

Immunology

How to give your vaccine a boost

Lifestyle choices around the time of a vaccination can affect your immune response to it. **Helen Thomson** explores how to give it the best shot at success

SIMPLE behaviour changes could improve how your body responds to a covid-19 vaccination and the speed at which you are protected from the coronavirus, evidence from studies on other vaccines suggests. These factors could be so important that some scientists believe that ignoring them could reduce the overall success of the covid-19 vaccine roll-out.

More than 130 million doses of vaccine against covid-19 have been administered at the time this magazine went to press. But not everyone who gets a shot will respond in the same way. Although the majority will build their immunity over the following weeks, a small percentage of

"We know so much about how stress affects vaccine response, I'd be surprised if it didn't apply to covid-19"

people won't become immune at all (see page 12). But even among those who do respond, factors such as age, sex, stress levels and the time of day that you receive a vaccine may affect how strong that immunity is, how quickly you build it, how long it lasts and what side effects you might encounter.

"While you can't change your age, there are psychological, social and behavioural strategies that can substantially impact the immune system's response to any vaccine," says Janice Kiecolt-Glaser, director of the Institute for Behavioral Medicine Research at Ohio State University.

Kiecolt-Glaser's experiments around 30 years ago were some of the first to show the impact we can have on our body's response to vaccination. During a stressful exam period, she and her colleagues vaccinated medical students against the viral disease hepatitis B. Those students who

were most stressed took the longest to build up a protective antibody response. Likewise, a study of individuals looking after people with dementia showed that the caregivers had a smaller antibody response to flu shots than non-caregivers, and their immunity declined significantly faster six months later.

Our immune system consists of much more than just antibodies, but they are the best proxy for vaccine effectiveness in studies, says Anna Whittaker, who looks at the effects of lifestyle factors on immune health at the University of Stirling, UK.

Further findings support these initial hints that stress affects our immune response to vaccines: in older people, a positive mood on the day of vaccination is associated with a higher antibody response to a flu shot.

"There is now such a rich literature of how stress can alter your response to vaccines, that I'd be surprised if there were no such effect with covid vaccination," says Kiecolt-Glaser.

Try not to stress

Although stress impacts the immune system in a myriad of ways, one mechanism probably involves adrenaline and cortisol, hormones that increase during stressful periods. Both hormones have a number of functions in our so-called fight-or-flight response. These include raising heart rate and suppressing digestion and the immune system – it is no use diverting precious resources to digesting food or getting rid of a cold virus when you are in a life-threatening situation.

Once the threat has passed, other mechanisms kick in to restore balance. But if you find yourself in a state of perpetual



People exercise during the pandemic in Hamburg, Germany

stress, the body is overexposed to these hormones, and immune cells are unable to respond normally. Such chronic stress creates a state in which we are more at risk of infection and experience low-level inflammation that can destroy healthy tissue. Stress can also indirectly impact the immune system via harmful coping methods, such as smoking or drinking more, sleeping less or eating more unhealthy foods.

But is it sufficient, let alone possible, to change our mood on the day of vaccination to improve our response or is a more long-term change in mindset necessary? In Kiecolt-Glaser's

study, the students' stress levels and social support as a group had been fairly similar across the academic year, suggesting that their divergent vaccine response was related to the exam period, and stress levels specifically around the time of vaccination.

It may be unrealistic to ask people not to be stressed during a pandemic, but another study may offer more practical advice. It showed that stress levels in the 10 days after vaccination may be more influential for antibody response than stress in the prior two days, and that stress-related sleep loss may be a key culprit.

Evidence for the benefits of sleeping well around a vaccination comes from several directions. For instance, healthy adults who sleep less than 6 hours on average



per night before a hepatitis B vaccination are less likely to mount an antibody response strong enough to fully protect them from being infected, compared with people who typically sleep more than 7 hours.

Likewise, a study that has yet to be published in which people had their sleep restricted for several consecutive nights prior to vaccination against hepatitis A had a lower antibody response compared with people who were allowed to sleep normally.

Slow-wave sleep, otherwise known as deep sleep, is probably involved. During this type of sleep, the brain stores long-term memories and clears out chemical junk that has accumulated during the day. It also creates a chemical and hormonal environment that

helps the immune system build a memory for the pathogens it has encountered through the day. There is some evidence that exercise can increase the amount of deep sleep you get the following night, as long as you don't do it just before bedtime.

To try and understand the most influential time to sleep well, Aric Prather at the University of California, San Francisco, looked at sleep over two weeks, pinpointing sleep duration on the two nights before flu vaccination as the best predictor of the immune response several months later. So while it may not be possible to de-stress, try to get some decent sleep around your vaccine. "It makes a whole lot of sense to me," says Kiecolt-Glaser. "I had my vaccine yesterday and I really made sure I slept well the last few nights."

Get friendly

Alongside stress and sleep, you may want to try to mitigate the effects of isolation. Even in young, healthy people, feelings of loneliness have been associated with a lower antibody response to flu vaccination. And having better social support or being married is linked to higher antibody responses to hepatitis B and flu vaccination, while bereavement is associated with lower such responses to the flu vaccine. The mechanism behind this is probably related to the increased levels of stress that can result from a lack of social support.

While it might not be practical for someone to make a bunch of new friends in the middle of a pandemic, you can reconnect and deepen the relationships you already have, says Sarah Pressman at the University of California, Irvine. She and her colleagues showed that social support in

15 mins

of upper body workout can boost the immune response to a flu shot

"Sleep duration on the two nights before flu vaccination is the best predictor of the immune response several months later"

the form of hugging is associated with a decreased risk of catching a cold. If you live with others, she suggests that a few extra hugs might not go amiss.

Pressman also recommends organising extra video catch-ups and talking to your family instead of simply "doomscrolling" online news. "Increasing your feelings of being supported will not only reduce your stress, but can also improve how you sleep at night, both factors we know matter for how vaccinations work for you," she says.

Something else you can control is your alcohol intake. In December, Anna Popova, the head of the Russian Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing, advised Russians to quit alcohol two weeks before their first coronavirus vaccine and to abstain until three weeks after their booster shot. Alexander Gintsburg, head of the Gamaleya National Center of Epidemiology and Microbiology in Moscow, which developed the Sputnik V vaccine, said that drinking alcohol after getting a coronavirus jab can impair the immune response and could even render the vaccine ineffective. Contrary to Popova, though, he recommended refraining from alcohol for three days after each injection.

Currently, there is no advice from the UK or US governments about drinking alcohol around your covid-19 vaccination.

A spokesperson for the World Health Organization said: "We have no specific guidance on this... but current evidence indicates that alcohol use has a clear impact on immune responses in high doses of consumption." Advice is at the discretion of national authorities, the spokesperson added. ➤

Having strong social support can increase antibodies after a vaccine



JOHN FEDELE/GETTY IMAGES

The effect of heavy alcohol use – six units in one sitting for women and eight for men – on the immune system’s response to other kinds of vaccination is well documented. Heavy drinking before and after a vaccine disrupts immune cell function, which can decrease the body’s ability to defend itself from a virus.

What about a tippie here and there? A study in macaques shows that moderate alcohol consumption – the equivalent in people of up to two units a day – actually appears to create a more robust response to vaccination using a member of the virus family that causes smallpox in humans. Macaques that drank moderately produced slightly more antibodies and other immune cells in response to the vaccine, compared with macaques that drank no alcohol.

Christopher Thompson, a biologist at Loyola University Maryland, says it is difficult to pinpoint exactly how drinking might impact your immune response to the covid-19 vaccine. This is complicated by the fact that the Pfizer/BioNTech and Moderna vaccines are mRNA-based, a technology that hasn’t been used for large-scale vaccination before.

“Women who exercised 45 minutes before a flu shot had a higher antibody response later”

Based on available data, he suggests that moderate alcohol consumption is unlikely to have much of an effect, so if you are an occasional drinker, you probably don’t have to change your lifestyle.

However, binge drinking will almost certainly decrease the vaccine’s efficacy and should be avoided for four weeks after each injection, says Thompson.



ANDREW MILLIGAN/POOL/AP VIA GETTY IMAGES

People in Edinburgh, UK, receive their coronavirus vaccines

As it takes about two weeks for an immune response to develop after vaccination, four weeks “gives a bit of a buffer zone”, he says.

On top of all that, make sure you are getting enough exercise. Not only will this improve your health more generally, helping to minimise stress and reduce risk factors like obesity and diabetes that can worsen covid-19 symptoms, but exercise is also intimately involved with your body’s ability to form an adequate response to a vaccine.

Several studies support this. For instance, people who already have an active lifestyle over the age of 62 have higher antibody responses to flu vaccination than those who are sedentary. People who received a tetanus vaccination after completing a marathon had a higher antibody response than

non-runners. And women who used an exercise machine in the 45 minutes before flu vaccination had a higher antibody response a month later than those who did no exercise.

Exercise triggers a transient increase in signalling proteins called cytokines that interact with all the immune cells. Weight training and other forms of resistance exercise also cause tiny tears in muscle, which are thought to activate the immune system in anticipation of these tears letting in possible pathogens.

These effects are generally less pronounced in younger adults, perhaps because their immune systems are already more effective. But in one study, young, healthy adults who performed a 15-minute upper body workout before receiving a flu vaccine saw a stronger immune response than a control group who rested before their shot.

One final benefit is that exercise

is a known analgesic. Kate Edwards at the University of Sydney in Australia says recent evidence shows that pain at the site of vaccination and subsequent side effects like swelling, reduced appetite and feeling unwell are all decreased by regular workouts. Kiecolt-Glaser adds that exercise might also help counter general fatigue, which is one of the main side effects associated with covid-19 vaccines.

Clock-watchers

Meanwhile, you may have read that the time of day you receive your vaccine could influence your response. This comes from a study that examined the immune response to flu or hepatitis A vaccine given in the morning or the afternoon. Men vaccinated in the morning exhibited a stronger antibody response to both vaccines than men who got their vaccine in the afternoon. No



difference was seen in women.

The underlying mechanism behind this effect is unclear, but the researchers are investigating the hypothesis that it may be related to rhythmic fluctuations of hormones that affect the immune system and may differ in men and women.

Whittaker, who led the study, says that it was indicative rather than definitive, and that timing hasn't yet been studied with any of the covid-19 vaccines.

"Having a vaccine in the afternoon or night is unlikely to reduce the efficiency of your immune system to be as poor as having no vaccine at all," she says. "Given the urgency and scale of the pandemic, the most important thing is to get vaccinated as soon as possible. Perhaps when we have more answers in the future and the situation is less urgent, then adjusting timing of vaccination is something that could be done."

There are few definitive answers as to what behaviours might affect the success of the covid-19 vaccination drives, and this is understandable, says Thompson. "There was not enough time to assess all of the social, family and medical histories of each patient [in the covid-19 vaccine trials] and correlate that with immunological outcomes. The vaccine companies were tasked to make a safe, effective vaccine as quickly as possible. So this is where their resources were focused."

However, others say it is vital to now look at our prior knowledge of how our behaviour has affected other kinds of vaccination. "Past evidence would suggest that not addressing these factors could reduce the overall success of the vaccine roll-out," says Kiecolt-Glaser. ■

Out of your hands

Some factors that affect our immune response to vaccines are beyond our control

Sex

The evidence is largely consistent on this: overall, women tend to have higher antibody responses to most

during the first week of life creates an adequate immune response in only 30 to 70 per cent of infants, but giving it after 4 weeks of age leads to immunity in nearly all infants.

Vaccine responses diminish in older people, whose antibodies also wane more rapidly after

varied considerably among the studies and it is too early to say how your gut microbes might affect covid-19 vaccination.

Prior infection

Good news for those who have already recovered from covid-19: immunity may last at least six months, with the body mounting a fast and effective response to the coronavirus upon re-exposure, according to a study last month.

Might this mean you also get a more effective response to the vaccine? It is hard to say.

People who have already encountered tetanus, for instance, tend to have a higher immune response after getting a booster vaccination than people who get the shot with no prior infection.

Likewise, people who have naturally encountered members of the flavivirus family, such as the virus that causes West Nile disease, have a higher antibody response to vaccines for other flavivirus diseases, such as dengue fever.

We might see something similar with covid-19, but we don't yet have data on this. What we do know is that the immunity someone gains from having had an infection varies from person to person, and both natural and vaccine-induced immunity can differ, so it is important to get vaccinated even if you have already recovered from the virus. ■

The jury is still out as to whether prebiotic and probiotic foods help with the immune response



SHUTTERSTOCK/DOCTERK

vaccines than men, creating a stronger immune response to dengue, hepatitis A, rabies and smallpox vaccination, among others. Given the early stage of covid-19 vaccine roll-out, it isn't yet clear whether we will see a similar sex difference in response to these shots.

Age

Probably the most well-researched factor here is age. Newborn babies produce low levels of antibodies in response to vaccines, and the antibodies they passively acquired from their mother during pregnancy can interfere with vaccine response, although it isn't well understood why this might be.

The optimal age to start vaccination differs depending on the pathogen you are protecting against. For instance, giving the oral polio vaccine

4 weeks

The age after which a polio vaccine works best

receiving vaccines. One reason for this is that the thymus, where virus-destroying T-cells mature, begins to degrade in old age.

Microbiome

It is early days, but the make-up of your gut bacteria could play a role. Some small studies have shown that prebiotics and probiotics, which are known to affect our microbiome, might improve the immune response to vaccination, including for diphtheria, hepatitis A and flu.

However, the type used and how long they were taken for



YULIA GRYZHEVSKA/LAMY