New Study Will Examine How Robustly Individuals Respond to COVID-19 Vaccination

Could emotional wellbeing and good sleep promote a lasting antibody response to the COVID-19 vaccine?

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The rapid development of COVID-19 vaccines with impressively high effectiveness offers hope that the pandemic will someday soon be under control. But as more people are vaccinated, new questions emerge about what factors might contribute to long-term effectiveness.

A vaccine works by activating an individual's immune system to create antibodies to the virus. And while the approved vaccines are highly effective, not everyone responds equally well. We know from a long history of research on the flu that older adults tend to show a weaker response to vaccines. Other factors, such as high levels of psychological stress and lack of sleep, are also associated with weaker antibody responses to various vaccines.

Researchers at UC San Francisco recently received a National Institutes of Health COVID-19 grant to study the effects of stress and sleep on vaccine responses. The new study, called BOOST, will investigate how these factors might influence the long-term effectiveness of the antibody response.

"While the COVID vaccination is extremely effective in the short run, if antibodies are not well maintained, people may lose protection from the virus," said Elissa Epel, PhD, a professor and vice chair of UCSF's Department of Psychiatry. Epel is one of two primary investigators on this study. "A weak response, and new variants of COVID-19, may lead to the need for booster shots to maintain protection. Thus, understanding the predictors of a robust SARS-CoV-2 antibody response, and especially antibody maintenance to theCOVID vaccination, will become a critical public health issue in our future."

Flu's Clues

Age is an important factor not only in predicting COVID-19 severity, but also in predicting a sluggish response to vaccinations. Initial response to COVID-19 vaccines appears to be somewhat lower with age, and prior research suggests that vaccine responses might wane more rapidly in

older people. Factors influencing the duration of antibody responses to COVID-19 vaccination are not yet known.

The new UCSF study will examine age effects, but also the factors that may promote better immune function across ages, such as sleep and emotional wellbeing.

Researchers will also study the difference between markers of the biological age of the immune system and chronological age, which may also predict a strong vaccination response.

Is Age Just a Number?

While chronological age is measured in years, the biological age of immune cells can be measured with various indicators, including telomeres.

Telomeres are the protective caps at the ends of chromosomes, and longer telomeres indicate a more youthful immune system, with cells that can go on to divide more robustly when exposed to antigens. The length of immune cells may be a particularly important indicator for predicting a robust vaccination response. Elizabeth Blackburn, PhD, a Nobel laureate and consultant on the UCSF study, was one of the pioneers who discovered this cellular aging system. The research team, including Blackburn, has studied telomeres in immune cells for several decades.

The UCSF research team has found that lifestyle factors, such as chronic stress and poor sleep, may shorten telomeres. Shorter telomere length predicts more severe infection with a cold virus, more severe COVID-19 symptoms, and poorer antibody response to flu vaccination. Now the team will test whether telomere length predicts COVID-19 vaccination response better than chronological age.

The Role of Sleep in a Pandemic

It's old hat, but still just as relevant, even in a pandemic: we need more sleep.

"Insufficient sleep has emerged as a key predictor of how well our immune system responds to vaccination," said Aric Prather, PhD, an associate professor in the Department of Psychiatry and co-PI of the UCSF study. He and his research team have found that shorter sleep duration increases susceptibility to developing a cold following rhinovirus infection and muted antibody responses to both the flu vaccine and hepatitis B vaccination series.

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In the study, participants will report on their sleep, and some participants will wear a biosensor ring to accurately measure sleep patterns. "This study will help shed light on when sleep might be critical during the vaccination process to mount the strongest protective response," said Prather.

Related to sleep, but certainly separate from it, is the way that stress – all too common in the

pandemic – may, ironically enough, impair immune function and drag out the pandemic.

Stressed Out Antibodies

Chronic stress is known to impair viral immunity. A history of studies show that psychosocial stress predicts an impaired peak antibody response to influenza vaccination. The BOOST researchers will study whether the same relationship holds true of our immune responses to the COVID-19 vaccination.

This may be particularly important to understand because this has been a period of immense stress for most, ;including the death of loved ones, financial loss, and parenting stress from school closures. Meanwhile, the need for social distancing has resulted in isolation, loneliness, and lower social support, said Epel, who has been studying the effects of stress on health, including climate distress.

“In California, we have a confluence of challenges due to COVID, and on top of that we have the wildfires and smoke that will revisit us this fall,” she said. “We will be measuring how much individuals are exposed to numerous pandemic challenges, as well as factors that protect us from stress – such as social support and purpose in life, and how well we can live with the stress of uncertainty.”

This will be one of the first and largest studies to examine the impact of factors like age and stress on vaccination effectiveness, which Epel thinks signals the next phase of this pandemic where we focus on recovery. Hopefully, the insights gleaned from the study will help us promote optimal immune function for vaccinations and other challenges.

“Even during this period that has caused so much suffering, people find ways to experience purpose, connection, and joy. That is as basic to our survival as our stress responses,” said Epel.

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