and Related Disorders 2019.
- Full extensive French version with tables on sfsep.org

DISCLOSURES

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RECOMMENDATIONS

Question 1: Are vaccines associated with an increased risk of MS?

1. Vaccines in general are not associated with an increased risk of MS or occurrence of a first demyelinating episode of the central nervous system, including hepatitis B and human papillomavirus vaccines (Grade B).

Question 2: Are vaccines associated with an increased risk of relapse in MS? of worsening of disability?

2a. Vaccines in general are not associated with an increased risk of relapse in a patient with MS. (Grade B) An increased risk of relapse after vaccination against yellow fever cannot be excluded (Grade C).

2b. Influenza and BCG vaccines have no impact of short-term accumulation of disability. Impact of other vaccines on disability has not been studied yet (Grade C).

Question 3: Are vaccines as effective in people with MS as in the general population (regardless of treatment)?

3. Available data on the efficacy of inactivated vaccines, in patients with MS and without disease-modifying treatment, suggest that it is similar to the general population, particularly for mono-and trivalent influenza vaccines. No studies are available for live attenuated vaccines (Grade C).

Question 4: Are vaccines as effective in people with MS exposed to disease-modifying treatments?

4a. Interferon bêta

The vaccine response to influenza of patients treated with interferon beta is not decreased compared to healthy controls and untreated MS (Grade B). The vaccine response to Meningococcus, Pneumococcus, and Diphtheria-Tetanus, in patients treated with interferon beta, is not decreased compared to healthy controls and untreated MS (Grade C). The other vaccines were not studied.

4b. Glatiramer acetate

The vaccine response to influenza in patients with MS treated with glatiramer acetate may be reduced compared to healthy controls and untreated MS (Grade C). The other vaccines were not studied.

4c. Dimethylfumarate

The vaccine response to Meningococcus, Pneumococcus and diphtheria-tetanus vaccines in patients with MS treated with dimethylfumarate appears to be comparable to that of MS treated with interferon beta (Grade C). It is advised to apply immunization recommendations for immunocompromised patients (Expert recommendation).

4d. Teriflunomide

The vaccine response to influenza in patients treated with teriflunomide is decreased compared to MS treated with interferon beta (Grade B). The other vaccines were not studied. It is advised to apply immunization recommendations for immunocompromised patients (Expert recommendation).

4e. Mitoxantrone

The vaccine response to influenza in patients treated with mitoxantrone is insufficient compared to healthy controls (Grade C). The other vaccines were not studied. It is advised to apply immunization recommendations for immunocompromised patients (Expert recommendation).

4f. Natalizumab

The vaccine response in patients treated with natalizumab is reduced for influenza, but not for tetanus, compared to healthy controls (Grade B). The other vaccines were not studied. It is advised to apply immunization recommendations for immunocompromised patients (Expert recommendation).

4g. Fingolimod

The vaccine response in patients treated with fingolimod is reduced compared to healthy controls, untreated MS and interferon beta treated patients (Grade B). It is advised to apply immunization recommendations for immunocompromised patients (Expert recommendation).

4h. Alemtuzumab

The data are insufficient to evaluate the vaccine response in patients treated with alemtuzumab. It is advised to apply immunization recommendations for immunocompromised patients (Expert recommendation).

4i. Ocrelizumab

The vaccine response in patients treated with ocrelizumab is effective but decreased after 12 weeks for tetanus, Pneumococcus and influenza compared with non-treated and interferon-beta-treated MS (Grade B). It is advised to apply immunization recommendations for immunocompromised patients (Expert recommendation).

4j. Cladribine

No vaccine has been studied in patients with MS treated with cladribine. It is advised to apply immunization recommendations for immunocompromised patients (Expert recommendation).

4k. Cyclophosphamide (off-label)

No vaccine has been studied in patients with MS treated with cyclophosphamide. It is advised to apply immunization recommendations for immunocompromised patients (Expert recommendation).

4l. Methotrexate (off-label)

No vaccine has been studied in patients with MS treated with methotrexate. The vaccine response in patients with rheumatoid arthritis treated with methotrexate is satisfactory. It is advised to apply immunization recommendations for immunocompromised patients (Expert recommendation).

4m. Azathioprine/mycophenolate mofetil (off-label)

No vaccine has been studied in patients with MS treated with azathioprine or mycophenolate mofetil. It is advised to apply immunization recommendations for immunocompromised patients (Expert recommendation).

4n. Rituximab and other anti CD20 (off-label)

No vaccine has been studied in patients with MS treated with rituximab and other anti-CD20 (except ocrelizumab). It is advised to apply immunization recommendations for immunocompromised patients (Expert recommendation).

Question 5: What prevention methods should be offered to patients with MS?

5a. The vaccination calendar of the general population should be applied to any patient with MS unless there is a specific contraindication (Recommendation of the Haut Conseil de la Santé Publique, article L3111-1, Code de la Santé Publique).

5b. It is recommended to update the vaccination calendar as soon as possible after the diagnosis of MS and before any disease-modifying treatment is introduced (Recommendation of the Haut Conseil de la Santé Publique, article L3111-1, Code de la Santé Publique).

5c. Seasonal flu vaccination is recommended for patients with MS who are treated with immunosuppressive drugs or with a significant disability (or any other reason recommended for influenza vaccination), unless there is a specific contraindication (Recommendation of the Haut Conseil de la Santé Publique, article L3111-1, Code de la Santé Publique). For all other MS patients, seasonal flu vaccination should be proposed annually (Expert recommendation).

5d. There is no vaccine restriction associated with immunomodulators (interferon beta and glatiramer acetate) (Grade B).

5e. Under immunosuppressants and in any other case of immunosuppression, live attenuated vaccines are contraindicated. Recommended vaccines are those of the vaccination calendar for the general population and vaccines specifically recommended in immunocompromised patients (influenza and Pneumococcus in particular) (Recommendation of the Haut Conseil de la Santé Publique, article L3111-1, Code de la Santé Publique).

5f. It is recommended to apply to the immediate entourage of an immunocompromised person the vaccination calendar, seasonal influenza vaccination and varicella vaccination in case of negative serology (Recommendation of the Haut Conseil de la Santé Publique, article L3111-1, Code de la Santé Publique).

RESULTS

Neurologists should double check vaccination status as soon as possible after MS diagnosis and before the disease-modifying treatment (DMT) introduction.

The French vaccinal calendar should be applied to MS patients and they should be advised to receive seasonal influenza vaccine.

If possible, serological status, including A, B, C hepatitis, measles, mumps, pertussis, rubella, varicella-zoster should be checked before starting a DMT. In case of treatment-induced immunosuppression, MS patients should be informed about infections risks and vaccine standards from the French High council of Health should be applied.

Live attenuated vaccines are contra-indicated in MS patients currently or recently treated with immunosuppressive drugs, including corticosteroids; other vaccines can be proposed whatever the treatment, but their effectiveness may be partly reduced with some drugs.

CONCLUSION

Physicians and patients should be aware of the updated recommendations for immunizations and MS. Practice guidelines will be delivered by the French MS Society for the medical and patients communities.

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