How do people with MS respond to COVID-19 vaccines?

What does research tell us about how DMTs affect the body's immune response to COVID-19 vaccines?

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Vaccines are vital in the ongoing fight against the coronavirus. However, some disease modifying therapies (DMTs) used to treat MS may affect the body's ability to produce an immune response to COVID-19 vaccines. This article summarises the latest research.

How do vaccines help our body fight COVID-19?

When infection strikes, B cells, T cells and macrophages are the key defenders of our immune system. Macrophages are white blood cells that eat and then digest germs and dying cells. They leave parts of the invader behind – these are known as antigens. The body recognises the antigens and stimulates antibodies to attack them. Antibodies are created with the help of B cells in a process known as a 'humoral response'[1]. (See glossary).

Antibody production can be triggered either by a vaccine or infection and generates memory B cells. Memory cells remain in the body so if they ever come in contact with

the virus again, the immune system's memory cells can recognise it more readily and fight it better. Meanwhile, T cells attack already infected cells in a process called a 'cellular response'[2]. (See glossary).

Some DMTs may weaken the immune response to COVID-19 vaccines

In vaccine clinical trials, healthy individuals were primarily enrolled, to ensure that the response to the vaccine is not altered by medications or health conditions. For instance, in the original Pfizer/BioNTech vaccine trials, individuals receiving treatment with immunosuppressive therapy or corticosteroids for an autoimmune disease were excluded. These criteria make it difficult to understand how people with MS respond to vaccines.

DMTs used to treat MS target the immune system, either by affecting the function of B or T cells, or by reducing the number of these cells in circulation. If B cells are targeted by the DMT, the body's ability to create antibodies may be reduced. This means that a vaccine may be less effective for those who are taking, or have recently taken, some DMTs. Several published or preprint articles have reported this.

These findings are supported by other studies in the US, Italy, France, Switzerland and Israel. These studies found a poor antibody response to rituximab (Rituxan), ocrelizumab (Ocrevus), and fingolimod (Gilenya), but better antibody response in individuals treated with cladribine (Mavenclad), alemtuzumab (Lemtrada), and natalizumab (Tysabri). Individuals on cladribine, alemtuzumab, and natalizumab seem to have a higher number of B cells in circulation compared to individuals on rituximab and ocrelizumab, and this may explain why they were able to produce more antibodies.

A clinical trial is ongoing to understand the ofatumumab (Kesimpta) response to COVID-19 vaccines, and we are waiting to learn more about the effects of ponesimod (Ponvory) and ozanimod (Zeposia) on antibody response. It is probable that they will be similar to siponimod (Mayzent) and fingolimod.

Treatment timing matters

The timing of treatment may play a role. When a person has an infusion of certain DMTs that reduce levels of B-cells – in particular ocrelizumab, ofatumumab and rituximab – the level of B cells in that person is reduced, but then slowly rises again. If there is a long gap between infusion and COVID-19 vaccine, more antibodies are often generated in response to the vaccine. This is because B cell production has recovered, meaning more B cells are in circulation. Individuals treated with other highly intensive DMTs like alemtuzumab or cladribine generally do not require as

long for the immune system to return to normal, allowing the immune system to create more antibodies in response to the vaccine.

The immune response beyond antibodies – T cells join the fight

As mentioned earlier, the immune system responds to germs in two main ways: a humoral response via B cells, and a cellular response via T cells. Even if a person does not produce a strong antibody response to vaccination, T cells can still have a critical role in forming an immune response. A few recent preprints have shown that some people on B cell-reducing DMTs like rituximab and ocrelizumab have a good T cell response to mRNA vaccines (e.g. Moderna and Pfizer vaccines) – despite a poor antibody response. It is less clear exactly how the T cells work, but they could play a crucial role in preventing severe COVID-19.

Summary

Many DMTs target T cells in one way or another. But DMTs like fingolimod or B cell-reducing therapies like rituximab reduce the number of B cells available. Studies show that individuals treated with fingolimod, siponimod, rituximab, and ocrelizumab have a poor B cell-driven antibody response to COVID-19 vaccines. But, individuals on cladribine, natalizumab, and alemtuzumab seem to create a more robust antibody response.

The number of B cells appears to be linked to how many antibodies are made. The more B cells in circulation, the easier it is to make more antibodies. That being said, even if there is no antibody production, it seems there can be some T cell response. In other words, if you take ocrelizumab, rituximab, or fingolimod, your immune system may still respond to the vaccine in other ways. This means that if the virus strikes, the T cells can help reduce the severity of the illness.

There are many pieces to this puzzle including vaccine timing, age, vaccine type, how long you have been on DMTs, B cell count and T cell response. The amount of information is growing, and we are learning more and more every day.

Conclusion

For detailed recommendations, please see the MSIF global COVID-19 advice for people with MS.

Glossary

- **Antibody**: A protein used by the immune system to identify and remove invaders, such as viruses.
- **Antigen**: A molecule present on the outside of a virus, normally triggering an immune response. Antibodies bind to antigens, and can cause the virus cell to be killed.
- **B cell**: B lymphocyte, a group of immune cells, all performing different functions – see humoral response.
- [2]**Cellular response**: The immune response inside infected cells by T cells. Killer T cells (or CD8+ T cells), seek out and destroy cells infected with the virus. Others, called helper T cells (or CD4+ T cells) are important for various immune functions, including stimulating the production of antibodies and killer T cells. T cells are activated after a virus has infected the body. They are important for fighting an ongoing infection. The killer T cell response could mean the difference between a mild infection and a severe infection requiring hospitalisation. It is also possible that they can reduce the amount of infection transferred to the community.
- **COVID-19**: Coronavirus disease (COVID-19) caused by SARS-CoV-2
- [1]**Humoral response**: Also known as antibody-mediated immunity. B cells bind to the antigens on the surface of the virus. In addition to antigens, B cells need a second signal to be activated – for instance by helper T cells. When both stimuli are present, B cells can become plasma cells and memory B cells. The plasma cell releases antibodies into the blood circulation. Memory B cells produce antibodies bound to the cell's surface and are highly specific against the virus. Memory B cells live for a long time, allowing the human body to react much faster and stronger when facing the same virus.
- **Seroconversion**: Development of antibodies against a virus in the blood serum – either after infection or immunisation (vaccination).
- **Preprint**: a type of scientific paper that comes before a formally peer-reviewed article in a scientific journal. Preprints are often non-formatted articles available for free. It allows the data to be shared as quickly as possible. However, in rapidly evolving fields, research is either refuted or replicated soon after publication. The public can also comment and post their reviews on other channels such as social media.
- **SARS-CoV-2**: the coronavirus causing the illness COVID-19.
- **T cell:** T lymphocyte, a group of immune cells. Some types include CD4+ helper, CD8+ killer, and T memory cells, all performing different functions (see cellular response).
- **Vaccination:** giving a vaccine to aid the immune system, to develop protection from disease (immunisation)