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BRIEF19

A daily review of covid-19 research and policy

RESEARCH BRIEFING

Vaccine-related covid-19 antibodies pass to infants through breast milk.

One of the wonders of childbirth is that mothers pass on certain aspects of immunity to their newborn infants. The ability to pass immunologic protection along can come via the placenta or breast milk and the specifics vary depending on the type of immunity and the particular disease. Fortunately, in the case of covid-19, naturally acquired antibodies are passed from mothers to children via the placenta during pregnancy, and now a new study published in *JAMA* shows that mothers can pass antibodies acquired from the Pfizer/BioNTech vaccine to their children through breast milk. This implies that mothers who get infected before or after birth, but who are breastfeeding, can supply their own infants with immunologic protection gained from vaccination.

This study, which took place in Israel, recruited 84 women who were breastfeeding at the time and who voluntarily chose to be vaccinated. Breast milk samples were collected before vaccine administration, two weeks later and then weekly for six weeks. The researchers primarily studied whether antibody levels (Immunoglobulin G, which are long-term antibodies found in the blood, and Immunoglobulin A, which are antibodies that line mucous membranes, including in the gastrointestinal tract) produced by the vaccine were present in breast milk. The researchers also monitored whether the women in the study suffered any adverse events from the vaccine itself.

The results indicated that 62 percent of subjects had an elevation of immunoglobulin A levels two weeks after the first vaccine dose and a week after the second dose. The number rose to over 86 percent a week after the second dose. For Immunoglobulin G, the levels were low at first. But after the second dose, the levels skyrocketed in nearly 92 percent of the recipients by week 4, reaching 97 percent by week 5 and 6. This second finding in particular may be another argument in favor the two-dose regimen. Some experts have suggested spacing the vaccine doses out to allow more people to get their first shot sooner. However, the rapid rise in Immunoglobulin G levels after the second dose implies that the second jab kicks the immune system into a higher gear quickly. That being said, it's possible that such a rise in these antibodies would have happened at week 4 regardless of whether or not a second dose was received and that their appearance in breast milk reflected normal lags in Immunoglobulin G production.

The only vaccine-related side effects were injection site pain and fatigue. Four infants developed a fever with cough and congestion during the study, and only one infant required hospital admission to rule-out a bacterial infection.

The results of this study suggest that after vaccination with a covid-19 mRNA vaccine, some antibodies to covid-19 appear early, and others emerge later, remaining in breast milk for at least 6 weeks. However, the study was unable to determine, based on its design and small number of events, if the fever in the four infants was at all related to the immunoglobulins in the breast milk or simply due to other factors, including the common cold. However, that seems unlikely. In general, breast milk supplies nutrients and antibodies to infants without incident all the time. One more new antibody would not be expected to change that.

In sum, the results of this study are *very* encouraging and corroborate US Centers for Disease Control and Prevention and American College of Obstetricians and Gynecologists recommendations supporting maternal covid-19 vaccination. —*Joshua Niforatos, MD, MTS*

POLICY BRIEFING

Johnson & Johnson vaccine rollout paused in the United States. Why baseline rates are everything.

The bad news is that in the United States, 6 women ages 18-48 appear to have developed a rare but serious blood clotting disorder after receiving the Johnson & Johnson vaccine. One died and another is still fighting for her life. The good news is that around 1 million women in that age range received the vaccine without incident, saving many, many lives in the process. Even if more cases of this apparently vaccine-induced condition are found—which is likely—we need to watch out for something very important: proper comparisons.

Today, many experts floated a variety of numbers about blood clots online and on television. This can be helpful but may also lead us astray. First of all, we need to understand the baseline rates of abnormal blood clots, in order to distinguish signal from noise. For example, in the Johnson & Johnson trial, around 1 in 2000 people reported abnormal clots had developed; the punchline is that this occurred in the *placebo group*. Around 1 in 1700 people who received the vaccine also reported such clots. The difference was not statistically different. The fact that it took millions of doses in both the US and Europe for a handful of these more serious cases (which cause a kind of stroke) to emerge suggests that clinically *relevant* clots are rare indeed. But I actually assume that there very likely many more clots in both arms of the Johnson & Johnson trial than we will ever know about. In fact, in a sense there are many that we should not even *care* about. Why? Because most of the undiscovered clots were so mild (or asymptomatic) that they were clinically *irrelevant*. (By clinically irrelevant, I mean that they did not actually require treatment, and led to little or no symptoms, and no long-term effects were caused.)

There are two key things to know about blood clots. First, not all blood clots are created equal. Some cause no symptoms at all and pose no risk. In fact, treating these clots with blood thinners may do more harm than good and may not be warranted. Second, the more clinicians look for blood clots in dangerous places like the legs, lungs, and brain, the more of them you find. However, clinicians rarely find important ones that were not already highly suspected. This means that when doctors and other healthcare providers are over-zealous in testing for blood clots, they frequently find blood clots that resemble danger, but are not actually dangerous. I worry that in the coming days and weeks, the rate of blood clots among Johnson & Johnson vaccine recipients will increase substantially. It's likely, however, that most of these clots will not be dangerous. What we really care about is how many dangerous clots occurred, like the ones in the brain found in many of the patients in the AstraZeneca/Oxford studies published last week and the Johnson & Johnson reports. The same is true for most blood clots caused by oral contraceptive pills (OCPs) made of hormones. The rate of blood clots sounds pretty high among women taking hormonal OCPs, (my friend Dr. Angela Rasmussen, who I respect greatly, tweeted a statistic that one in 3,000 women on OCPs develops abnormal blood clots). But the number of these clots that are truly dangerous events is far lower, in actuality. In the coming weeks, we need to make sure we are using the same power microscope, metaphorically speaking, to compare the rates of blood clots related to the Johnson & Johnson vaccine to other more common causes. After all, what matters is not just how often these problems occur, but how often they have any meaningful effect on those who develop them. If a far higher number of people are found to have developed vaccine-related blood clots than currently suspected, the larger question will be just how many of these events were truly dangerous.

Ultimately, the most important decision to be made is not whether or not to receive a coronavirus vaccine. It's whether to receive a coronavirus vaccine or covid-19. To make that risk-benefit calculation, what matters is the rate of serious covid-19 by age and sex (which we generally know) and the rate of serious vaccine-induced blood clotting problems by age and sex (which we are just starting to study). Once we know the answer to that question, we can safely decide how to proceed. But if we ask the wrong question, we are consigned to a guaranteed wrong answer.

—Jeremy Samuel Faust, MD MS

US approaching full vaccine eligibility.

Last week President Biden pushed the deadline for vaccinating all Americans forward, a landmark date in the ongoing struggle to overcome the pandemic. Initially set for May 1st, he has now targeted April 17th, given the success of having vaccinated one hundred and sixty million Americans along with many doses waiting to be shot into arms.

Recall that while the National Academies of Science, Engineering, and Medicine (NASEM) published their recommended eligibility schedule as the vaccine candidates were still applying for authorization, it was left to the states to determine their own distribution plans, which led to regional inconsistencies due to differing timelines.

Many states have had an accelerated plan that has allowed them to offer vaccines to everyone sixteen years and older, though such efforts have not been entirely successful. A recent report covered by *Brief19* showed that the number of doses could not keep up with the expanded pool, resulting in regional shortages that largely mitigated any progression to wider eligibility. The people who have suffered the most when this happens are the most at-risk, like those in the correctional system. With supplies stretched thin, there is no clear solution about how to ensure vulnerable populations don't get left behind. *Various*.

—Brief19 Policy Team

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