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Guillain-Barré syndrome (GBS) & vaccines: The risks and recommendations

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Guillain-Barré syndrome, or GBS, was recently described as a rare side effect following receipt of adenovirus-based COVID-19 vaccines, such as the J&J/Janssen version used in the U.S. GBS has also been found to be a rare consequence of influenza vaccination. What people may not realize is that GBS is also a consequence of COVID-19 or influenza infections, as well as other viral, and some bacterial, infections, so we wanted to take a closer look at what GBS is, how it relates to vaccines, and the recommendations related to vaccines for those who previously experienced GBS.

What is Guillain-Barré syndrome?

GBS involves an untoward interaction between two body systems — the immune system and the nervous system. In short, the immune system mistakenly attacks the nervous system, specifically the “peripheral nerves,” meaning nerves that are not part of the brain or spinal cord but are in all other parts of the body. As a result of the attack, people with GBS can experience a range of symptoms. The hallmark symptom is muscle weakness, which can be minor (e.g., tingling) or debilitating (e.g., paralysis of limbs or immobilization of muscles necessary for breathing). People with GBS can have difficulty walking, seeing, swallowing, speaking and chewing. Likewise, GBS can result in severe muscle pain, lack of coordination, heart and blood pressure abnormalities, digestive problems and incontinence. Often, the symptoms worsen over a period of a few days up to a few weeks, with the worst effects typically occurring about four weeks into the syndrome.

Because of the paralysis, people affected by GBS are often hospitalized to treat the disease or its complications, which can include pneumonia, bed sores, or as previously mentioned, trouble breathing or eating. Once stabilized, people with GBS often require physical and occupational therapy to regain skills that involve muscles weakened during the acute phase of illness. While GBS can be life-altering, particularly during the acute phase, most people completely recover and few die if they receive appropriate medical care. Recovery, however, is often slow, taking months or years. About 30 of every 100 people continue to experience weakness more than three years after the original event, and about 15 of 100 have long-term weakness that requires assistance, such as a walker, wheelchair or other support. Very few people, about 3 of every 100, experience a recurrence GBS-related weakness years after the original bout.

What causes GBS?

Even though it is understood that the immune system attacks the peripheral nervous system, what causes this to happen is not completely understood. However, some viral and bacterial infections are known to trigger the development of GBS, including recent infections with:

- *Campylobacter jejuni*, a bacterium that causes diarrheal illness
- Influenza
- Cytomegalovirus (CMV)
- Epstein-Barr virus (EBV)
- Human immunodeficiency virus (HIV)
- *Mycoplasma pneumoniae*, a common cause of so-called “walking pneumonia”
- Varicella, the virus that causes chickenpox
- Zika virus
- SARS-CoV-2, the virus that causes COVID-19

In the case of *Campylobacter*, which causes about 4 of every 10 cases of GBS in the U.S., antibodies generated against the infection also attack the nerves. However, it is not known whether that is also how the other infections lead to GBS. Three possible mechanisms have been suggested:

1. Proteins from these pathogens and those of the nerves are similar enough that antibodies produced to fight the pathogen also attack the nerves, such as happens with *Campylobacter*.
2. The pathogen alters the nerves, causing them to be viewed as foreign by the immune system, which then attacks them.
3. The infection causes changes to the immune system that make it less efficient at distinguishing between self- and non-self-proteins.

Also, of note, while we don't know everything about the causes of GBS, it is known that GBS is not contagious, so someone with GBS will not transmit it to another person. Likewise, we know that GBS is not inherited, meaning if someone in a person's family has had GBS, this does not make that person more likely to also develop GBS. About 3,000 to 6,000 cases of GBS occur each year in the U.S., and it tends to occur most often in men and those older than 50 years of age.

Do vaccines cause GBS?

In a rare number of instances, GBS has been associated with vaccination. In each case, GBS has also been identified following infection with the virus or bacterium that the vaccine protects against:

Influenza vaccines

- 1976 swine flu vaccine — This vaccine was attributed to GBS in about 1 of 100,000 recipients.
- 2001 H1N1 flu vaccine — This vaccine was associated with a GBS risk of about 1 to 5 cases per million doses.
- Annual influenza vaccine — Studies of subsequent influenza vaccines showed variable rates of GBS following vaccination. But a meta-analysis, which is a study that evaluates the design and findings of several previously published studies, identified an average of about 1 case of GBS per million vaccine recipients. Importantly, this analysis also identified a rate of about 17 cases of GBS per million influenza infections, indicating that vaccination actually decreases the risk of developing GBS.

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Rabies vaccine — Early versions of rabies vaccine made using cells from the nervous system were associated with increased risk of GBS, but the rabies vaccines currently used in the U.S. do not use nervous system cells, so this risk is no longer an issue.

Smallpox vaccine — While no longer routinely used, the vaccinia virus used to protect against smallpox was also a rare cause of GBS.

Oral polio vaccine — GBS occasionally followed receipt of the live, weakened polio vaccine given orally, commonly referred to as OPV. This vaccine is no longer used in the U.S. The inactivated polio vaccine, given as a shot, is not associated with GBS.

Tetanus-toxoid-containing vaccines — Evidence of GBS following receipt of tetanus toxoid and tetanus-toxoid-containing vaccines is based on case studies, meaning reports of individual experiences, as opposed to placebo-controlled studies. Typically, case studies are used to alert other providers and scientists to an observation and to generate a hypothesis to test in a controlled study. In this case, placebo-controlled studies are not possible since most people have received tetanus-containing vaccines. With this in mind, and based on a clear occurrence of GBS following receipt of tetanus toxoid in an individual, the Institute of Medicine (IOM) indicated that since tetanus-containing vaccines are based on tetanus toxoid, the risk of GBS following receipt of a tetanus-containing vaccine is plausible. However, if GBS follows receipt of tetanus-containing vaccines, it would be extremely rare based on the small number of times it has been reported and the large number of tetanus-containing vaccines that have been administered.

Shingles vaccine — Earlier in 2021, the FDA required the addition of a warning label to the Shingrix® vaccine, citing an increased risk of about 3 cases per million vaccine doses. Importantly, this increased risk occurred in about 6 of one million people 65 years of age and older during the six weeks after receipt of the first dose of this vaccine. Because this is a two-dose vaccine and GBS typically only occurs after the first dose, the overall risk is described as 3 cases per million doses. Of note, the FDA indicated that causality has not been established, but this would be biologically plausible based on a couple of experiences. First, on occasion, GBS can follow varicella infections, which are caused by the same virus as shingles. Second, shingles occurs because the virus that causes chickenpox lives silently in the nerves after a chickenpox infection. When someone's immune system is weak, the virus activates to cause shingles. Depending on which nerves are involved during an occurrence of shingles, some people experience muscle weakness.

COVID-19 adenovirus-based vaccines — A GBS risk warning has also been added to the J&J/Janssen COVID-19 vaccine after an increased risk of about 7 or 8 cases of GBS per million doses was identified in the six weeks following receipt of this version of the COVID-19 vaccine. The risk is greatest among men between 50 and 64 years of age, but GBS can also occur in women and individuals outside of this age range. A similar increased risk of GBS has not been identified following receipt of the mRNA COVID-19 vaccines.

Other vaccines have been studied, but were not associated with increased rates of GBS, including currently used versions of MMR (measles, mumps, rubella), HPV, meningococcal conjugate, polio (shot), pneumococcal, varicella (chickenpox), *Haemophilus influenzae* type b, rabies, hepatitis A and hepatitis B vaccines.

Are vaccines recommended for people who have had GBS?

Considerations related to vaccines and GBS are described by vaccine:

Influenza vaccine — Perhaps the biggest misconception related to GBS and vaccines concerns influenza vaccine. Many people with a history of GBS — and some doctors — believe that if they have had GBS, they cannot ever get the influenza vaccine. However, this assumption is not correct. Here is the story:

- **History of GBS within six weeks of getting an influenza vaccine** — These individuals have what is called a “precaution” for influenza vaccine. A precaution means that the individual and their doctor should consider the potential risks and benefits before getting any future doses of influenza vaccine. If the individual also has other health conditions that increase their risk of severe outcomes from influenza infection, they may, together, decide that the risk is worth taking. However, if the individual is otherwise healthy and not at increased risk from influenza, they will likely decide that the dose of vaccine is not worth the risk of GBS. These are very individualized decisions that should be made with a patient and their healthcare provider together as no one answer is right for everyone.
- **History of GBS not associated with an influenza vaccine** — These individuals can get influenza vaccine. They have neither a precaution nor a contraindication, which is a reason to forgo a vaccine, for influenza vaccine.

Tetanus-containing vaccines — People who had GBS within six weeks of receipt of a tetanus-containing vaccine have a precaution against receipt of tetanus-containing vaccines and should discuss the potential risks and benefits with their healthcare provider. As with influenza, if their GBS was not associated with a six-week window of receiving tetanus vaccine, they can get tetanus-containing vaccines.

Shingles vaccine — While the FDA recently required a notification about the risk of GBS following receipt of Shingrix, changes have not been made to the vaccine recommendations. Because the vaccine is recommended starting at 50 years of age and the risk of GBS increases in those 65 years and older, most people should have received the shingles vaccine before the risk of GBS increases. Likewise, the rates of GBS are rare and more likely to occur after the first dose, and shingles can limit daily activities, as such, even those over 65 years of age and their healthcare providers may decide that the benefit still outweighs the risk.

COVID-19 vaccines — Despite the finding that risk for GBS is increased following receipt of the J&J/Janssen COVID-19 vaccine, the CDC has not recommended a preference of one COVID-19 vaccine over another for people with a history of GBS; however, people with a history of GBS may still consider discussing the options with their healthcare provider or seeking an mRNA-based COVID-19 vaccine since those have not been associated with GBS.

If a person develops GBS following receipt of COVID-19 vaccine, the case should be reported to the Vaccine Adverse Events Reporting System, or VAERS. (vaers.hhs.gov/reportevent.html)

Three key takeaways

In sum, when thinking about GBS and vaccines, the following are important:

1. If a vaccine is associated with GBS, so, too, is the disease it is protecting against, so the risk of GBS is not eliminated by forgoing vaccination.
2. In addition, the risk of GBS is typically lower for the vaccine than if the disease is contracted naturally.
3. Most people with a history of GBS can still get an annual influenza vaccine (and other vaccines as well).

If you have any comments about this newsletter or suggestions about how we can make our program more helpful, please send them to contactPACK@chop.edu.