Vaccines against SARS-CoV-2 will have side effects—that's a good thing

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In 2021 hundreds of millions of people will be vaccinated against SARS-CoV-2. The success of that COVID-19 vaccination campaign will heavily depend on public trust that the vaccines are not only effective, but also safe. To build that trust, the medical and scientific communities have a responsibility to engage in difficult discussions with the public

about the significant fraction of people who will experience temporary side effects from these vaccines.

I am an immunologist who studies the fundamentals of immune responses to vaccination, so part of that responsibility falls on me.

Simply put, receiving these vaccines will likely make a whole lot of people feel crappy for a few days. That's probably a good thing, and it's a far better prospect than long-term illness or death.

Immunology's 'dirty little secret'

In 1989, immunologist Charles Janeway published an article summarizing the state of the field of immunology. Until that point, immunologists had accepted that immune responses were initiated when encountering something foreign—bacteria, viruses, and parasites—that was "non-self."

Janeway suspected that there was more to the story, and famously laid out what he referred to as "the immunologist's dirty little secret": Your immune system doesn't just respond just to foreign things. It responds to foreign things that it perceives to be dangerous.

Now, 30 years later, immunologists know that your immune system uses a complex set of sensors to understand not only whether or not something is foreign, but also what kind of threat, if any, a microbe might pose. It can tell the difference between viruses—like SARS-CoV-2—and parasites, like tapeworms, and activate specialized arms of your immune system to deal with those specific threats accordingly. It can even monitor the level of tissue damage caused by an invader, and ramp up your immune response to match.

Sensing the type of threat posed by a microbe, and the level of intensity

of that threat, allows your immune system to select the right set of responses, wield them precisely, and avoid the very real danger of immune overreaction.

Vaccine adjuvants bring the danger we need

Vaccines work by introducing a safe version of a pathogen to a patient's immune system. Your immune system remembers its past encounters and responds more efficiently if it sees the same pathogen again. However, it generates memory only if the vaccine packs enough danger signals to kick off a solid immune response.

As a result, your immune system's need to sense danger before responding is at once extremely important (imagine if it started attacking the thousands of species of friendly bacteria in your gut!) and highly problematic. The requirement for danger means that your immune system is programmed not to respond unless a clear threat is identified. It also means that if I'm developing a vaccine, I have to convince your immune system that the vaccine itself is a threat worth taking seriously.

This can be accomplished in a number of ways. One is to inject a weakened—what immunologists call attenuated—or even killed version of a pathogen. This approach has the benefit of looking almost identical to the "real" pathogen, triggering many of the same danger signals and often resulting in strong, long-term immunity, as is seen in polio vaccination. It can also be risky—if you haven't weakened the pathogen enough and roll out the vaccine too fast, there is a possibility of unintentionally infecting a large number of vaccine recipients. In addition to this unacceptable human cost, the resulting loss of trust in vaccines could lead to additional suffering as fewer people take other, safer vaccines.

A safer approach is to use individual components of the pathogen,

harmless by themselves but capable of training your immune system to recognize the real thing. However, these pieces of the pathogen don't often contain the danger signals necessary to stimulate a strong memory response. As a result, they need to be supplemented with synthetic danger signals, which immunologists refer to as "adjuvants."

Adjuvants are safe, but designed to inflame

To make vaccines more effective, whole labs have been dedicated to the testing and development of new adjuvants. All are designed with the same basic purpose—to kick the immune system into action in a way that maximizes the effectiveness and longevity of the response. In doing so, we maximize the number of people that will benefit from the vaccine and the length of time those people are protected.

To do this, we take advantage of the same sensors that your immune system uses to sense damage in an active infection. That means that while they will stimulate an effective immune response, they will do so by producing temporary inflammatory effects. At a cellular level, the vaccine triggers inflammation at the injection site. Blood vessels in the area become a little more "leaky" to help recruit immune cells into the muscle tissue, causing the area to become red and swell. All of this kicks off a full-blown immune response in a lymph node somewhere nearby that will play out over the course of weeks.

In terms of symptoms, this can result in redness and swelling at the injection site, stiffness and soreness in the muscle, tenderness and swelling of the local lymph nodes and, if the vaccine is potent enough, even fever (and that associated generally crappy feeling).

This is the balance of vaccine design—maximizing protection and benefits while minimizing their uncomfortable, but necessary, side effects. That's not to say that serious side effects don't occur – they do –

but they are exceedingly rare. Two of the most discussed serious side effects, anaphalaxis (a severe allergic reaction) and Guillain-Barré Syndrome (nerve damage due to inflammation), occur at a frequency of less than 1 in 500,000 doses.

Vaccination against SARS-CoV-2

Early data suggest that the mRNA vaccines in development against SARS-CoV-2 are highly effective—upwards of 90%. That means they are capable of stimulating robust immune responses, complete with sufficient danger signaling, in greater than nine out of 10 patients. That's a high number under any circumstances, and suggests that these vaccines are potent.

So let's be clear here. You should expect to feel sore at the injection site the day after you get vaccinated. You should expect some redness and swelling, and you might even expect to feel generally run down for a day or two post-vaccination. All of these things are normal, anticipated and even intended.

While the data aren't finalized, more than 2% of the Moderna vaccine recipients experienced what they categorized as severe temporary side effects such as fatigue and headache. The percentage of people who experience any side effects will be higher. These are signs that the vaccine is doing what it was designed to do—train your immune system to respond against something it might otherwise ignore so that you'll be protected later. It does not mean that the vaccine gave you COVID-19.

It all comes down to this: Some time in the coming months, you will be given a simple choice to protect yourself, your loved ones and your community from a highly transmissible and deadly disease that results in long-term health consequences for a significant number of otherwise healthy people. It may cost you a few days of feeling sick.

Please choose wisely.

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