January 2021 Newsletter

Accelerating research towards a cure for multiple sclerosis

Vaccines and MS – The Science Behind the Guidance

Immunity is an extensive topic that can be most simply defined as protection from disease. When germs, such as bacteria or viruses, enter the body, they start to reproduce. This invasion, called an infection, is what causes illness. The immune system recognizes these germs as foreign invaders and responds by making proteins called antibodies which help destroy the germs. The first time a person is exposed to a germ, their antibodies may not act fast enough to prevent them from becoming sick, but by eliminating the attacking germs, the antibodies do help them get well. Antibodies also provide protection from future infections. They remain in the bloodstream and provide protection if the same germs attack again, destroying them before they cause illness.

Blood contains three types of white blood cells for fighting infection. Macrophages consume and digest foreign particles, such as viruses and bacteria. They leave behind parts of the invading agents called antigens, which the body identifies as dangerous. B-lymphocytes produce antibodies that attack the antigens left behind by the macrophages. T-lymphocytes attack cells in the body that have been infected. The first time the body

encounters a bacteria or virus, it can take several days for the immune system to fight the infection. Once it has been resolved, both B- and T-lymphocytes form memory cells that remember the same pathogen and provide a rapid response to future infections.

Vaccines help develop immunity by imitating an infection. This type of infection almost never causes illness, but it does cause the immune system response described above. Antibodies destroy the "vaccine germs" just as they would the "disease germs." Sometimes, after getting a vaccine, the "imitation infection" can cause minor symptoms, such as a fever, which are normal and expected as the body builds immunity. However, it typically takes a few weeks for the immune system to produce memory cells after vaccination. Therefore, it is possible that a person infected with a bacteria or virus just after vaccination could get sick because the vaccine has not had enough time to provide protection.

There are several different types of vaccine. **Live-attenuated vaccines** contain a weakened form of the living virus or bacteria. These vaccines are the closest thing to a natural infection and are very effective, however not everyone can receive them. For example, they are not recommended for people with MS on a disease modifying therapy (DMT). **Inactivated vaccines** are made from the killed version of the germ that causes a disease. These vaccines usually don't provide as much protection as live vaccines. Often, multiple doses are necessary to build up and/or maintain immunity. Some bacteria, such as diphtheria and tetanus, produce toxins (poisons) in the body. **Toxoid vaccines** contain weakened toxins (called toxoids). When the immune system receives this type of vaccine, it learns how to fight off the natural toxin. **Subunit, recombinant, polysaccharide and conjugate vaccines** are made from specific pieces of the germ, such as its protein, sugar or casing. These vaccines provide a very strong immune response that's targeted to key parts of the germ. They can be used more generally than live vaccines, including people with weakened immune systems and chronic conditions like MS.

There are several reasons that individuals receiving a vaccine for the first time may need more than one dose. As mentioned above, more than one dose of inactivated vaccines is usually needed to build more

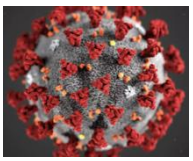
complete immunity. For other vaccine types, immunity may begin to wear off. At that point, a "booster" dose is needed to bring immunity levels back up. In the case of flu vaccines, individuals need to get a dose every year because the flu viruses causing disease may be different from season to season. Every year, flu vaccines are made to protect against the viruses that research suggests will be most common.

The capacity of traditional vaccines to either cause or exacerbate MS and other demyelinating diseases has been studied extensively. Researchers in Sweden evaluated more than 789,000 subjects who received the human papillomavirus (HPV) vaccine. They found no increased risk of MS or other demyelinating diseases such as optic neuritis (ON), neuromyelitis optica, transverse myelitis (TM), or acute disseminated encephalomyelitis (ADEM) following HPV vaccination. A 2014 study found no association between Hepatitis B (HBV) or HPV vaccination and the risk of MS, ADEM, TM, ON or clinically isolated syndrome (CIS), up to three years later. A 2016 literature review found no change in the risk of developing MS after vaccination against HBV, HPV, seasonal influenza, MMR (measles, mumps and rubella), variola, tetanus, BCG (Bacillus Calmette–Guérin), polio or diphtheria. Researchers in Belgium investigated whether or not influenza vaccination affects the clinical course of relapsing remitting MS. Subjects were examined clinically as well as with MRI scans three weeks before vaccination, the day of vaccination, and three weeks after vaccination. Investigators found no exacerbations in the pre- or post-vaccination period. On MRI, a greater number of lesions appeared at the end of the pre-vaccination period as compared with post-vaccination. Researchers concluded that influenza vaccine has no clinical or subclinical short-term effect on the activity of MS. A 2001 study also concluded that tetanus, HBV, or influenza vaccination did not increase the short-term risk of relapse in subjects with MS.

According to the National MS Society (the Society), preventing infections through vaccine use is a key part of medical care for people with MS. Therefore, it is recommended that those living with the disease receive traditional vaccines according to the standard vaccine schedule. However, before receiving any vaccine, individuals with MS should consult with their healthcare provider as some DMTs affect which vaccines are appropriate and

safe. Special considerations with regards to vaccinations and MS, and information on individual vaccines can be found on the Society's website.

RNA (or messenger RNA) vaccines are a new type of vaccine. Messenger RNA (mRNA) molecules carry the genetic information needed to make proteins. They carry these instructions from the DNA in the nucleus of the cell to the cytoplasm where the proteins are made. An mRNA vaccine delivers the genetic instructions for making a bacterial or viral protein (or just a piece of it) to cells. Production of these proteins triggers an immune response in the body that provides protection from the "real" virus. Interest has grown in these vaccines because they can be developed in a laboratory using readily available materials. This means the process can be standardized and scaled up, making vaccine development faster than traditional methods of making vaccines. Researchers have been studying and working with mRNA vaccines for years for conditions like the flu, rabies, and cytomegalovirus (CMV). The recent COVID-19 vaccines are among the first to be approved for use in humans. These vaccines deliver instructions for coding a critical section of the coronavirus's spike protein. This protein is easy for the immune system to attack because it sits on the virus's outer surface. It's also indispensable to the virus, as it's required for entry into the cells. Researchers believe these vaccines will be effective against any new form of COVID-19 that may occur due to mutation because the virus can't alter its spike protein to escape immune detection.



The Society recently released a COVID-19 vaccine guidance for people with MS that is based on data from the general population in the vaccine clinical trials and data from studies of other vaccines in MS. According to the Society, the vaccines are safe and effective for people with MS to use along with their MS medications. As stated in the guidance, "Most people with relapsing and progressive forms of MS should be vaccinated. In addition, members of the same household and close contacts should also get a COVID-19 vaccine when available to decrease the impact of the virus. People with progressive MS, those who are older, those who have a higher level of physical disability, those with certain medical

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conditions (e.g., diabetes, high blood pressure, obesity, heart and lung disease, pregnancy), and Black and Hispanic populations are among groups with the highest risk for hospitalization due to COVID-19. Individuals in these high risk groups are especially encouraged to get the vaccine as soon as it becomes available." The currently available COVID-19 vaccines require two doses. According to the Society's guidance, "You need to get both doses for it to work. If you've had COVID-19 and recovered, you should also get the vaccine…Please review the full guidance to learn more about COVID-19 vaccines and MS." It's important to note that, as with traditional vaccines, the decision to get the COVID-19 vaccine is best made in partnership with one's healthcare provider. In addition, this guidance only applies to the approved mRNA vaccines in the United States (Pfizer BioNTech and Moderna). As there are different vaccines available in other countries, this guidance may not apply to those living outside of the US.

Natural infections can be deadly or cause severe health complications. Even though it may cause side effects, vaccination is one of the best ways to prevent them. Individuals with MS should consult with their doctor before receiving any vaccinations to be sure the medications they are taking will not cause complications. While the new COVID-19 vaccines offer a glimmer of hope during this uncertain time, the number of people with MS that participated in the vaccine clinical trials isn't known, so data on the safety and effectiveness of COVID-19 vaccines in those with MS is not yet available. Targeted clinical trials involving people with MS and other autoimmune conditions are needed to determine their safety and effectiveness in these populations. The Society's guidance will be updated and become more detailed as more is learned from these studies. The core of ACP's mission is to facilitate research efforts such as these, which will provide clarity for people with MS as they make healthcare decisions to stay as healthy as possible during the pandemic and beyond.